

Original Research Article

Scrub typhus: a hospital-based study in the northern districts of West Bengal, India

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ABSTRACT

Background: Scrub typhus caused by *Orientia tsutsugamushi*, is a mite-borne zoonotic acute febrile illness. Geographically, it is confined to the Asia-Pacific region and important re-emerging infection in India. Clinical diagnosis of scrub typhus from other acute febrile illness is very difficult due to nonspecific symptoms and the relative absence of eschar in the Indian population. Case fatality rate varies from 30-70% depending on the clinical suspicion, delay in diagnosis and treatment. Antibody-based serological tests are the mainstay of diagnosis. IgM enzyme-linked immunosorbent assay (ELISA) against *O. tsutsugamushi* is helpful for the diagnosis of scrub typhus within the first week of illness.

Methods: The aim of the study was to determine the prevalence of the disease in Northern districts of West Bengal, India using IgM ELISA.

Results: Out of 577 serum samples tested 10.05% were positive for IgM antibodies. Majority of cases were below 40 years of age with higher prevalence in female patients. The disease showed a seasonal trend with a peak during the monsoon and later months. The case fatality rate among ELISA positive cases was 32.76%.

Conclusions: Significant seropositivity against scrub typhus among cases of acute febrile illness with relatively higher mortality indicates that scrub typhus should be included in the differential diagnosis and confirmed by IgM ELISA.

Keywords: IgM ELISA, *O. tsutsugamushi*, Scrub typhus, West Bengal, Zoonosis

INTRODUCTION

Scrub typhus is an important public health problem in the 'Tsutsugamushi triangle' extending from Japan to Russia in the north, to Australia in the south, and Pakistan in the west. It is a re-emerging disease in India. Epidemic outbreaks of scrub typhus were reported from the sub-Himalayan belt, extending from Jammu to Nagaland and from Tamil Nadu, Pondicherry, and Chennai, India.¹⁻³

Scrub typhus, also known as tsutsugamushi disease, is caused by the arthropod-borne gram-negative obligate intracellular bacillus *Orientia tsutsugamushi*.⁴ Wild rats of subgenus *Rattus* are the natural hosts for the vector, a

Leptotrombidium mite. Approximately 5 to 14 days after an infected vector bite, patients begin to show manifestations of infection. They present with non-specific flu-like symptoms, fever, rash, and eschar at the site of the bite, headache, myalgia, cough, generalized lymphadenopathy, nausea, vomiting, and abdominal pain. Patients often present with pyrexia of unknown origin of varying severity.⁵⁻⁷ An eschar at the site of chigger bite is a classical feature of scrub typhus. It begins as a papule at the site of the bite and following ulceration, forms a black crust with an erythematous border. When present, it appears before the onset of fever and other symptoms.^{6,8} Though, the pathognomonic sign of scrub typhus, the presence of eschar varies from 7%-80% of patients

depending on the geographic areas and studies. It is more easily found on Caucasian and East Asian patients than on dark-skinned South Asian patients.⁸⁻¹⁰ Severe multi-organ manifestations include hepatitis, acute renal failure, pneumonitis, acute respiratory distress syndrome (ARDS), myocarditis, septic shock, acute meningitis and meningoencephalitis, pericarditis, and disseminated intravascular coagulation (DIC) may occur in a varying proportion of patients.^{6,7,10} Central nervous system involvement is often the predominant clinical manifestation in scrub typhus infection, and 12.5-26% of patients present with acute meningitis or meningoencephalitis.^{11,12} Absence of eschar or presence of nonspecific symptoms and low index of suspicion, leads to the delayed diagnosis. Though treatment is affordable and often successful with dramatic response to doxycycline, the case fatality varies between 30-70% in untreated cases.^{13,14} Therefore, early diagnosis is very essential to start treatment and prevent complications. There are several tests available for diagnosis of scrub typhus. Weil-Felix test is the cheapest and readily available, but results are unreliable due to low sensitivity. Indirect immunofluorescence antibody test is the gold standard, but not cost effective for resource-limited countries and needs expertise for preparation and interpretation. Cell culture or molecular detection using polymerase chain reaction is possible, but they are not readily available and not routinely used for diagnosis. IgM ELISA is quite satisfactory in comparison to the gold standard. In primary infection, a significant IgM antibodies titer is observed at the end of the 1st week and IgG antibodies appear at the end of 2nd week. In the case of re-infection IgG antibodies are detected by the end of the 1st week with variable IgM antibody titer.^{15,16} The study was conducted to know the prevalence of scrub typhus infection among febrile patients in a tertiary care hospital using IgM ELISA and assess clinical feature and outcome of serologically positive patients in the northern part of West Bengal, India.

METHODS

The study was conducted in the department of microbiology, North Bengal medical college, West Bengal, India. As a rural tertiary care hospital in the Northern part of West Bengal, it caters the needs of patients from all the seven districts of this region and also from neighboring states of Bihar, Assam, and Sikkim as well as Bangladesh, Bhutan, Nepal. The northern part of West Bengal is one of the humid regions of the Himalaya with the highest rainfall of about 3000mm. The Climate varies between the tropical heat of the valleys and alpine cold of the snowy regions with a mean annual range of temperature of 10-degree centigrade.

Study technique

A total of 577 consecutive, non-repetitive serum samples of both sexes and all the ages were collected from the

patient with acute febrile illness from January 2016 to December 2018. Under aseptic measures, about 5ml of blood was collected in a sterile vial. The vial was left at room temperature and the blood was allowed to clot for separation of serum. The serum was then further separated by centrifuging (REMI-R-24) the blood at 3000 rpm for 8 min. Scrub typhus specific IgM antibody was detected using Scrub typhus detect TM IgM ELISA, In Bios International, Inc, Seattle, WA 98104, USA. Detail history, treatment and, outcome of positive cases was done retrospectively.

Statistical analysis

Data were compiled in MS excel sheet and analysis was done.

RESULTS

During the study period, a total of 577 serum samples were collected for detection of *O. tsutsugamushi* specific IgM antibodies by ELISA. Of these, 58 (10.05%) tested positive for IgM antibodies against *O. tsutsugamushi*. Year wise distribution of scrub typhus positive cases over the study period is shown in (Table 1).

Table 1: Trend of scrub typhus positivity during the study period (2016-2018) (N=577).

Year	Total cases examined	No. of positive cases	Percentage
2016	182	13	7.14
2017	207	22	10.63
2018	188	23	12.23
Total	577	58	10.05

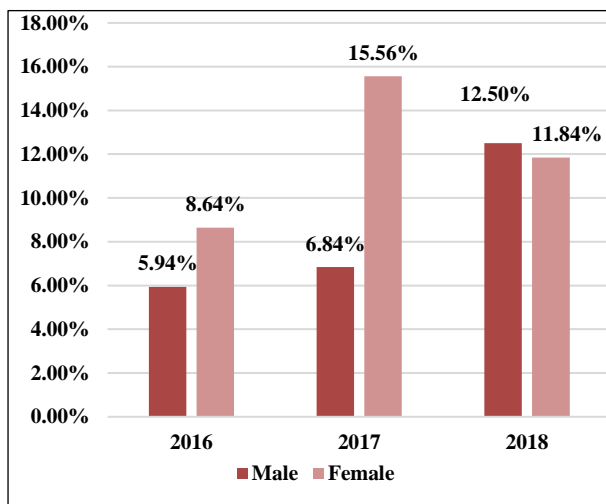
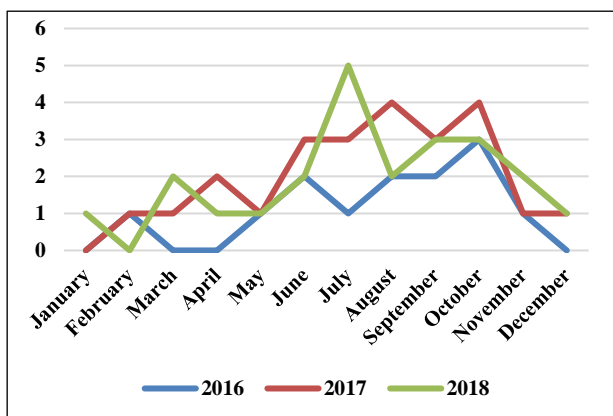
Majority of cases were below 40 years of age (Table 2). The number of adult male and adult female positive patients were 8.5% (28/330) and 12.15% (30/247) (Table 3 and Figure 1). The number of positive cases increased from June to October. Thereafter, both the number of samples and positive test results gradually decreased. This showed a seasonal trend of the disease in the monsoon and later months, as shown in (Figure 2). A retrospective analysis of the clinical presentation of serologically positive patients found that a prolonged fever with a mean duration of 10.5 days was the predominant symptoms. The eschar, though a characteristic of scrub typhus was detectable in only 13.3% of patients. Other clinical findings included hepatomegaly and lymphadenopathy. 68.7% had complications such as acute respiratory distress syndrome, hypotension, and acute kidney injury or presented with features of acute meningitis or acute meningoencephalitis like headache, loss of sensorium, seizure with meningeal signs in varying combinations.

Table 2: Age-wise distribution of study population and scrub typhus IgM positive cases (N =577).

Age (Years)	2016	2017	2018	Total no. of scrub typhus IgM positive	Percentage
<10	2 (65)	8 (80)	4 (50)	14 (195)	7.18
11-20	3 (38)	5 (50)	5 (29)	13 (117)	11.11
21-40	4 (37)	3 (39)	8 (45)	15 (121)	12.4
41-60	2 (29)	5 (32)	4 (53)	11 (114)	9.65
>60	2 (13)	1 (6)	2 (11)	5 (30)	16.67

Table 3: Year-wise scrub typhus positivity among male and female.

Year	Total case examined	Total no. of scrub typhus IgM positive		Percentage	
		Male	Female	Male	Female
2016	182	6 (101)	7 (81)	5.94	8.64
2017	207	8 (117)	14(90)	6.84	15.56
2018	188	14 (112)	9 (76)	12.5	11.84
Total	577	28 (330)	30 (247)	8.5	12.15

**Figure 1: Sex-wise distribution of scrub typhus positive cases (n= 58).****Figure 2: Seasonal trends of scrub typhus positive cases (2016-2018) (n=58).**

During the course of the study, 19 patients expired (32.76%). All other serologically positive patient was treated with doxycycline and showed remarkable improvement.

DISCUSSION

Rickettsial diseases are re-emerging in the Indian subcontinent, with a more varied geographical distribution. Scrub typhus, despite being a common rickettsial disease in India, is one of the neglected zoonosis of public health importance. It affects a large part of North and East India (Kashmir, Himachal Pradesh, Assam and Sikkim) and some parts of South India (Eastern and the Western Ghats) and considered re-emerging in the eastern and southern part.

Despite an endemic zone, there has been no previous significant report on scrub typhus in the northern region of West Bengal, India.

Scrub typhus, as a common entity in the tropics, should be suspected in patients from endemic areas with a high risk of environmental exposure and acute febrile illness. The prevalence of scrub typhus cases was 10.05% in present study, similar to other studies from India.^{17,18} However, Takhar RP et al, and Sinha P et al, showed a higher prevalence in their studies.^{19,20} Most of the patients in present study were between 11-40 years of age. It was also found that scrub typhus positivity is highest among female. Sinha P et al, and Medi D et al, also showed similar age and sex distribution.^{20,21} People with more outdoors activities have more chance of chigger bite. The men in these regions usually migrate to nearby cities for work. Women look after the agricultural work and working in the tea garden for plucking tea leaf. Hence, they have more chance of contact with the vector and

chigger bite. The disease is more prevalent in the cooler months that coincide with increased in scrub vegetation and favors the growth of vector. Mathai E et al, reported an increase in scrub typhus cases during the cooler months and the same has been reported in international studies also.^{22,23} This phenomenon was also observed in present study where the majority of cases were after the monsoon leading to winter.

Most of the patients in present study presented with persistent high-grade fever with other non-specific symptoms and eschar were not present in all cases (13.3%). Takhar RP et al, showed the prevalence of eschar was 12.1%, whereas Mathai E et al, reported the presence of rash in 22% of cases and Chrispal A et al, reported a 45.5 % prevalence of eschar in their study.^{19,22,24}

Scrub typhus is a multi-organ dysfunction syndrome. About 68.7% of our patients presented with multiple organ involvement during the course of treatment and complications usually develop within the first week of illness. Takhar RP et al, showed similar multi-organ system involvement and Narvencar KP et al, found hepatic dysfunction, respiratory distress, circulatory collapse, and acute renal failure were very common.^{19,25}

Patient outcomes in present study were favorable with the regimen of doxycycline. The outcome depends on the circulatory load of *O. tsutsugamushi*, early or late presentation and treatment modality. High mortality is mainly due to delayed presentation or diagnosis and organ dysfunction.²⁶ Mortality rate of 32.76% in present study was quite similar to Lai CH et al, (15-30%) and Griffith M et al, while slightly higher compared to other studies from India by Mahajan SK et al, (14.2%) and Rungta N et al.²⁷⁻³⁰

Diagnosis of scrub typhus is quite difficult in India due to its non-specific clinical presentation, the absence of eschar in a large number of patients and lack of availability of specific tests. A high index of suspicion and careful clinical, laboratory and epidemiological evaluation is an essential tool for early diagnosis of scrub typhus in resource-limited countries like India.

CONCLUSION

Scrub typhus is very much prevalent in both southern and northern districts of West Bengal, India. The study points toward the definite possibility of the existence of many other undiagnosed cases in these locations, previously unknown for scrub typhus, and highlights the necessity for increased sensitivity among the physicians for suspecting scrub typhus. It should be considered in the differential diagnosis of patients with acute febrile illnesses, including those presenting with acute meningitis or meningoencephalitis or multi-organ dysfunction. A careful search for an eschar, particularly in the hidden areas is very useful for diagnosis, though it

may not be present in many cases. Empirical therapy with Doxycycline may be lifesaving when clinical suspicion is high.

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