



## Probing into the Recent Occurrence of Scrub Typhus Cases in and around Kolkata

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### Abstract

*Scrub typhus is endemic in India. Right now scrub typhus is enjoying its status as a re-emerging disease and is often causing trouble in diagnosis due to absence of specific rash or eschar. In our institution, we observed a seasonal rise of febrile illnesses that coincided with monsoon rain, and decided to investigate the probable etiological role of scrub typhus among the undiagnosed fever cases. This prospective study was conducted from the middle of May to the end of August in 2019. All febrile patients who tested negative for malaria, dengue, urinary tract infections, enteric fever and other pyogenic infections were included in this study. Those who became serologically reactive for Scrub typhus IgM antibody by ELISA were considered as established cases of scrub typhus. The seroprevalence of scrub typhus among undiagnosed fever cases was 33.9% with a resultant mortality of 11.8%. Fever (100%), headache (92%) and myalgia (62%) were the commonest symptoms followed by lymphadenopathy, vomiting, diarrhea, pain abdomen, rash and rarely eschar. Meningoencephalitis (12%) was the commonest complication followed by acute kidney injury which along with hepatitis often led to fatal multi organ failure. Thus, scrub typhus should be considered at the earliest in the differential diagnoses for acute undiagnosed fever with nonspecific features in endemic countries like ours.*

**Keywords:** *Scrub typhus, IgM ELISA, undiagnosed fever, non-specific features, meningoencephalitis.*

### Introduction

Scrub typhus is a well known zoonosis characterised by an acute febrile illness that can range from a self-limiting illness to fatal multi-organ failure. The disease is transmitted by bites of the 'chiggers', the larval stage of the trombiculid mite, which harbours the rickettsial pathogen – *Orientia tsutsugamushi*<sup>[1]</sup>.

This febrile illness is endemic in a wide zone of the renowned 'Tsutsugamushi triangle' bounded by Japan in the east, Pakistan in the west, Russia in the north and northern Australia in the south; thus covering China, Korea, Indonesia, Malaysia, India and the islands of western Pacific and Indian ocean. However, recent reports have enlisted occurrences of scrub typhus in several regions outside this

'infamous' triangle of rickettsial disease<sup>[2],[3]</sup>. India faced several outbreaks of scrub typhus since 1960s, the first reported cases being from Himachal Pradesh<sup>[1]</sup>. Later on, the disease "virtually disappeared" due to use of insecticides for vector control, changes in lifestyle and empirical treatment of pyrexia with chloramphenicol and tetracycline group of drugs. The apparent well controlled status of the disease was enjoyed until recently when the disease reemerged in several regions of India namely Himachal Pradesh, Tamilnadu, Kerala, Karnataka, Madhya Pradesh, Jammu and Kashmir, Bihar, West Bengal, Uttaranchal, Rajasthan and Meghalaya<sup>[1],[4]-[7]</sup>. West Bengal faced scrub typhus outbreak few years ago<sup>[8]</sup>. Still, there are less than required awareness about this potentially fatal zoonotic disease as aptly mentioned by WHO- "Scrub typhus is probably one of the most underdiagnosed and under-reported febrile illnesses requiring hospitalization"<sup>[1]</sup>.

In our institution, we have observed a seasonal rise of febrile illnesses coinciding with the monsoon rain who had negative laboratory reports for malaria, dengue, urinary tract infections and other pyogenic infections. Most of them presented with non-specific flu-like symptoms with development of fatal complications like meningitis or multi organ failure (MOF) in certain percentage of patients. There were varied response with empirical antibiotics like doxycycline or azithromycin. Keeping in mind the endemicity of scrub typhus, we suspected that a silent outbreak of scrub typhus is going on in this particular area. We intended to evaluate the seroprevalence of scrub typhus IgM antibody by ELISA method which is considered as one of the confirmatory tests to detect acute scrub typhus disease<sup>[4]</sup>.

### Materials and Methods

This prospective study was carried out from starting of May to the end of August, this year with rise in acute undiagnosed fever cases attending this tertiary care hospital catering primarily urban population. A detailed history taking and thorough clinical examination followed by laboratory screening was

done for detection of malaria parasites, dengue, Japanese encephalitis, enteric fever, urinary tract infection and other pyogenic infections. Serum from patients who were negative for all those etiology were further evaluated for scrub typhus serology. All the serum samples were aliquoted and stored at -20°C till further testing. Scrub typhus IgM antibody was detected by using Scrub Typhus IgM ELISA kit (InBios) following the manufacturer's guidelines. The absorbance was measured with primary filter at 450nm without any secondary filter. All the data were analysed methodically to determine statistical significance.

### Results

In the last three and half months, 251 patients presented with febrile illnesses. Out of them, 85 were serologically confirmed by scrub typhus IgM ELISA with a seroprevalence of 33.9%, having 53% males and 47% females among them. Among all the patients, 52% were from Kolkata whereas rest were mostly from semi-urban populations in the surrounding cities with scattered cases from some distal rural belts. (Table-1)

Fever and malaise for a duration of 5-14 days were the commonest findings found in majority of patients followed by headache, myalgia, lymphadenopathy, and gastrointestinal symptoms. Classical rash and eschar, the hallmarks of the disease, were rarely found, and till date we could not find any respiratory symptoms like cough or ARDS.(Table 2) Complications developed in 11 cases, with development of isolated meningoencephalitis in 3 cases. Multi organ failure occurred in 6 cases- presenting with any two of the followings- meningoencephalitis, acute kidney injury and hepatitis denoted by raised hepatic enzymes. Isolated fatal liver dysfunction was found in a solitary case. The overall mortality reached 11.8 % with CNS and renal involvement as the prime important prognostic markers.

**Table 1:** Demographic characteristics of the scrub typhus reactive patients with percentage (n=85)

Demographic characteristics	No. Of patients (%)
Regional distribution	
Kolkata	44(52)
Outside Kolkata	41 (48)
Gender	
Male	45 (53)
Female	40 (47)
Age Groups	
0-5yrs	4 (5)
6-18yrs	28(33)
19-45 yrs	33(39)
45-60 yrs	12 (14)
>60 yrs	8 (9)
Duration of illness	
<5 days	19 (22)
5-14 days	58 (68)
» 15 days	8 ( 9)

**Table 2:** Clinical presentations in Scrub typhus patients (n=85)

Clinical signs /symptoms	No. of patients (%)
Fever	85 (100)
Malaise	85 (100)
Headache	78 (92)
Myalgia	53 (62)
Lymphadenopathy	43 (50)
Rash	11 (13)
Eschar	1 (1.2)
Vomiting	49 (58)
Diarrhoea	30 (35)
Pain abdomen	20 (24)
Raised liver enzymes	7 (8)
Acute kidney injury	8 (9)
Seizures	10 (12)
Meningitis	10 (12)
Altered sensorium	10 (12)
Multi organ failure (MOF)	6 ( 7)

## Discussion

Scrub typhus can be designated as ‘today’s most important rickettsial disease, worldwide’, accounting for up to 23% of all febrile episodes, with an occurrence of estimated 1 million cases annually while over one billion people are at risk.<sup>[1],[2],[9]</sup> Scrub typhus is an important reemerging pathogen in India as proven by several outbreaks reports in the last 10 years from various states like Tamil Nadu (2001–2002), Pondicherry (2008) Meghalaya (2010), Himachal Pradesh (2011), Nagaland (2011)<sup>[8]</sup>. Indeed, it is the commonest rickettsial disease in the Indian

subcontinent. In West Bengal, scrub typhus is endemic in the sub-Himalayan belt by rendering a favorable habitat to the mite-vector due to abundance of bushy vegetation, tea gardens, grassy fields and forests with adjacent cleared outskirts. Regular outbreaks were reported from Kurseong and Mirik in Darjeeling district of West Bengal (2005, 2010-2012)<sup>[10]</sup>. Recently, scrub typhus cases were reported from urban areas, too. Studies have pointed out important role of rodents in transmission of urban scrub typhus as well as role of various recreational activities like jogging, doing yoga or playing in a park, thus increasing the possibilities of mite or chigger bites<sup>[11]</sup>. In this background it took us some time to convince our clinicians that scrub typhus may be an important differential diagnosis in cases attending this urban-based hospital with acute undiagnosed fever rapidly progressing to meningitis or fatal multi organ failure.

Starting from May, we observed a sharp rise of cases from the second half of June to the end of August, fairly coinciding with the monsoon rain. Similar seasonality of scrub typhus was observed by R Thomas and co-workers who commented that the increased humidity was favorable for hatching of mite eggs thus increasing the chances of chigger-bite<sup>[12]</sup>. In South India, disease-peak was used to be observed in rainy and cooler months of the year<sup>[4]</sup>. Li T et al in their study concluded that in a particular region, this seasonality was dependent on the climate, temperature and degree of rainfall in that very area<sup>[13]</sup>.

In our study, out of 85 confirmed cases, 53% were males and 47% females with a male preponderance of 1.1. GM Varghese and group found 48% males and 52% females in their study in South India<sup>[4]</sup>.

The majority of cases (52%) were clustered in various urban slums in the metropolitan city of Kolkata, whereas cases from suburban and rural areas cumulatively were 48%.

86% cases occurred in 6- 60 years of age group, indicating involvement of active young and adult population, 5% cases in under 5 children and 9% cases in the geriatric age group. The patient

population varied among the previous studies depending on the socio-demographical characteristics. A study from South India found mean age of patients 45 +/- 15 years<sup>[4]</sup>.

A diverse clinical spectrum was observed in our study. 92% of the febrile patients came with duration of illness between 5 days to 2 weeks. The common cluster of symptoms include fever, malaise, headache (92%), myalgia (62%), vomiting (58%), lymphadenopathy (50%) and diarrhoea (35%). Pain abdomen (24%) were commoner than rash (13%). Eschar was found rarely (1.2%). We have not seen cough or respiratory distress or development of ARDS in any of the cases. These findings were similar to that of other studies save respiratory involvement, for which they found cough and breathlessness in significant proportion of cases,<sup>[14],[15]</sup> and eschar in a variable but higher proportion of cases<sup>[16]</sup>.

Case fatality rate was approximately 12% in our study. Studies from south India found a declining trend of mortality- from 14% in 2002-2003 to 9% in 2014<sup>[4],[17]</sup>. Studies from northern India pointed out a similar declining trend from 17.2% in 2004 to 14% in 2006<sup>[5],[18]</sup>.

Serious complications like meningoencephalitis, acute kidney injury, hepatitis were not uncommon in our study. Fatal fulminant hepatitis occurred in 1.2% cases. Acute kidney injury was found in 9% cases which is lower than that observed by Attur et al<sup>[19]</sup>. Isolated meningoencephalitis occurred in 6% in our study with a 60% fatality which was significantly higher than the non-meningitis group (p-value less than 0.05). Other studies found that CNS involvement in scrub typhus has shown an extended spectrum of manifestations commonest being meningitis, meningoencephalitis or encephalitis<sup>[20]</sup>. Several studies in India pointed out the rate of occurrence of meningoencephalitis in scrub typhus in 23.3, 9.5 and 14 percent of cases<sup>[4],[5],[15]</sup>. Varghese et al. observed multi organ failure in a very high proportion – 34% of cases and pulmonary dysfunction as the commonest complication (33.4%) followed by acute renal failure (18%). They found a significantly higher

mortality rate of 25% among the multi-organ failure group in comparison to that of 7% in patients without MOF<sup>[4]</sup>. On the other hand, we found only 7% of cases with MOF, but the relative mortality due to MOF was a striking 83% which means MOF is a significant prognostic marker with a p-value of less than 0.05.

### Conclusions

Scrub typhus should be considered as a potentially fatal cause of acute febrile illnesses presenting with non-specific symptoms like fever, headache, myalgia and lymphadenopathy. GI symptoms like nausea, vomiting, diarrhoea, may be present in a fair number of cases. In endemic tropical countries like India, the eschar may not be present or even pass unnoticed. Similarly, rashes may be inconspicuous in dark skinned people if not absent.

Febrile illness that leads to newly onset seizures or altered sensorium or acute encephalitis syndrome may have scrub encephalitis. So, in all non-JE AES cases the possible role of scrub typhus should also be ruled out by ELISA or other confirmatory tests. As it is a potentially fatal disease which rapidly turns into complications like multi-organ failure, high degree of clinical suspicion followed by laboratory confirmation may lead to significant reduction in mortality and morbidity from this disease.

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