

**A STUDY OF COMPLICATIONS OF SCRUB TYPHUS IN CHILDREN AT A TERTIARY HOSPITAL OF UTTARAKHAND**

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**ABSTRACT**

**Objective:** Present study aims to evaluate the complications of scrub typhus in children admitted to Himalayan Institute of Medical Sciences, Dehradun; a tertiary hospital situated in terai belt of Uttarakhand State in India.

**Method:** Seventy nine children diagnosed with scrub typhus fulfilled the inclusion criteria and were analyzed in this cross sectional study. The diagnosis was confirmed by IgM ELISA test. The study was carried out over a period of one year. **Results:** The 79 subjects had 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 presented during the monsoon season. The common complications observed were meningitis (30.38%), severe thrombocytopenia (26%), pneumonia (20.2%), shock (3.8%), ARDS (3.8%), pleural effusion (3.8%) and myocarditis (1.27%). There were 3 deaths with an overall mortality of 3.8%. **Conclusion:** This study will help the clinicians in early diagnosis of scrub typhus and related complications. Meningitis is observed to be more common complication of scrub typhus in the present study. The study provides clue for timely interventions and thus prevent life threatening morbidity and mortality. Advanced and extensive research on this life threatening disease is required to decrease the burden on health facilities.

**KEYWORDS:****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.<sup>[1]</sup> Scrub typhus is endemic to a part of the world known as the "tsutsugamushi" triangle which includes South and East Asia and Pacific. Scrub typhus is regarded as a life threatening disease in children. Serious complications of scrub typhus 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 complications of scrub typhus in children from Uttarakhand. The geographic area is characterized by i) high vegetation growth and high humidity due to irrigated agriculture round the year, and ii) flood prone streams. The first report on occurrence of scrub typhus in Uttarakhand was in 2010, when 9 adult cases of scrub typhus were reported.<sup>[2]</sup> The cases of scrub typhus have dramatically increased thereafter and till 2014 approximately 400 adult and 150 pediatric cases were reported from Uttarakhand state.<sup>[3,4]</sup> This requires an urgent need for research in this area so as to provide appropriate information on this subject for timely intervention to prevent life threatening complications.

**MATERIALS AND METHODS**

Himalayan Institute of Medical Sciences, Dehradun is a tertiary hospital situated in terai belt of Uttarakhand State in India the study was conducted at this hospital over a period of one year. All pediatric patients with age less than 18 years who 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 were included in the study.

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 detect<sup>TM</sup> IgM ELISA system from In BiosInternational, Inc. Seattle USA*). Other common infectious conditions (malaria, Dengue, Tuberculin, HIV etc) that could clinically mimic scrub typhus were ruled out by performing appropriate tests. 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 were performed at presentation for all cases and were repeated if necessary. The data was entered into a

Microsoft Office excel spreadsheet and analyzed using descriptive statistics.

## 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, 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.

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 mm<sup>3</sup>) in 37 (47%) children. Severe anemia (hemoglobin < 6.0 g %) was present in 6 (7.5%) children and severe thrombocytopenia (platelet count <50,000/mm<sup>3</sup>) in 21 (26.5%).

Meningoencephalitis was the most common complication seen in 31% children. One fifth children presented with pneumonia. Other complications encountered in the present study were pleural effusion, acute kidney injury (AKI), acute respiratory distress

syndrome (ARDS). Three children died with a mortality rate of 4%.

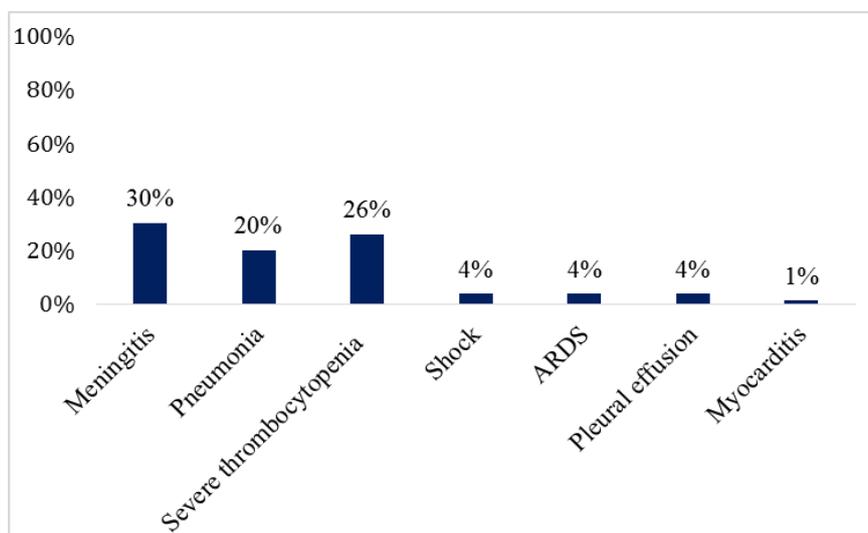
## DISCUSSION

Scrub typhus is an acute febrile illness. 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 complications associated with scrub typhus. 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.<sup>[5,6]</sup>

In the present study 67% patients were from rural area and 33% from urban area. Bhat *et al.* in their study on scrub typhus have reported that 90% children were from rural area and 10% from urban.<sup>[4]</sup> A study from a tertiary hospital in south India found 58% children to be from urban area and 42% from rural area.<sup>[7]</sup> Males predominated the present study population (65%), as also reported by other authors in their studies.<sup>[4,5,8]</sup>

Scrub typhus is a life threatening disease in children. Serious complications of scrub typhus usually occur in second week of illness. These include meningitis, shock, ARDS, AKI, pleural effusion, myocarditis, severe thrombocytopenia and bleeding. Relative occurrence of various complications due to scrub typhus in patients in present study is depicted in figure 1.



**Figure 1: Distribution of various complications.**

Meningitis was seen in 24 (30.38%) patients in present study. The same has been reported in other previously conducted studies.<sup>[4,5]</sup> Pneumonia was reported in 16 (20.2%) cases in the present study. Digra *et al.* and Bhat

*et al.* found pneumonia in 9.5% and 9.6 % of their cases.<sup>[4,9]</sup> Hypotension refractory to fluids and requiring inotropic support (shock) was observed in 3.8 % of cases in the present study as compared to 44% and 34 %

reported by two respective studies.<sup>[5,7]</sup> Pleural effusion and ARDS was reported in 3 children each (3.8%) in the present study which was less than reported previously. Palanivel *et al.* found pleural effusion in 61% patients whereas Kumar *et al* reported it in 14%.<sup>[5,7]</sup> ARDS was reported in 18% cases by Kulkarni *et al.*<sup>[10]</sup> 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.*<sup>[5]</sup> 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.*<sup>[8,9]</sup> Other authors have reported a mortality rate ranging from 0-15%.<sup>[4,11-14]</sup> A comparison of common complications of scrub typhus observed in present study and that reported in some previous pediatric studies is presented in table 2.

**Table 2: Reported complications (in percentages) of scrub typhus in various studies.**

Complications	Present study	Bhat <i>et al.</i> <sup>[4]</sup>	Kumar <i>et al.</i> <sup>[5]</sup>	Palanivel <i>et al.</i> <sup>[7]</sup>	Huang <i>et al.</i> <sup>[8]</sup>	Digra <i>et al.</i> <sup>[9]</sup>	Kulkarni <i>et al.</i> <sup>[10]</sup>
Meningitis	30.3%	30.6	6	6	21	19	64
Pneumonia	20.2	9.6	3	15	7	9.5	4
Shock	3.8	17.7	34	44	-	-	-
ARDS	3.8	9.6	9	4.5	-	-	18
Pleural effusion	3.8	8	14	61	-	-	-
Myocarditis	1.27	4.8	34	-	-	14	10
Mortality	3.8	6.4	3	12	0	0	11.5

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.

Meningitis is a common complication of scrub typhus in children. Children with meningitis tend to present early with fever, altered sensorium, seizures and meningeal signs. CSF examination reveals a lymphocytic pleocytosis, raised proteins and a normal glucose level. These children respond promptly to appropriate antibiotics like doxycycline and azithromycin, as do children without meningitis. Timely recognition of complications is of paramount importance to ensure a favorable outcome.

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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