

**SCRUB TYPHUS: CLINICO-LABORATORY PROFILE OF CHILDREN IN
UTTARAKHAND**

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ABSTRACT

Objective: Scrub Typhus is a common rickettsial disease presenting as an acute febrile illness with multisystem involvement. Objective of this study is to evaluate the clinical features of scrub typhus in children brought to Himalayan Institute of Medical Sciences, Dehradun (a tertiary hospital, located in foot hills of Himalaya in north India). **Method:** Seventy nine children diagnosed with scrub typhus fulfilled the inclusion criteria and were analyzed in this study conducted over a period of one year. The diagnosis was confirmed by IgM ELISA test. **Results:** Out of 79 subjects, 52 were male and 27 were female with a male female ratio of 1.9:1. Fifty three (67.09%) resided in rural area while 26 (32.91%) resided in urban area. Most of the patients (91%) presented during the months of August to November. All of the patients presented with fever with the mean duration of fever on presentation was 9.07 days. Other common symptoms observed were nausea (62.03%), anorexia (32.91%), abdominal pain (29.11%), headache (27.85%), breathing difficulty (25.32%), altered sensorium (21.52%) and convulsion (15.19%). The common signs observed were hepatomegaly (89.87%), splenomegaly (78.48%), pallor (51.90%), edema (43%), hypotension (22.78%), tachypnoea (21.52%), meningeal signs (21.52%), and eschar (17.72%). There were 3 deaths with an overall mortality of 3.8%. All these children presented late with manifestation of shock and multi organ dysfunctions. **Conclusion:** This study provides useful clinical and laboratory clues to help clinicians in early diagnosis of scrub typhus so as to institute appropriate antibiotic treatment to prevent the life threatening complications and mortality.

KEYWORDS: Scrub Typhus, tachypnea, manifestation.**INTRODUCTION**

Scrub typhus is an acute febrile illness caused by obligate, intracellular, gram-negative bacteria, *Orientia tsutsugamushi*, and is characterized by an eschar, lymphadenopathy and multisystem involvement.^[1] Scrub typhus is endemic to a part of the world known as the "tsutsugamushi triangle". This geographical triangle extends from northern Japan and far eastern Russia in north, northern Australia in south to Pakistan and Afghanistan in west. This geographical area includes South and East Asia and Pacific.

Rickettsial infections are being grossly under diagnosed in India because of i) their non-specific clinical presentation, ii) low index of suspicion among clinicians, iii) limited awareness about the disease and iv) lack of diagnostic facilities.^[2] Scrub typhus is regarded as a life threatening disease in children. Serious complications of scrub typhus usually occur in the second week of illness, which include acute respiratory distress syndrome (ARDS), pneumonia, meningitis / meningoencephalitis,

acute kidney injury (AKI), myocarditis, severe thrombocytopenia and bleeding.

There is a paucity of studies on clinical profile and complications of scrub typhus in children from various states of India especially from Uttarakhand in northern part of India. Hence we undertook this prospective observational study, to analyze the clinical profile of scrub typhus in children.

MATERIALS AND METHODS

The study was conducted at Himalayan Institute of Medical Sciences, Dehradun; a university teaching hospital in Uttarakhand over a period of one year. All pediatric patients below the age of 18 years were included in this study. These children presented with fever for more than 5 days with one or more of the following clinical features: rash, edema, hepatosplenomegaly, lymphadenopathy, eschar, altered sensorium and seizures, and a positive serological test (IgM ELISA) for scrub typhus.

The diagnosis of scrub typhus was suspected on the basis of clinical and laboratory features. The diagnosis of scrub typhus was confirmed by an IgM ELISA test (*Scrub typhus detectTM IgM ELISA system from In Bios International, Inc. Seattle USA*). Other common infectious conditions that could clinically mimic scrub typhus were ruled out by performing the following tests: peripheral smear and rapid antigen test for malaria, Dengue (NS1 antigen, IgM antibody) test, Widal test, urine and blood cultures. Tuberculin test, leptospira serology and an HIV enzyme-linked immunosorbent assay (ELISA) were performed when clinically indicated. Relevant patient information (age, sex, address, medical history, duration of fever, associated symptoms, vital signs, and the general and systemic examination findings) was recorded in a predesigned proforma. Laboratory investigations including complete blood counts, chest X-rays, tests for renal and liver function, urinalysis and serum electrolyte estimation

were performed at presentation for all cases and were repeated if necessary.

RESULTS

Seventy nine patients were diagnosed with scrub typhus on the basis of clinical features and a positive IgM ELISA for scrub typhus. The age of patients ranged from 0.17 to 17 years. Of the total 79 patients, 23 (29%) were less than or equal to 5 year age, 19 (24%) were in 6-10 years range, 28 (36%) were in the range of 11 to 15 years and the rest 9 (11%) were between 16 to 18 years. Fifty two (65.82%) were males and 27 (34.18%) were females with a male to female ratio of 1.9:1. Two thirds of these children (67%) belonged to rural area and 33% belonged to the urban area. The distribution of various symptoms, signs and laboratory findings of these 79 patients is given in Table 1. Figure 1 graphically depicts relative distribution of different signs.

Table 1: Clinical and laboratory profile of 79 children with scrub typhus.

Laboratory Investigations				
Symptoms	No. (%)	Parameter	No. (%)	Mean \pm SD
Fever	79 (100)	Hemoglobin (g%)	79 (100)	10.15 \pm 1.92
Vomiting	49 (62)	<6	06 (7)	
Anorexia	26 (33)	6-11	50 (63)	
Abdominal pain	23 (29)	>11	23 (29)	
Headache	22 (28)	TLC ($\times 10^3/\text{mm}^3$)	79 (100)	10233 \pm 5228
Breathlessness	20 (25)	Platelet ($\times 10^3/\text{mm}^3$)	79 (100)	115.06 \pm 103.45
Convulsion	12 (15)	<50	21 (26)	
Myalgia	11 (14)	50-100	16 (20)	
Diarrhea	10 (12)	100-150	19 (24)	
Cough	06 (07)	>150	23 (29)	
Oliguria	03 (04)	AST > 40 U/L	56 (72)	
Arthralgia	02 (03)	ALT > 40 U/L	50 (63)	

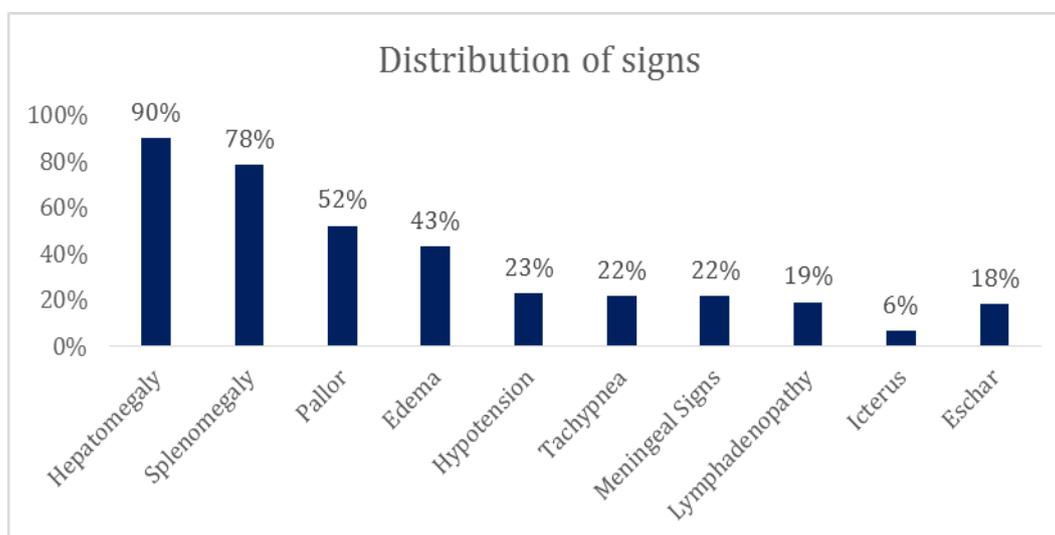


Figure 1: Distribution of different signs.

All 79 patients presented with fever. Vomiting (62%), anorexia (33%), abdominal pain (29%) were other common symptoms. Headache, breathlessness and rash were present in 28%, 25%, 11% of patients respectively.

Common signs observed were hepatomegaly (90%), splenomegaly (78%), edema (43%). Eighteen patients had hypotension and 17 had meningeal sign. Eschar was observed in 18% of patients. Anemia (hemoglobin <

11.0 g%) was present in 56 (71%), thrombocytopenia (platelet count $<1,000,000 \text{ mm}^3$) in 37 (47%) children. Severe anemia (hemoglobin $< 6.0 \text{ g } \%$) was present in 6 (7.5%) children and severe thrombocytopenia (platelet count $<50,000/\text{mm}^3$) in 21 (26.5%).

DISCUSSION

Scrub typhus is an acute febrile illness caused by rickettsiae, *Orientia tsutsugamushi*. The disease is transmitted to humans through the bite of an infected chigger, the larval stage of trombiculid mite. These mites and wild rodents act as reservoir, and between the two, the infection perpetuates in nature.

This hospital based descriptive study elaborates the clinical profile of scrub typhus in pediatric patients. Seventy nine patients fulfilled the inclusion criteria and have been analyzed in this study. Most of the patients (91%), presented between the months of August and November. This period coincides with and immediately follows the monsoon season and is associated with peak growth of scrub vegetation. Similar observations have also been reported in two other studies.^[3,4]

The occurrence of scrub typhus also varies with area of residence. In the present study 67% patients were from rural area and 33% from urban area. Bhat *et al.* reported 90% children were from rural area and 10% from urban.^[5] A study from a tertiary hospital in south India found 58% children to be from urban area and 42% from rural area.^[6] Males predominated the study population (65%), as also reported by other authors in their studies.^[3,5,7] The male predominance can be attributed to higher prevalence of exposure to chiggers among boys, due to more outdoor activities. However a single study from south India has reported a female predominance with a male: female ratio of 1:1.3.^[6]

Distribution of patients in age groups was found to be nearly uniform over 0 to 18 years; 23 (29.11%) patients were < 5 years of age, 19 (24.05%) patients were between 6 to 10 years, 28 (35.44%) patients were in age group 11-15 years and 9 (11.39%) patients were in age group 16-18 years. Similar observations were noted in a study conducted at a tertiary hospital from north India.^[5] In contrast, a study by Huang *et al.* shows that children 0 to 5 years constituted 50% of cases, children aged 6 to 10 years constituted 35.7% of cases, and children aged 11 to 13 years constituted 14.3% of cases.^[7] Thus it cannot be conclusively stated that scrub typhus predominantly occurs in any particular pediatric age group.

The clinical manifestations of scrub typhus in children are nonspecific and likely to be confused with other febrile illnesses. Fever was the most common symptom seen in all the 79 cases and the median duration of fever was 9 days (range 2 to 25 days) similar to findings of other two studies.^[5,6] Other common symptoms observed in the present study were nausea, abdominal pain, breathing difficulty, headache in 62%, 29%, 25% and

28% respectively. Cough was reported in 6 (7.59%) patients. Seventeen patients (21.5%) had altered sensorium and 15% patients had convulsion in the present study. The common clinical signs observed in the present study were hepatomegaly, splenomegaly and pallor in 90%, 78% and 52% children respectively. Comparable findings were observed in two similar studies.^[6,8] Hypotension (23%), edema (22%), meningeal sign (22%) were observed in the present study similar to other studies.^[5,9] Eschar is a black necrotic lesion resembling a cigarette burn, usually found in areas where skin is thin, moist or wrinkled and where the clothing is tight like axilla, genitalia and inguinal area. Eschar was seen in 18% children in the present study. Though the presence of an eschar is a pathognomic sign of scrub typhus however its absence does not rule out the disease. Eschar has been reported in 0-80% of cases with scrub typhus and may be difficult to find in dark skinned population.^[2] Nineteen percent children with scrub typhus had lymphadenopathy in the present study however; Bhat *et al.* have reported lymphadenopathy in 42% and Kumar *et al.* in 37% of their patient.^[3,5]

On analyzing laboratory investigations anemia, thrombocytopenia and leucocytosis were frequently observed. Anemia ($<11\text{gm/dl}$) was found in 68.3% patients and severe anemia ($< 6 \text{ gm/dl}$) in 3.8% similar to another study.^[5] Seventy seven percent of children had thrombocytopenia (Platelet count $< 1, 50,000/\text{mm}^3$) with 21(26%) having severe thrombocytopenia (Platelet count $< 50,000/\text{mm}^3$). Similar finding of severe thrombocytopenia have been reported in 2 other studies.^[3,5] Hepatic dysfunction (AST and ALT levels $> 40\text{U/L}$) was reported in 56 (72%) and 50 (63%) patients in the present study. Bhat *et al.* reported AST and ALT levels of $> 40 \text{ U/L}$ in 47% and 48% cases respectively.^[5] Renal dysfunction (creatinine $>1.2 \text{ mg/dl}$) was seen in 5 (6.3%) patients. Serum creatinine of $>1.2\text{mg}\%$ was reported in 11% cases in study from north India.^[5]

Scrub typhus is a life threatening disease in children. Mortality in 3.8% of cases was reported in the present study which was comparable to the mortality of 3% cases in study by Kumar *et al.*^[3] Palanivel *et al.* have reported an overall mortality of 12% cases while as no mortality was reported in the studies of Huang *et al.* and Digra *et al.*^[7,9] Other authors have reported a mortality rate ranging from 0-15%.^[5,10-13]

The clinical manifestations of scrub typhus in children are nonspecific and likely to be confused with other common acute febrile illnesses. Eschar though pathognomic is not found in all cases. Thus when a child presents with acute febrile illness, maculopapular rash, hepatosplenomegaly, thrombocytopenia and features suggestive of capillary leak, diagnosis of scrub typhus should be suspected and an eschar, if found is very useful for confirming diagnosis. Clinical suspicion of scrub typhus warrants immediate empirical therapy with Doxycycline or Azithromycin pending serological

confirmation, as delay in treatment would result in life threatening complications. Timely recognition of complications is of paramount importance to ensure a favorable outcome.

CONCLUSION

Scrub typhus is emerging as common febrile illness in north India during and immediately following the monsoon season. The common presenting sign and symptoms are fever, hepatosplenomegaly, rash, eschar. The clinicians should be aware of these signs so as to start empirical antibiotics therapy till the serological results are available. This study provides useful clinical and laboratory clues to help clinicians diagnose scrub typhus at earliest and thus prevent the complications. But, further research, on a larger scale is warranted for this life threatening disease.

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