

# Post-disaster outbreak of scrub typhus in Sub-Himalayan region of Uttarakhand

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## ABSTRACT

**Background:** In June 2013, flash floods caused a great loss of human life and infrastructure in the Sub-Himalayan region of Uttarakhand, India. An outbreak of scrub typhus caused by *Orientia tsutsugamushi* occurred in the district of Chamoli, Rudraprayag and Pauri Garhwal after the disaster. The present study was conducted with the objective to describe this outbreak in terms of time, place, person and clinical features and to compare the outbreak with the pre-disaster status of the area. **Materials and Methods:** This study was conducted in Veer Chandra Singh Garhwali Government Medical Science and Research Institute, Srinagar, Pauri Garhwal from June to December 2013. Study subjects were patients from disaster-affected areas. Definition criteria were used for clinically suspected, probable and confirmed cases of scrub typhus. All the samples were subjected to immunochromatographic test out of which 229 were confirmed by ELISA. **Results:** A total of 283 samples of patients with undiagnosed fever were tested and 229 (80.9%) showed the presence of IgM antibody by ELISA against scrub typhus. The maximum number of cases (213) were found between July and November and were mainly confined to the districts mentioned above. The main clinical features were gastrointestinal symptoms (53%), rash (51%), myalgia (71%), acute respiratory distress syndrome (ARDS) (2%), hepatorenal syndrome (1.7%), coagulopathy (18%) and eschar occurred only in five cases (2%). **Conclusions:** An increase in the number of cases of scrub typhus was observed after the floods in Uttarakhand, which suggests that a post-disaster epidemic had occurred. Scrub typhus should also be considered in the differential diagnosis of acute febrile illness with gastrointestinal symptoms, rash, myalgia, ARDS, hepatorenal syndrome and coagulopathy. Eschar being pathognomonic, may not always be seen, and its absence does not rule out scrub typhus.

**Key words:** Outbreak, post-disaster, scrub typhus

## INTRODUCTION

In June 2013, there was a great loss of human life and infrastructure caused directly by a flash flood, mainly in the district of Chamoli, Rudraprayag and Pauri Garhwal, Uttarakhand, India. This was followed by outbreaks of disease, especially scrub typhus which occurs due to the introduction of *Orientia tsutsugamushi* through the skin by the bite of a larval stage (chigger) trombiculid mite.<sup>[1]</sup> Scrub typhus is widespread in the so-called 'tsutsugamushi triangle' which includes Japan, Taiwan, China and South Korea on the North, India and Nepal on the west and Australia and Indonesia on the South.<sup>[2]</sup> In India, epidemics of scrub typhus have been reported from Northern, Eastern and Southern regions.<sup>[3-11]</sup> Although the disease is

endemic in our country, it is grossly underdiagnosed owing to the non-specific clinical presentation, lack of access to the specific diagnostic facilities in most areas and low index of suspicion by the clinicians.<sup>[12]</sup> The true burden of this disease is still unknown in the state of Uttarakhand which requires urgent attention to establish the prevalence of the disease.

The present study was undertaken to find the prevalence of scrub typhus after flash floods in the region and

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correlate the demographic profile and clinical features of the patients.

**MATERIALS AND METHODS**

The study was conducted in a tertiary care teaching institution in the district of Chamoli, Rudraprayag and Pauri Garhwal, Uttarakhand. All patients belonging to disaster-hit areas, presenting with febrile illness, from June 2013 to December 2013, were evaluated. As per the WHO recommended surveillance standards, definition criteria were used for clinically suspected (a case that is compatible with the clinical description), probable (a case compatible with the clinical description with occurrence at same location and time) and confirmed cases (a suspected case with laboratory confirmation) of scrub typhus.

Other probable diagnoses such as malaria, leptospirosis, dengue fever, viral pharyngitis, enteric fever and urinary tract infection were ruled out by history, clinical examination and appropriate laboratory investigations. The patients were subjected to a battery of investigations such as bleeding and clotting time, prothrombin time, urine analysis, complete blood count, platelet count, rapid antigen test for malaria, smear for malarial parasite, serology for leptospirosis and dengue haemorrhagic fever, Widal tube agglutination and blood culture, renal function tests and liver function tests.

The patients were also subjected to additional investigations such as chest X-ray and abdominal ultrasonography, as per the indication.

Blood samples (5–8 ml) were collected, and serum sent to the laboratory for the patients who remained febrile and no aetiological diagnosis could be ascertained. Samples were subjected to the immunochromatographic test (ICT) by SD Bioline and the test for specific IgM antibodies against *O. tsutsugamushi* using a commercial ELISA kit (In BiOS International Inc., USA). The ELISA kit uses *O. tsutsugamushi* derived recombinant antigen mix. The tests were carried out as per the manufacturer’s instructions.

The patients having IgM antibodies against *O. tsutsugamushi* in their serum samples were diagnosed as having scrub typhus. Numerous complications such as hepatitis, disseminated intravascular coagulation, acute renal failure (ARF), acute respiratory distress syndrome (ARDS), meningitis and myocarditis were also recorded during the study.

**RESULTS**

A total of 283 patients with undiagnosed fever were included in the study and out of these 229 were positive for IgM antibody against scrub typhus. Of the 229 patients, 133 (58%) were females, the rest being males [Figure 1].

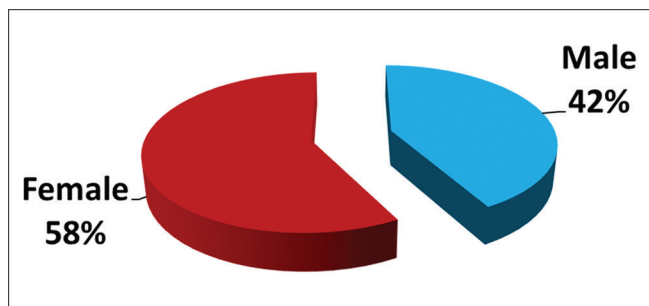


Figure 1: Sex distribution of the patients (n = 229)

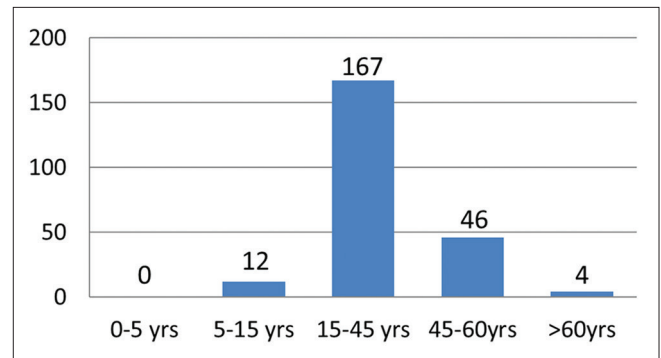


Figure 2: Age distribution of patients (n = 229)

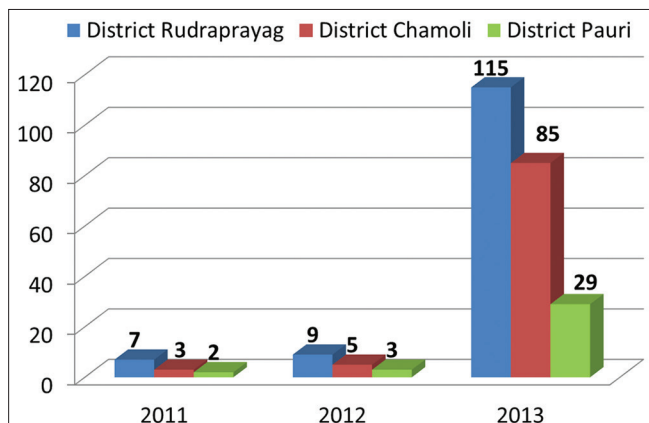


Figure 3: District wise comparison of 3 years

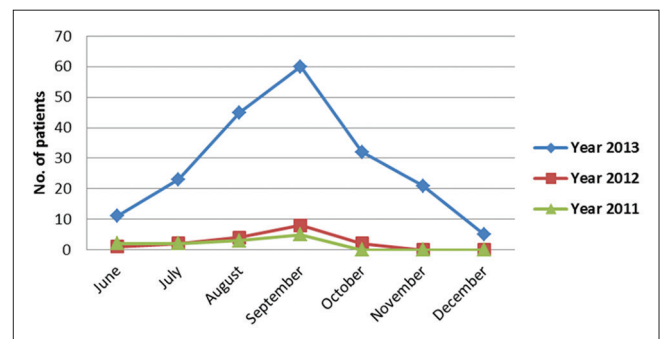


Figure 4: Month wise distribution of the patients

The youngest patient was 7 years old while the oldest was aged 68 years [Figure 2]. All the patients belonged to the three main disaster-affected districts. The number of cases reported from the concerned districts were 12, 17 and 229 in the year 2011, 2012 and 2013, respectively [Figure 3]. The cases were seen mainly in the months between August and November [Figure 4].

The common symptoms noted were fever, myalgia, nausea and vomiting, followed by breathlessness, gastrointestinal complaints such as abdominal pain and sometimes associated with loose motion, rash and jaundice. The most common signs seen were lymphadenopathy (56%) and maculopapular rashes (51%). Eschar, which is considered to be the pathognomonic feature, was rare in the present study; only five of them had the presence of eschar with lymphadenopathy [Table 1].

Out of 283 patients, 242 were found to be positive by ICT by SD Biotline, whereas IgM ELISA confirmed positive results for 229 only [Table 2].

Among the other laboratory investigations, leucocytosis (51%) was the most commonly found parameter, followed by raised serum transaminases (21%) thrombocytopenia (18%) and bilirubinemia (7.4%) [Table 3]. ARDS (2%) and ARF (3%) were the main complications noted in the study [Table 3].

**DISCUSSION**

There have been reports of outbreaks of scrub typhus from various parts of the country in the recent past with serological evidence of the widespread prevalence of spotted fevers and scrub typhus in the Himalayan states and other states of Southern India.<sup>[3,4,6-10]</sup>

After the Kedarnath floods which mainly affected the districts of Rudraprayag, Chamoli and Pauri Garhwal, there was a surge in the cases of scrub typhus in these areas. As compared to other outbreak-related studies, the present study shows a larger number of cases [Table 4] that were referred to our hospital, a tertiary care centre. This may be due to the fact that a large number of people were left stranded because of damaged roads and were exposed to the mite bite for a longer duration of time. Further, in the immediate post-monsoon period (September to early months of the next year), there is growth of secondary scrub vegetation, which is the habitat for trombiculid mites (mite islands).<sup>[12]</sup> In the present study, most of the cases were seen during the months of August to November [Figure 4]. Such a post-monsoon surge was reported earlier also.<sup>[4-6,8,10]</sup>

**Table 1: Clinical presentation (n=229)**

Symptoms	n (%)	Signs	n (%)
Fever with chills	225 (98)	Lymphadenopathy	128 (56)
Headache	190 (83)	Maculopapular rash	117 (51)
Myalgia	163 (71)	Splenomegaly	2 (1)
Cough	158 (69)	Crackles/rhonchi	16 (7)
Nausea/vomiting	121 (53)	Pleural effusion	2 (1)
Abdominal pain	126 (55)	Altered sensorium	0
Diarrhoea	11 (5)	Eschar	5 (2)
Breathlessness	34 (15)	Hepatomegaly	18 (8)

**Table 2: Diagnostic tests (n=283)**

Test	Number of patients (%)
ICT	242 (85.5)
IgM ELISA	229 (80.9)
IgM + ICT	229 (80.9)
Eschar + IgM + ICT	5 (2.2)

ICT: Immunochromatographic test

**Table 3: Complications of scrub typhus (n=229)**

Complication	Number of patients (%)
ARDS	5 (2)
Shock	Nil
Meningitis	2 (1)
Renal impairment (creatinine>1.5 mg/dl)	4 (1.7)
Raised bilirubin (>1.2 mg/dl)	17 (7.4)
Raised serum transaminases	49 (21)
Leucocytosis (>12,000/µl)	117 (51)
Thrombocytopenia (<1 lac/cmm)	41 (18)

ARDS: Acute respiratory distress syndrome

**Table 4: Comparison of studies**

	Vellore	Shimla	Pondicherry	Present study
Number of cases	27	21	50	229
Fever	5-20	5-25	3-60	4-28
Nausea/vomiting (%)	48	43	58	53
Cough (%)	44	NA	40	69
Myalgia (%)	52	38	38	71
Lymphadenopathy (%)	NA	53	30	56
Jaundice (%)	26	53	10	7.4
Rash (%)	22	10	14	51
Eschar (%)	4	10	46	2
IgM ELISA positive (%)	-	-	-	81

NA: Information not available

The present study showed that women (58%) were more affected than males (42%) [Figure 1]. This can be explained by the fact that in our state, women make the major workforce in the fields that's why they are more exposed. Studies from other part of the world also suggest female preponderance which is in concordance with the present study.<sup>[13,14]</sup>

The disease presents as an acute febrile illness with non-specific signs and symptoms. In our study, the

most common presentation seen was that of fever with myalgia (71%) or with rash (51%). Another important finding was a predominance of gastrointestinal signs and symptoms such as nausea and vomiting (53%), abdominal pain (55%) and diarrhoea (5%). This finding assumes importance, as there is limited available information on the relationship between scrub typhus and gastrointestinal dysfunction.<sup>[15]</sup> Since clinical presentation of fever with rash/myalgia occurs in many other febrile illnesses such as dengue fever or leptospirosis, presence of gastrointestinal complaints could be used as a differentiating feature for suspecting scrub typhus as suggested by some of the other studies too.

A necrotic eschar at the inoculating site of the mite is pathognomonic of scrub typhus;<sup>[1,2]</sup> however, it is rarely seen in Southeast Asia and the Indian subcontinent.<sup>[4,6,10]</sup> In our study, the eschar was seen only in 2% of patients. Lymphadenopathy (56%) was commonly present in the present study which is in accordance with the other studies [Table 2].<sup>[7,15]</sup>

Occurrence of capillary leak was a significant finding perceived in the study. *O. tsutsugamushi* infects vascular endothelium leading to vasculitis and organ dysfunction.<sup>[16]</sup> Capillary leak because of injury to vascular endothelium may ultimately lead to the development of rashes. However, this finding needs to be validated in a large number of patients. In the present study, thrombocytopenia was the most common finding, followed by signs of impaired liver function, as evidenced by elevated serum transaminases and ARDS without multiorgan dysfunction. This finding was in accordance with many other case series.<sup>[4,6,15]</sup> Other laboratory findings noted were leucocytosis and low serum albumin. While low serum albumin and leucocytosis are thought to be associated with severe scrub typhus.<sup>[17,18]</sup> These findings again need to be validated in a larger sample size. The complications in scrub typhus usually develop after the first week of illness<sup>[1]</sup> and are directly related to the blood load of *O. tsutsugamushi*.<sup>[17,19]</sup>

The mainstay of diagnosis in scrub typhus is serology.<sup>[20]</sup> The gold standard serological tests are immunofluorescence antibody test or indirect immunoperoxidase assay<sup>[20]</sup> but are out of reach in our country owing to high costs. The Weil–Felix test (WFT) is the cheapest test presently available and extensively used in our country.<sup>[3,5-7,10]</sup> The WFT demonstrated low sensitivity<sup>[21]</sup> in diagnosing acute rickettsial infections and low specificity.<sup>[22,23]</sup> Therefore, the use of the WFT should be discouraged in the diagnosis of acute rickettsial infections. In the present study, we performed ELISA test for IgM antibodies against *O. tsutsugamushi* for diagnosis. This test has shown good sensitivity and specificity<sup>[3,20,24]</sup> and has been adequately

validated.<sup>[4]</sup> Since the ICT has given the considerable number of false positivity, so its result should be interpreted in conjunction with ELISA.

A comprehensive report of the findings was sent to the district health authorities. The district authorities in turn directed the local health centres to carry out extensive control measures through health education, insecticide spraying, prophylactic treatment and periodic survey in the affected area leading to containment of the outbreak.

All the patients, serologically diagnosed of having scrub typhus, and also the patients with clinical features strongly suggestive of scrub typhus, were advised doxycycline in the dosage of 100 mg twice a day for 10 days.

## CONCLUSIONS AND RECOMMENDATIONS

In conclusion, our study suggests that scrub typhus should be considered in the differential diagnosis of acute febrile illness associated with gastrointestinal symptoms, rash, myalgias including those with organ dysfunctions such as hepatorenal syndrome, coagulopathy or ARDS. Although eschar is pathognomonic of the disease, it may not be commonly seen, and its absence does not rule out scrub typhus. Delay in treatment may lead to complications and higher mortality. As patients respond to doxycycline or macrolides, empirical treatment with these antibiotics may be given in cases where there is a strong suspicion of scrub typhus. The findings of the study may also be used for better disaster preparedness.

It has been often observed that at the time of the rehabilitation of the disaster victims, the health authorities are usually more concerned about food- and water-borne diseases, but the present study established that in temporary living conditions, populations are more prone to mite bite; hence, it is recommended that while sitting around or camping, ground covers and tents with closed floors should be used. The people entering in the affected area should wear closed footwear, boots with socks and long trousers, exposed area of skin and clothing should be treated with mite repellents.<sup>[25]</sup>

In the end, what is needed is better awareness among not only the clinicians and the health authorities but also among the general public for better diagnosis and treatment of scrub typhus which has long been ignored as a potential public health problem in the event of disaster.

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### Conflicts of interest

There are no conflicts of interest.

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