Indian J Med Res 153, April 2021, pp 503-507
DOI: 10.4103/ijmr.IJMR_1223_19

Quick Response Code:

First seroprevalence report of scrub typhus from the tribal belts of the Nilgiris district, Tamil Nadu, India

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***Background & objectives*: Scrub typhus, an acute febrile Rickettsial disease is caused by the bacterial pathogen *Orientia tsutsugamushi* which is spread by the bite of infected chigger mite vectors belonging to the family Trombiculidae. A study was undertaken to find out the prevalence of scrub typhus among the indigenous population from Nilgiris, Tamil Nadu.**

***Methods*: This study was conducted among 214 patients with fever of unknown aetiology and a recent history of febrile illness attending the Nilgiris Adivasi Welfare Association medical facilities available at Nilgiris district, Tamil Nadu. Serum samples were tested for scrub typhus IgM enzyme-linked immunosorbent assay.**

***Results*: Overall, 13 (6.07%) of the 214 samples tested were positive for scrub typhus. This is the first seroprevalence report of scrub typhus from the indigenous people belonging to *Irula*, *Kurumba*, *Paniyar*, and *Kota* tribes from the Nilgiris district, Tamil Nadu.**

***Interpretation & conclusions*: Early diagnosis and effective management will protect this indigenous population from this disease. This report would help in creating awareness regarding scrub typhus infection among clinicians and public health authorities in the region and take appropriate measures for treatment and control.**

Key words Enzyme-linked immunosorbent assay - first report - scrub typhus - the Nilgiris district - tribals

Scrub typhus (ST) is an emerging vector-borne zoonotic infectious disease spread by *Orientia tsutsugamushi* and transmitted through infected trombiculid chigger mite vectors[1]. About one billion people are estimated to be at the risk of contracting scrub typhus each year and an estimated one million people are affected every year with this disease[2]. Mortality rates in untreated patients range from 0 to 30 per cent depending on the geographic area, Orientia strain and the time of intervention[3]. The spread of scrub typhus closely follows the distribution pattern of rodent species *Rattus rattus*. The endemic region is usually known as the 'tsutsugamushi triangle' and has an area of about 13 million km^2 this area spans across northern Japan and far-eastern Russia in the north, the geographic area around the Solomon Sea, into northern Australia in the south and Pakistan and Afghanistan in the west[4]. In India, there are reports of a resurgence of ST from northern, north-eastern, western and southern States[5]. The cases of ST in Tamil

Nadu have been reported from Vellore, Thirupattur, Thiruvannamalai, Dharmapuri and Krishnagiri by the Institute of Vector Control and Zoonoses, Hosur and Christian Medical College, Vellore[3,6]. This disease is under-diagnosed in India due to its non-specific clinical presentation, limited awareness among clinicians and lack of diagnostic facilities[7]. This cross-sectional study to detect ST among patients presenting with fever was hence undertaken in the Nilgiris district, Tamil Nadu as no report on ST from this area in the Western Ghats is available to date.

Material & Methods

The Nilgiri hills have an elevation of 900-2636 meters above the mean sea level. Its topography is rolling and steep, and the cultivable land falls under the slopes[8]. It has an area of 2452.50 km^2 with a population of 762,000. Dams have been constructed wherever possible to harness natural springs. During summer, the temperature varies between 10°C and 25°C, and during winter from 2°C to 21°C.

This is a cross-sectional observational study was conducted in the Nilgiris district between October 2014 and March 2016 among the patients with fever of acute undifferentiated febrile illness of unknown aetiology and recent history of febrile illness attending the Nilgiris Adivasi Welfare Association (NAWA) health care institutions at Nilgiris district in Tamil Nadu, India. This study was approved by the Institutional Human Ethics Committee of ICMR-Centre for Research in Medical Entomology (CRME), Madurai. Patients with the acute undifferentiated illness of more than one week attending the aforementioned NAWA health facility were included in this study. Patients with immunodeficiency (HIV/AIDS), and malignancies were not included in this study and neither were patients with fever of more than 4 weeks.

The medical officers from the NAWA healthcare institutions of Nilgiris district assisted in the clinical examination and collection of blood samples. Patient consent was obtained before collection of samples and the serum samples drawn were screened for IgM against *O. tsutsugamushi* using enzyme-linked immunosorbent assay (ELISA) kits (Scrub Typhus Detect; Detect™ IgM ELISA, InBios International, Inc., WA, USA). This is a qualitative ELISA for the detection of IgM antibodies in human serum to *O. tsutsugamushi*-derived recombinant antigen. An optical density value of >0.5 indicated IgM positivity[9].

A total of 214 sera samples were tested for IgM antibodies against ST infection as per the manufacturer's specifications. A pre-designed pro forma was used for patient data collection and analyzed using Epi Info™ ver. 7.2.3.1 (CDC, Atlanta, USA)[10]. Due to limited sample size Chi-square test and odds ratio (OR) were used for statistical analysis. The study sites are shown in Figure using software Epi Map of Epi Info™ ver. 7.2.3.1 (CDC, Atlanta, USA).

Results & Discussion

Two hundred and fourteen serum samples were drawn from fever-affected people (suspected ST cases) and were tested for *O. tsutsugamushi* infection using IgM ELISA (Table I). IgM ELISA is easy to perform test and a sensitive and specific test for ST which does not need trained personal and specific instrument like a fluorescent microscope as required in immunofluorescence assay test[11]. Overall, 13 (6.07%) of the 214 samples tested were positive for ST. The percentage of samples positive among males (n=55) and females (n=159) were 5.45 and 6.29 per cent, respectively. The percentage serum positivity was 12.20, 10.26, 4.76 and 1.41 from Gudalur, Coonoor, Kotagiri and Ooty, respectively (Figure). No positives in males were reported from Kotagiri and Ooty. The year-wise variations of ST IgM positivity varied among blocks. Gudalur and Kotagiri showed more during the two years cause of the study. The youngest ST patient was a 21 yr old female and the oldest was a 65 yr old man. The mean age was 44.62±15.1247 (mean±SD; range 21-65 yr). The most common clinical symptoms observed among the 13 confirmed ST patients were fever for one to three weeks (100%) and myalgia (100%). Other symptoms included cough (69%), headache (38.5%) and eschar (7.7%). Only one ST case had the characteristic eschar in the leg. One serum sample screened by IgM ELISA showed visible (>3 OD) value and the sample was represented from Kota tribe with fever for two weeks.

Based on rainfall, the survey months were classified into two seasonal groups as rainfall and dry season months. Rainfall season months were June (south-west monsoon rainfall) and October (north-east monsoon rainfall). Dry season months were December (cool-dry). February (cool-dry), and March (hot-dry). Positivity was more in dry months (8.62%) than in the rainy months (5.40%), but there was no seasonal difference (χ^2=0.3934, df-2, P<0.05), OR-0.573 (95% confidence interval was 0.1795-1.829)

Table I. Gender wise scrub typhus (ST) IgM positives reported in the Nilgiris district (2014-2016)

Block	Male			Female			Total		
	Number of sera tested	Number positive	Per cent positive	Number of sera tested	Number positive	Per cent positive	Number of sera tested	Number positive	Per cent positive
Kotagiri	19	0	0.00	44	3	6.82	63	3	4.76
Coonoor	8	1	12.50	31	3	9.68	39	4	10.26
Ooty	12	0	0.00	59	1	1.69	71	1	1.41
Gudalur	16	2	12.50	25	3	12.00	41	5	12.20
Total	55	3	5.45	159	10	6.29	214	13	6.07

and most of the cases were reported during December 2014 (18.52%). No positive case was recorded in February 2015 and March 2016 (Table II). There was a significant difference in the positivity among the months surveyed (χ^2=34.2315, df-5, P<0.05).

This study reported the detection of ST from the indigenous people belonging to Irula, Kurumba, Paniyar and Kota tribes from Nilgiris district, Tamil Nadu (Table III). Tribe Kota was found affected only during the first year of the study (2014-2015) with a significant difference in positivity of χ^2=12.5582, df-6, P<0.05. These blocks were Kothagiri, Coonoor, Ooty and Gudalur. There was a significant difference among the blocks for serum positivity (χ^2= 29.065, df-3, P>0.05).

Un-surveyed places like Nilgiris district, which were previously assumed to be non-endemic areas have started to show *O. tsutsugamushi* activity. ST was not usually diagnosed here due to the low level of clinical signs and symptoms, and the non-availability of proper

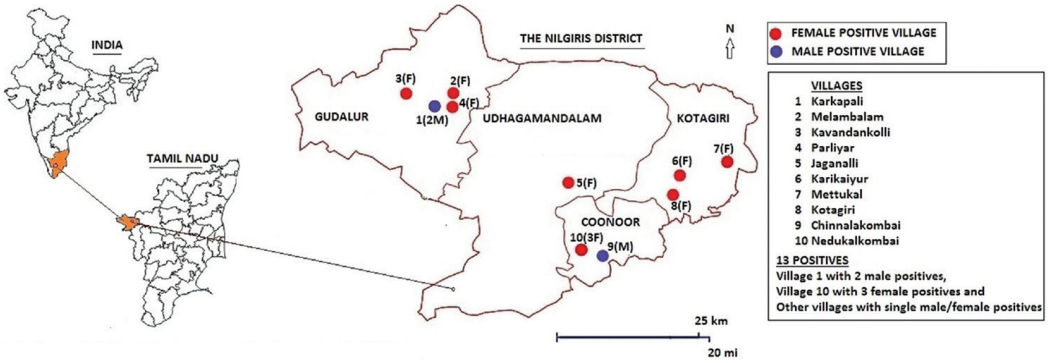

Figure. Study sites in the Nilgiris district, Tamil Nadu. *Source*: *https://www.cdc.gov › epiinfo*. Map generated in English (US) 7.2.3.1 version of EPI INFO TM Website (CDC, Atlanta, USA)

Table II. Scrub typhus IgM positive cases detected in Nilgiris district (2014-2016)

Month	Season	Total number of samples	Number positive	Per cent positive
October 2014	Rainy (N.E. monsoon)	75	3	4.00
December 2014	Dry (winter)	27	5	18.52
February 2015	Dry (winter)	27	0	0.00
June 2015	Rainy (S.W. monsoon)	55	4	7.27
October 2015	Rainy (N.E. monsoon)	26	1	3.85
March 2016	Dry (summer)	4	0	0.00
Total		214	13	6.07

S.W. monsoon, south west monsoon; N. E. monsoon, northeast monsoon

Table III. IgM positive ST cases detected among different group present in Nilgiris district (2014-2016)

Tribe	Total number of serum	Number positive	Per cent of positive
Irula	91	4	4.40
Kurumba	39	4	10.26
Kota	19	1	5.26
Toda	27	0	0.00
Kattu Naikar	4	0	0.00
Paniyar	33	4	12.12
SC community	1	0	0.00
Grand total	214	13	6.07

assays[12]. However, the failure of timely diagnosis of scrub typhus might lead to significant morbidity and mortality[9,13]. Treatment part of this disease is easy, by administering antimicrobials if diagnosed timely. Surveillance is therefore essential in such areas. Several studies have been undertaken to find out the prevalence of scrub typhus from South India, especially from Tamil Nadu and Pondicherry[14-16].

The diagnosis of acute ST requires a demonstration of the IgM antibody positivity to *O. tsutsugamushi*[17,18]. The ST prevalence rate varied from 8 to 60 per cent in different countries[19]. In this study, the overall seroprevalence of ST was 6.07 per cent in Nilgiris district, Tamil Nadu which is much less than all the other places studied from Krishnagiri[20], (31%), Vellore[21] (47.5%, Tamil Nadu, Pondicherry[15] (72%); Tirupati[22] (58.21%), Andhra Pradesh[23] (39%); Arunachal Pradesh[24] (40.3%); Delhi[25] (42.6%); Uttarakhand region[26] (59.5%) and Deoria and Gorakhpur district Uttar Pradesh[27] (18.9%). This is to note that, in many parts of the country, a sudden increases in ST cases are being reported.

Regarding the seasonal ST prevalence in India, it occurs during monsoon seasons. The rainy season is always favourable for the development of grassland where the proliferation of vectors takes place with an inevitable contact with the human host[4,28]. More cases were reported during December and thus cool months are favourable for ST infection in the Nilgiris area. In South India, particularly in Tamil Nadu and Pondicherry, the monsoon starts in October and ends in February, however more ST cases were reported from August to October each year from Uttarakhand region[26].

The present study documents the detection of ST and provides evidence on its occurrence in and around in the Nilgiris region of Tamil Nadu. This is the first seroprevalence report of ST from the indigenous people belonging to Irula, Kurumba, Paniyar and Kota. In this hilly district, due to deforestation, this area is under the risk of spreading this infection to nearby places cultivated. Inter-sectoral, co-ordinated and well-defined control efforts should hence be undertaken in this ST vulnerable area to save the unaffected and susceptible groups of the population against this disease.

Risk factor analysis undertaken in Gorakhpur, Uttar Pradesh, has suggested that the constant exposure of these people to the natural environment (going out for defecating playing outdoor games, undertaking agricultural work) is the reason for contact with the chigger mites[27].

Due to the varied clinical presentation, absence of eschar in many patients and lack of availability of specific serological tests, ST diagnosis is and often delayed leading to fatality in India[11]. Otherwise, the treatment schedule is simple, with doxycycline as the drug of choice. Early diagnosis and subsequent control strategies in these areas can reduce mortality. Active surveillance should be undertaken in these areas to understand the magnitude of this re-emerging neglected tropical disease[28]. Due to the prevalence of ST from this area, the need for its consideration in the differential diagnosis is to be emphasized. Differential diagnosis fever of unknown origin along with dengue, malaria, and leptospirosis should be routinely undertaken for the confirmation of ST which are the other common endemic infections in these areas and control of ST should be focused on public education, rodent/shrew control, and habitat modification. Additional prospective studies are also required with molecular tools and vector surveys to confirm the findings.

***Financial support & sponsorship*:** This work was supported by the ICMR-CRME intramural research grant.

***Conflicts of Interest*:** None.

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