

## ORIGINAL ARTICLE

# Clinical Manifestations and Complications of Scrub Typhus : A Hospital Based Study from North Eastern India

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## Abstract

**Objectives:** To study the different clinical manifestations and complications associated with scrub typhus.

**Methods:** A hospital based prospective observational study of patients of acute febrile illness above 18 years age. Diagnosis was based on clinical and serological data.

**Results:** A total of 61 patients were diagnosed with scrub typhus, with males more than females. Most (42.37%) belonged to 18 to 30 years age group. Fever with headache was the commonest presentation (94.91%). Multiorgan dysfunction syndrome was the most common complication (16.94%). The mortality rate was 8.47%.

**Conclusion:** The study reveals the clinical manifestations and complications of a well known mite borne disease in the state of Meghalaya. The varied presentations and high mortality requires a high index of suspicion. The study highlights the clustering of cases during the months of September to November.

## Introduction

Scrub typhus also known as tsutsugamushi disease<sup>1</sup> is an acute febrile illness caused by *orientia tsutsugamushi*, a bacterium from the family *rickettsiaceae*.<sup>2</sup> Scrub typhus is widespread in so called "tsutsugamushi triangle" which extend from Pakistan, India and Nepal in the west, to south-eastern Siberia, Japan, China and Korea in the north to Indonesia, the Philippines, northern Australia and the pacific islands in the south.<sup>3</sup> In India, the disease had occurred amongst troops during World War II in Assam and West Bengal, and in 1965 Indo Pak war.<sup>4</sup> In India, epidemics of scrub typhus have been reported from Pondicherry and Goa in south,<sup>5,6</sup> Utrakhand in north India.<sup>7</sup> Cases of scrub typhus were also reported from eastern India among the paediatric age group.<sup>8</sup> Although the disease is endemic in our country, it grossly remains under diagnosed owing to the non-specific clinical presentation, lack of access to the specific diagnostic facility and low index of suspicion by the clinician.

In north eastern India particularly in the state of Meghalaya, this disease is well known among the local people since long time who called the disease as "niangsohot" which mean organism associated with chestnut. Majority of cases are seen during the month of July to November but it is not uncommon to find cases in the rest of the year. In spite of being an endemic disease in this part of India many cases were remained undiagnosed mostly due to lack of high index of suspicion by the clinician and non availability of specific diagnostic test for the disease. It is a common observation that when the disease like malaria, typhoid, leptospirosis and fever due to localised causes were excluded, a good percentage of cases among the patients with acute febrile illness were ultimately diagnosed to have scrub typhus.

Complication associated with scrub typhus is not uncommon and some time proved to be fatal. Common complications associated with scrub typhus are acute kidney injury,

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hepatitis, ARDS, meningoencephalitis, myocarditis and septic shock. Effective treatment in the form of doxycycline, azithromycin are available but in spite of that large number of patients develop complication with high mortality mostly because of delayed in the diagnosis and late initiation of specific treatment.<sup>9</sup>

Keeping this clinical scenario in mind effort has been made to conduct an observational prospective study on scrub typhus among the adult patients admitted in the department of general medicine, North Eastern Indira Gandhi Regional Institute Of Health And Medical Sciences (NEIGRIHMS), a tertiary care institute under the ministry of health and family welfare, Government of India, located in the capital city of state Meghalaya which is a referral centre for entire north east India.

## The Aims and Objective of the Present Study

To study the different clinical manifestation and complication associated with scrub typhus.

## Material and Methods

We did a hospital based prospective observational study in the department of general medicine, NEIGRIHMS, Shillong.

### Inclusion criteria

All patients with acute febrile illness above 18 years of age admitted in the department of general medicine from 7<sup>th</sup> January 2013 to 6<sup>th</sup> January 2014 with diagnosis of scrub typhus.

### Exclusion Criteria

Patients diagnosed to have some other associated infection.

Patient having co-morbid condition like chronic renal failure, chronic liver disease, patient with known neoplastic disease etc.

Diagnosis of scrub typhus has been made if patient fall in any of the following three groups:

Group A: Acute febrile illness with eschar specific for scrub typhus plus serological test positive for scrub (in Weil-Felix test titre for OXK more or equal to 1:160 or immunochromatographic card test (IgM, IgG and IgA) positive for scrub typhus).

Group B : Acute febrile illness + Weil-Felix test titre for OXK more than or equal to 1:320.

Group C: Acute febrile illness highly suspicious of scrub typhus plus Weil-Felix test titre for OXK equal to 1:160 or immunochromatographic card test (IgM, IgG and IgA) positive for scrub typhus plus response to doxycycline.

All patients of the acute febrile illness were subjected to a battery of investigation as per the

institute protocol and also the special investigation for particular cases were done as according to the institute protocol. Investigations done were complete blood count, platelet count, urine routine examination with microscopy, renal function test, liver function test, bleeding time, clotting time, prothrombin time/ international normalised ratio (INR), rapid diagnostic test for malaria, peripheral blood smear for malarial parasites, urine for dark field microscopic test for leptospirosis, Widal test, serological test for dengue and blood culture. Radiological investigation includes chest X-ray, ultrasonography abdomen and CT brain or MRI brain where indicated. Other test includes lymph node fine needle aspiration cytology for lymphadenopathy. For the diagnosis of scrub typhus serological test done were by Weil- Felix test (PROGEN, Tulip Diagnostics (P) Ltd.) and lateral-flow-format immunochromatographic test (ICT) for the detection of *O. tsutsugamushi* IgM, IgG and IgA antibodies (SD Bioline Tsutsugamushi, Standard Diagnostic, Inc. Korea) which has good sensitivity.<sup>10</sup>

For the diagnosis of associated complication for the ease of comparison same standard definitions were used as of other study on scrub typhus.<sup>6</sup>

Multiple-organ dysfunction syndrome (MODS): Dysfunction of more than one organ, requiring intervention to maintain homeostasis.

Acute kidney injury: A rise in serum creatinine of more than 1.6 mg/dl or urine output less than 400 ml/24 hrs failing to improve after adequate rehydration.

Acute respiratory distress syndrome (ARDS): Bilateral alveolar or interstitial infiltrates on chest radiograph and PaO<sub>2</sub>/FiO<sub>2</sub> less than or equal to 200 mmHg.

Hepatitis: Rise in 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 the upper limit of normal value.

Pancreatitis: Rise in threefold or more above the normal level of serum amylase and serum lipase level with typical pain upper abdomen of pancreatitis or radiological evidence of pancreatic involvement.

Meningitis: Altered sensorium with feature of meningeal irritation like neck rigidity, positive Kernig sign with elevated protein and/or polymorphic leucocytosis on CSF analysis.

Disseminated intravascular coagulation(DIC) was defined as clinical manifestation of bleeding along with thrombocytopenia and elevated coagulation profile (raised fibrin degradation products, prolonged prothrombin time/INR, activated partial thromboplastin time, aPPT): Platelet count < 80,000/L or 50% decrease in platelet count from highest value recorded over previous 3 days.

**Myocarditis:** Myocarditis was defined as presence of systolic global left ventricular wall motion abnormalities on 2D echocardiography along with ECG changes and clinical findings consistent with left ventricular dysfunction in a previously normal individual.

**Shock:** Systolic blood pressure of < 90 mm Hg for at least 1 h despite adequate fluid resuscitation was labelled as shock.

All patients diagnosed to have scrub typhus or those with strong clinical suspicion of scrub typhus were treated with doxycycline in the dose of 100 mg twice daily PO for 10 days unless it is contraindicated like pregnancy. In cases where doxycycline was not used azithromycin in a dose of 500 mg once daily for 5 days given. As per indication other supportive measure were given like haemodialysis, mechanical ventilation, blood transfusion, inotropic agent etc.

## Result and Observation

Total 61 patients were diagnosed to have scrub typhus in the present study but 2 patients were excluded because one patient had associated

pulmonary tuberculosis on DOTS and another having neurocysticercosis on anti epileptic drugs. Most of the patients were reported from the month of September to November although the cases were reported throughout the year. As shown in Table 1 male patients 35(59.3%) outnumber female patients 24(40.7%) that include three pregnant women one of whom had spontaneous abortion. Majority of the patients were young belong to age group 18-30 years (42.37%) and 31-40 years (28.81%). Patients with acute febrile illness were only included in the present study. As shown in Table 2 commonest presentation was fever with headache in 59(94.91%) number of patients. Other common sign and symptoms on presentation include lymphadenopathy, cough, dyspnoea, eschar, altered sensorium, jaundice, hepatomegaly, splenomegaly and oliguria. Distribution of lymphadenopathy which were painful in most of the instance in decreasing order were cervical 13(22.03%), inguinal 12(20.34%), generalised 5(8.47%) and axillary 1(1.69%). Eschars found were mostly of sub centimetre in size having firm adherent black scab with red margin. Eschars were mostly found in inguinal region (11.86%). Almost all patient who having eschar had single except two (3.39%) whom had multiple eschars, one had multiple eschars at inguinal region and other had eschar at two different site. Locations of eschars observed in lower limb in decreasing order of frequency were upper thigh, foot, popliteal fossa and gluteal region. Uncommon presentations in the present study include haemoptysis, epistaxis, rash and neck rigidity. Others include seizure and cholangitis with cholecystitis in 2(3.39%) and 1(1.69%) patient

**Table 1 : Age and sex distribution**

Age group	18-30 years	31-40 years	41-50 years	51-60 years	> 60 years
Male:	15	12	6	1	1
35(59.3%)	(25.42%)	(20.33%)	(10.16%)	(1.69%)	(1.69%)
Female:	10	5	6	2	1
24(40.7%)	(16.94%)	(8.47%)	(10.16%)	(3.38%)	(1.69%)
Total: 59	25	17	12	3	2
	(42.37%)	(23.72%)	(20.34%)	(5.08)	(3.39%)

**Table 2 : Signs and symptoms at presentation and investigation findings**

Signs and symptoms	n-(%)	Investigation	n-(%)
Fever	59(100%)	Haemoglobin less than 11 gm/dl	21(35.59%)
Headache	56(94.91%)	Leucocytosis (> 11,000/cumm)	16(27.12%)
Cough	29(49.15%)	Leucopenia (< 4,000/cumm)	3(5.08%)
Dyspnoea	19(32.20%)	Platelet (less than or equal to 1,50,000/cumm)	19(32.20%)
Lymphadenopathy	Cervical 13(22.03%)	Platelet count less than 80,000/cumm	7(11.86%)
	Inguinal 12(20.34%)	Hyperbilirubinaemia (> 1 mg/dl)	37(62.71%)
	Axillary 1(1.69%)	Sr Bilirubin (> 3 mg/dl)	16(27.12%)
	Generalised 5(8.47%)	SGOT (> 50 U/L)	49(83.05%)
Eschar	Inguinal 7(11.86%)	SGOT (> 150 IU/L)	28(47.46%)
	Lower limb 7(11.86%)	SGPT (50 U/L)	45(76.27%)
	Trunk 2(3.39%)	SGPT (> 150 IU/L)	12(20.34%)
	Axilla 1(1.69%)	ALKP (> 300 IU/L)	20(33.90%)
Rash	1(1.69%)	Sr creatinine (> 1.6 mg/dl)	16(27.12%)
Jaundice	9(15.25%)		
Oliguria	6(10.17%)		
Altered sensorium	11(18.64%)		
Neck rigidity	5(8.47%)		
Bleeding	Epistaxis 1(1.69%)		
	Haemoptysis 3 (5.08%)		
Hepatomegaly	13(22.03%)		
Splenomegaly	10(16.94%)		

**Table 3 : Complication and mortality**

Complications	no-(%)
Hepatitis	9(15.25%)
Acute renal failure	8(13.56%)
Pancreatitis	1(1.69%)
ARDS	7(11.86%)
MODS	10(16.94%)
Meningoencephalitis	5(8.47%)
Mortality	n-5(8.47%)

respectively. Investigation report has been shown in Table 2. Haemoglobin less than 11 gm/dl was present in 21(35.59%), leucocytosis in 16(27%), leucopenia in 3(5.08%), platelet count less than 80,000/cumm in 7(11.86%) number of patients. Deranged liver function were present in 49(83.05%) and deranged renal function in 13(27.12%) of patients respectively. Associated complications found were hepatitis in 9(15.25%) and acute renal failure in 8(13.56%) (These don't include patients having MODS), others include pancreatitis, ARDS, MODS and meningoencephalitis as shown in Table 3. 5 patients expired with a mortality rate of 8.47% in the present study.

## Discussion

Scrub typhus is a well-known mite born disease in the state of Meghalaya, the disease has a local name also (*niangsohot*). The state had observed many outbreak of scrub typhus in the recent past. Most of the cases were seen between the months of September and November, although cases were reported throughout the year, similar clustering of cases were also reported in other study from India.<sup>6,11,12</sup> Previous outbreak of scrub typhus in Meghalaya was also reported during the same period.<sup>8</sup> Most of the cases in present study were involved in outdoor activity, particularly fishing (angling) in pond, agriculture activity or collecting of firewood from jungle.

Patients usually present with fever, headache, malaise, suffused face, lymphadenopathy and eschar. It is so characteristic for scrub typhus that in the present study doxycycline was started empirically. In our study the commonest presentation was an acute febrile illness with severe headache (94.91%), which is global and throbbing in nature. Headache is so severe that many time patients took medical consultation because of headache only, although other study reported headache in only 14.3% of cases.<sup>11</sup> Lymphadenopathy usually painful, is a common finding in scrub typhus reported in 13 to 18% of patients<sup>6,12,13</sup> in present study lymphadenopathy was present in 52.54% of cases. Cervical lymphadenopathy (22.03%) is commonest, followed by inguinal (20.34%) but generalised lymphadenopathy was also present in 5 patients (8.86%). Though rash was reported in many

study as a common finding but in our study only one patient (1.69%) had rash on presentation.<sup>6,14</sup>

A necrotic eschar which is considered as a most useful diagnostic clues for scrub typhus was present in 17(28.81%) cases of our study population, though it was reported as high as 86.3% in some study but some studies from India reported of eschar in as less as 5.56% of patients.<sup>6,14-17</sup> It was expected to be less along with less number of patients with rash as area of study fall in region endemic for scrub typhus. In the present study commonest site for eschar was inguinal region (11.86%), followed by lower limbs (11.86 %) (thigh, popliteal region, buttock), trunk (3.39%) and axilla (1.69%). Almost all patients had single eschar, except two who were having multiple eschars. Hepatomegaly was present in 22.03% of cases and splenomegaly in 16.94% of patients though hepatosplenomegaly was reported to be a very common finding especially in children.<sup>18</sup>

As with other case series elevated SGOT (83.05%) and SGPT (76.27%) was present in majority of cases. One interesting finding we observed in our study was that raise in SGOT is more than raised in SGPT along with raised level of ALKP level. Raised bilirubin more than 3 mg/dl present in 16(27.12%) and raised serum creatinine of more than 1.6 mg/dl present in 16 (27.12%) of patients. Leucocytosis was noted in 27.12% patients but leucocytopenia was also present in 5.08% of patients. Platelet count of less than 150000/cumm was present in 32.20% cases.

Multiorgan dysfunction (MODS) and meningoencephalitis are the common complications associated with scrub typhus as is the ARDS with high mortality rate. MODS were reported as high as 50% of patients without meningoencephalitis and 76.5% with meningoencephalitis.<sup>12</sup> In our study MODS was present in 16.94%, meningoencephalitis in 8.47% and ARDS in 11.86% patients though other study reported meningoencephalitis as a more common complication (26%) and ARDS incidence same as present study(11.1%).<sup>19</sup> Pancreatitis and disseminated intravascular coagulopathy (DIC) are uncommon complication with few case reports; in present study one (1.69%) patient developed pancreatitis.<sup>20</sup> The case-fatality rate for untreated classic cases is 7% but would probably be lower if all mild cases were included;<sup>21</sup> but as the present study is a hospital based which include only admitted patients mortality is expected little higher (8.47%). Of those who had expired 4 out of five patients had MODS and one patient was having acute renal failure. 3(5.08%) patients had associated pregnancy in the present study, out of which one had spontaneous abortion, a common finding with other study also.<sup>22,23</sup> All cases were treated with doxycycline except those who were pregnant with an excellent result. Almost all patients show significant

clinical improvement within 2 to 3 days of starting of doxycycline. Three pregnant women were treated with azithromycin.

## Conclusion

The study shows the wide variety of clinical manifestation and complications of Scrub typhus, a well known mite borne disease in the state of Meghalaya. Due to the varied presentation and high mortality due to complications, a high index of suspicion is required. The study highlights the clustering of cases during the months of September to November. The study also shows the response of treatment with Doxycycline.

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