

Original Research Article

## Clinico-Laboratory Profile of Severe Pediatric Scrub Typhus

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**Abstract:** Scrub typhus is a mite-borne bacterial infection of humans caused by *Orientia tsutsugamushi* that causes a generalized vasculitis that may involve the tissues of any organ system. It is a re-emerging disease affecting many parts of India. We undertook a descriptive study to identify the clinical and laboratory features associated with severe scrub typhus in children. All children up to 18 years of age who presented with severe scrub typhus to the Pediatric Department of Nazareth Hospital between January 2014 and December 2014. A total of 75 cases were included. Results showed that the symptoms of severe scrub typhus were fever (100%), headache (58.7%), loss of appetite (46.7%) and cough (46.7%), vomiting (45.3%), abdominal pain (32%), breathing difficulty (25.3%), myalgia (24%) and altered sensorium (24%). Conjunctival redness was present in 44% of patients, pallor in 28% and eschar in 21%. Meningoencephalitis was seen in 58.6%. Pneumonia was the commonest respiratory complication seen in 24% cases. Hypotension and shock was found in 16% of patients. A MODS was seen in 42.6% cases. Laboratory findings were raised acute phase reactants, hypoalbuminemia, anaemia and hypocalcemia. There was only 1 death. Our findings suggest that the severe form of scrub typhus is very common and clinicians should have a high index of suspicion for severe scrub typhus when children present with fever, headache, conjunctival redness and eschar in an area endemic to scrub typhus. Identification of clinical signs like neck stiffness, low blood pressure and respiratory distress would help in timely recognition of complications such as meningoencephalitis, shock and pneumonia. Frequent monitoring of blood haemoglobin, platelet count, and serum albumin and serum calcium levels is warranted. Early intervention can significantly reduce morbidity and mortality.

**Keywords:** eschar, Meghalaya, meningoencephalitis, *Orientia tsutsugamushi*, pediatric, scrub typhus, north-east India, rapid diagnostic test

### INTRODUCTION

Scrub typhus is an acute, febrile, infectious illness that is caused by *Orientia* (formerly *Rickettsia*) *tsutsugamushi*. It is transmitted by the mite *Leptotrombidium deliense*. This is found only in areas with a suitable climate, plenty of moisture and scrub vegetation [1].

Scrub typhus is endemic to a part of the world known as the “tsutsugamushi triangle”, which extends from northern Japan and far-eastern Russia in the north, to northern Australia in the south, and to Pakistan in the west [2]. Approximately 1 million infections occur each year, and it is estimated that more than 1 billion people are at risk [3].

Scrub typhus may be mild or severe. After an incubation period of 6-21 days, the rickettsiae proliferate at the site of the chigger bite to form in

<50% of cases a necrotic eschar with an erythematous rim [4]. The onset of illness usually becomes manifest by fever, headache, and sometimes myalgia, cough, and gastrointestinal symptoms. Regional or generalized lymphadenopathy is common. A maculopapular rash is present in <50% of patients and involves the trunk and extremities and infrequently the hands or face.

Complications are interstitial pneumonia (30 to 65% of cases), meningoencephalitis and myocarditis. Other important complications that maybe seen include hypotension, multiple organ dysfunction, renal impairment, ARDS and MODS [5].

Scrub typhus may be diagnosed in the laboratory by: (i) isolation of the organism (ii) serology (iii) molecular diagnosis (PCR). Several serological tests are currently available for the diagnosis of rickettsial diseases like Weil-Felix Test (WFT), Indirect

Immuno fluorescence (IIF), Enzyme linked Immunosorbent assay (ELISA) etc [6]. Treatment of scrub typhus must be initiated early in the course of the disease. It is emphasized again that the only crucial factor for early diagnosis is high index of suspicion. Antibiotic therapy brings about prompt disappearance of the fever and dramatic clinical improvement. Rapid defervescence after antibiotic treatment is so characteristic that it is used as a diagnostic test for *O. tsutsugamushi* infection [7].

Though studies have been done in all parts of the country, no study in India has focused exclusively on the severe form of scrub typhus in children. With the severe form being the most important cause of morbidity and mortality, this study was undertaken to focus on this aspect of the disease.

## MATERIALS AND METHODS

**Study Design:** Descriptive Study

**Setting:** Hospital based; Children's Ward of Nazareth Hospital, Shillong.

**Duration of Study:** 12 months from January 2014 to December 2014

**Inclusion Criteria:** Children with signs and symptoms of severe scrub typhus, confirmed by using primary screening test (SD BIOLINE TSUSTUGAMUSHI rapid diagnostic test for antibody), after attaining informed consent from the mother / father / guardian.

**Exclusion criteria:** Patients whose parents have not consented for the study and patients with severe scrub typhus suffering from other co-infections

## METHODOLOGY

All children below 18 years of age diagnosed clinically as severe scrub typhus and testing positive with the SD BIOLINE TSUSTUGAMUSHI rapid diagnostic test (RDT) [Standard Diagnostics, Inc.; 156-68 Hagal-dong, Giheunq-qu Yongin-si, Kyonggi-do, Korea; Tel: 82-31-899-9700; Fax: 82-31-899-9740 <http://www.standardia.com>] for scrub typhus antibody were included in the study after taking informed consent.

Severe scrub typhus was defined as those cases with fever without a focus, having any of the following symptoms: eschar, maculopapular skin rash, headache, myalgia, generalized weakness, nausea, abdominal discomfort, lymphadenopathy and systemic involvement (CNS/RS/ CVS/GIS/Renal).

Central nervous system (CNS) involvement was defined by the presence of CNS related symptoms like altered mental states such as confusion, obtundation, stupor, or coma (without evident causes such as shock or hypoglycemia), or the presence of both severe headaches and neck stiffness. Involvement of respiratory system (RS) was defined by the presence of symptoms and signs supporting evidence of pulmonary edema, interstitial pneumonia, pleural effusion or the need for mechanical ventilation. Cardiovascular (CVS) organ dysfunction was defined as: Hypotension <5th percentile for age or systolic blood pressure <2 SD below normal for age, despite >60 mL/kg of isotonic intravenous fluid in 1 hour OR Need for vasoactive drug to maintain blood pressure in the normal range OR Two of the following: Unexplained metabolic acidosis: base deficit > 5.0 mEq/L; Increased arterial lactate: >2 times upper limit of normal; Oliguria: urine output <0.5 mL/kg/hr; Prolonged capillary refill: >5 sec; Core to peripheral temperature gap >3° C;

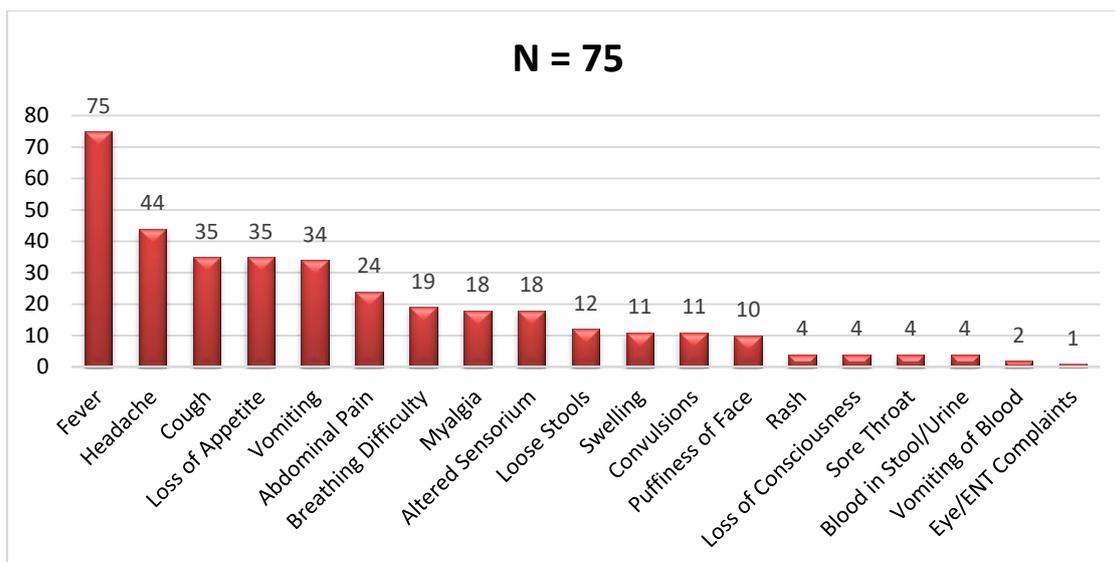
Gastrointestinal system (GIS) involvement was defined by the presence of symptoms, signs and investigation results supporting gastric ulcer, pancreatitis, and upper gastrointestinal bleeding. Renal failure was defined by urine output <0.3 mL/kg/hr for 24 hr or anuric for 12 hr. The following investigations were sent for all children included in the study: routine blood examination, Serum Electrolytes, Serum Creatinine, Platelet count, CRP, Prothrombin time with INR, SGPT, Serum Albumin, Urine Albumin and Serum Calcium. Additional investigations, if needed, were sent based on the organ system involved.

## RESULTS AND DISCUSSION

The total cases included in this descriptive study were 75. The mean age of the subjects was  $10 \pm 5$  years. Of these, 58 % were males. The mean duration of fever before admission was  $6.48 \pm 3.35$  days [Table 1]. In fact, all 75 patients presented with fever. 44 of the 75 complained of headache and 11 had convulsions [Figure 1].

**Table 1: Demographic Data of enrolled cases**

Characteristics	Severe Scrub Typhus (n=75)
Age, mean years $\pm$ SD	$10 \pm 5$
Mean Age of Males, years $\pm$ SD	$10.0 \pm 6.3$
Mean Age of Females, years $\pm$ SD	$13.69 \pm 4.8$
Gender, no. of male/no. of female (% of male)	44/31 (58.7)
Mean duration of Fever before admission, days	$6.48 \pm 3.35$
Length of hospitalization, mean days $\pm$ SD	$10.5 \pm 5.4$



**Fig 1:** depicts clinical features in the study group

The most common clinical sign was conjunctival redness seen in 44% of the patients [Table

2]. Pallor and lymphadenopathy was found in 28% and 13% respectively.

**Table 2: Clinical Signs on General Physical Examination**

Clinical Sign	Severe scrub typhus (n = 75)
Temperature (in deg C) Highest Mean ± SD	40.5 38.2 ± 1.9
Tachypnea, no. (%) of patients 2-12 months (>50/min) > 12 months (>40/min)	4 (5%) 16 (21%)
Conjunctival redness, no. (%) of patients	33 (44%)
Pallor, no. (%) of patients	21 (28%)
Icterus, no. (%) of patients	2 (3%)
Cyanosis, no. (%) of patients	6 (8%)
Eschar, no. (%) of patients	16 (21%)
Lymphadenopathy, no. (%) of patients	10 (13%)
Edema, no. (%) of patients	10 (13%)

The characteristic eschar was seen only in 21% of children [Figures 2 & 3]. On systemic examination,

58.6% of subjects showed features suggestive of CNS involvement [Table 3].



**Fig 2:** shows an eschar in the neck of a patient



**Fig 3: shows an eschar in the popliteal fossa of a patient**

Multiple organ dysfunction syndromes (MODS) were found in 42.6% of patients. Laboratory evaluation showed that 78.7% of the children had a raised ESR; 74.6% of the patients had anemia. Leukocytosis was seen in 46.7% of children and of these neutrophilia was found in 22.7% of patients whereas lymphocytosis was found in 54.7%. Neutropenia was seen in only 2.6% children.

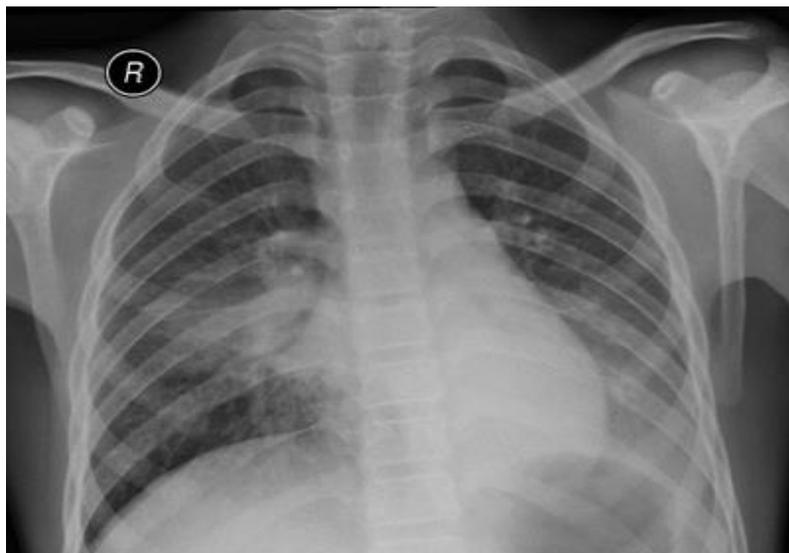
Thrombocytopenia was documented in 49.3%. Raised serum SGPT levels were seen in 66.7% patients. Hypoalbuminemia and hypocalcemia was found in 84% and 74.7% of patients, respectively. C - reactive protein was elevated in 82.7% and serum creatinine was elevated in 9.3% children. Hyponatremia was documented in 36% and hyperkalemia in 20% of children.

**Systemic Examination**

System Involved	Number of Patients	Percentage of Patients
Respiratory	25	33%
Cardiovascular	12	16%
Gastrointestinal	26	34.6%
Central Nervous	44	58.6%
Renal	0	0

CSF examination showed CSF protein was elevated (mean- 102.98 g/dl) and was associated with a lymphocytic predominance (mean- 81.14%). Radiographic findings of the 25 patients who presented with respiratory complaints showed that 10 patients were found to have interstitial pneumonia, 8 had

consolidation, 4 had pleural effusion and 3 of the patients had radiographic features suggestive of acute respiratory distress syndrome (ARDS). [Figures 4 & 5]. There was only one death among the seventy-five cases enrolled in the study.



**Fig 4: Shows a chest radiograph with right middle zone consolidation with left pleural effusion**



**Fig 5: Shows a chest radiograph with bilateral consolidation**

In the present study, all 75 children (100%) presented with fever similar to the findings documented by Dass *et al.*; [9] and Huang *et al.*; [10] Headache was the next most common symptom, seen in 58.7% of children, unlike other studies where headache ranged from 25 to 39.3% only [9, 10]. The presence of an eschar is a valuable clinical clue in the diagnosis of scrub typhus; however absence does not rule out the disease. The prevalence of eschars in patients diagnosed with scrub typhus has been reported as between 7%-80% [11, 12]. However, in the present study, eschar was seen in only 21% of the patients. Headache was one of the predominant complaints in 58.7% of the

children in the present study, comparatively higher than was seen in other studies. Dass *et al.*; [9] and Digra *et al.*; [13] reported headache in 25% and 39.3% of cases respectively.

On clinical examination, pallor was found in only 28% of the patients, considerably less, in comparison to findings by Palanivel *et al.*; [15] Conjunctival redness, was found in 44% of children in the present study, nearly similar to the study in Jammu and Kashmir, by Digra *et al.*; [13]

Lymphadenopathy has always been a characteristic feature of rickettsial infections. Studies from Taiwan (Huang *et al.*; [10]), Chennai (Palanivel *et al.*; [15]) and Dehradun (Jain *et al.*; [14]) had shown 42.9%, 59.7% and 42.1% cases of lymphadenopathy respectively. However, clinical examination revealed lymphadenopathy in only 13% of patients in the present study. Surprisingly, this finding is nearly similar to the findings of another study from the North-East region of India by Dass *et al.*; [9] which demonstrated lymphadenopathy in 12.5% of cases. These findings may suggest that scrub typhus less commonly presents with lymphadenopathy in this part of the country, as compared to other parts of the country and of the world.

Laboratory findings in the present study showed that hypoalbuminemia was found in 84% of cases. The Taiwan study by Huang *et al.*; [10] showed that hypoalbuminemia was present in 88.9%, whereas the Chennai study by Rajendran [19] detected hypoalbuminemia in 72% cases. CRP was raised in 82.7% of patients, correlating with findings by Jain *et al.*; [14] where CRP was raised in 89.4% cases. ESR too was elevated in 78.7% cases, whereas Jim *et al.*; [20] observed that CRP and ESR were raised in 95% and 88% patients respectively.

In the present study, meningoencephalitis was the most common complication seen in 58.6% patients, whereas other studies have reported incidence between 6% to 30% cases only [15, 9, 10]. This was rather an unusual finding and could probably suggest that serious complications in the North East region of India were restricted predominantly to the central nervous system. The next most common system involved was the gastrointestinal system, where 34.6% of patients were affected. These findings were similar to observations by Huang *et al.*; [10] wherein 35% of children were found to have hepatosplenomegaly. Other researchers however have found gastrointestinal involvement in the form of hepatomegaly ranging between 51.8% to 76% cases [13, 17, 22]. Multiple organ dysfunctions was found in 42.6% children, higher in comparison to Vivekanandan *et al.*; [5] where in 34% of patients had MODS.

## CONCLUSION

The present study evaluated the clinical and laboratory findings of severe scrub typhus in children. A higher incidence of meningoencephalitis was observed in this study than in previously published paediatric studies. Also, clinical signs such as conjunctival redness were more commonly observed than the typical eschar, which is characteristic of scrub typhus. Other features usually associated with scrub typhus, like rash and lymphadenopathy were less commonly found. Laboratory findings that were most common were raised acute phase reactants (ESR and

CRP), hypoalbuminemia, anaemia and hypocalcemia. CSF findings in the majority were an elevated protein associated with a lymphocytic predominance.

Physicians should consider scrub typhus when caring for patients with acute febrile illness in endemic areas. Identification of clinical signs like neck stiffness, hepatosplenomegaly and respiratory distress would help in timely recognition of complications such as meningoencephalitis, pneumonia and ARDS. This is of paramount importance to ensure a favorable outcome in pediatric patients with severe scrub typhus.

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