

Correspondence

Scrub typhus in hilly regions of north east India

Sir,

Scrub typhus (ST) belongs to a group of Rickettsial diseases caused by an obligate intracellular Gram-negative bacterium - *Orientia tsutsugamushi*. The bacterium is maintained in trombiculid mites through transovarial and transstadial transmission. Humans acquire the infection from the bite of infected larval stage of trombiculid mites, known as chiggers. Clinical spectrum varies from remaining asymptomatic to severely fatal. This disease is also known as tsutsugamushi disease (from *tsutsuga* meaning dangerous and *mushi* meaning insect or mite) and is endemic to a part of the world known as the tsutsugamushi triangle^{1,2}. In India, ST is considered as a re-emerging infectious disease³. The first ST infection in the country was reported from the States of Assam and West Bengal during the Second World War⁴. Outbreaks of ST have been reported in Himachal Pradesh, Sikkim, West Bengal, Puducherry, Uttarakhand and north-western part of the country¹. During 2010-2011, resurgence of ST was reported in Assam after a gap of 65 years, since its maiden report⁵. Thereafter, sporadic cases of ST in the State of Assam as well as from its neighbouring States have been reported⁶⁻⁹. Here we document the serosurveillance carried out in the States of Nagaland and Meghalaya demonstrating the wide presence of antibodies against ST in these regions.

During October 2013 - February 2014, serosurveillance was carried out by Regional Medical Research Centre (RMRC), Dibrugarh team. In certain areas of these States from where the ST cases were reported. Blood samples (3 ml) were collected from healthy individuals who were asymptomatic (absence of fever lasting for 5 days or more, absence of eschar,

rash, headache, acute respiratory disorders, *etc.*) at the time of collection from residential areas of positive case reporting areas of Phek district and West Garo Hill district of Nagaland and Meghalaya, respectively. Written informed consent was obtained from the participants of the study prior to collection. Samples were collected from individuals who voluntarily agreed to participate in the study. A total of 295 blood samples were collected; 145 samples were collected from Nagaland and 150 from Meghalaya. This study was approved by the institutional ethics committee of RMRC, Dibrugarh.

Serum samples were screened for presence of antibodies against *O. tsutsugamushi* recombinant proteins Gilliam, Karp and Kato - r56 antigens with a four step indirect ELISA assay^{10,11}. These recombinant antigens were procured from Naval Medical Research Center, Maryland, USA. The test was performed as described earlier^{10,11}. An optical density (OD) of ≥ 0.5 was considered as positive at 1:100 sample dilution. A positive result is defined as detecting a net absorbance of the sample greater than the mean of three negative control serum samples plus three times their standard deviation. Positive samples were further titrated at four-fold dilutions of 1:100, 1:400, 1:1600 and 1:6400. Samples with a total absorbance of ≥ 1.000 were considered as positive. Titres were determined as the inverse of the highest dilution with a net absorbance of ≥ 0.200 .

Overall, 45.1 per cent (133/295) samples had antibodies against *O. tsutsugamushi*. Titration results showed 48.1 per cent (64/133) positivity in 1:100; 3 per cent (4/133) in 1:400; 11.2 per cent (15/133) in 1:1600 and 37.5 per cent (50/133) in 1:6400 dilutions. Demographic characteristic showed both male and

Table. Seropositivity of scrub typhus among tested samples

States	Age groups (yr)	No. of sample tested			No. (%) of positive samples		
		Male	Female	Total	Male	Female	Total
Nagaland	0-20	14	6	20	2 (14.3)	1 (16.7)	3 (15)
	21-40	25	37	62	4 (16)	9 (24.3)	13 (20.9)
	41-60	14	16	30	10 (71.4)	10 (62.5)	20 (66.7)
	≥61	19	14	33	9 (47.3)	8 (57.1)	17 (51.5)
	Total	72	73	145	25	28	53
Meghalaya	0-20	37	43	80	18 (48.6)	20 (46.5)	38 (47.5)
	21-40	18	30	48	12 (66.7)	14 (46.7)	26 (54.2)
	41-60	4	15	19	4 (100)	10 (66.7)	14 (73.7)
	≥ 61	2	1	3	1 (50)	1 (100)	2 (66.7)
	Total	61	89	150	35	45	80

female to be almost equally affected in Nagaland, whereas in Meghalaya, female cases had preponderance over males in the ratio of 45:35 (Table).

Hospital based studies have shown a wide prevalence of ST from north western to southern part of India ranging from 8.8 per cent in the south to 59.6 per cent in the north^{12,13}. However, hospital based studies might not be a valid assessment of prevalence of ST in the community. Our study demonstrated 36.55 per cent (53/145) and 53.33 per cent (80/150) seropositivity in the States of Nagaland and Meghalaya, respectively. The ELISA assay used in this study has been proved to be highly specific and sensitive when compared to other whole cell and single recombinant antigen ELISAs¹¹. None of the positive cases had clinical symptoms of the disease. Not much difference in age, gender, ecosystem between seropositive and seronegative people was noted. Moreover, both seropositive and seronegative individuals had equal exposure to the risk factors.

It was observed that the seropositive individuals belonged to the physically active group involved in outdoor activities such as farming and agriculture. Granaries and rat burrows were found to be common in majority of the human dwellings. Moreover, north east India is highly vulnerable to climate change with a visible bearing on agriculture and forest sectors¹⁴. High prevalence of ST has been shown to be associated with changes in climate¹⁵. The emergence of ST may

possibly be associated with this climate change that potentially provides a suitable niche for rickettsial vectors *viz.* mites, fleas, ticks, *etc.* to proliferate and dissipate the rickettsial infection.

In our study eschars, the typical characteristic sign of ST, were not noted in seropositive individuals. This easily treatable disease can be fatal if undiagnosed/misdiagnosed and left untreated. Thus, for effective management of the disease, proper surveillance of epidemiological parameters and studies on the probable vectors is necessary. There is a need for health awareness programmes among the public in these endemic areas through which the local populace can be alerted to take personnel protection measures from insect bites. By adopting a good hygiene practice and sanitation for maintaining a clean living environment, getting rid of rodent habitats around the houses can significantly reduce the impact of scrub typhus.

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**Siraj A. Khan^{1*}, Vinotsole Khamo²,
Helen J. Uriah³, Trishna Bora¹ &
Prafulla Dutta¹**

¹Entomology and Filariasis Division,
Arbovirology Group, Regional Medical Research
Centre (ICMR), N.E. Region,
Dibrugarh 786 001, Assam

²Department of Pathology &
Healthcare Laboratory & Research Centre,
Naga Hospital Authority, Kohima 797 001,
Nagaland & ³Integrated Disease Surveillance
Programme Office, West Jaintia Hills 793 150,
Meghalaya, India

*For correspondence:
sirajkhanicmr@gmail.com

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