

## Seroprevalence of Scrub Typhus in a Tertiary Care Hospital of Upper Assam

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### ABSTRACT

**Introduction:** Scrub typhus is an acute febrile infectious illness caused by *Orientia tsutsugamushi*, transmitted to humans by the bite of the larva of trombiculid mites. The study was undertaken to know the seroprevalence of Scrub typhus among clinically suspected cases and its association with different parameters like age, gender, geographical location, season etc.

**Methods:** This prospective cross-sectional hospital based study was carried out on consecutive non repetitive clinically suspected cases satisfying the case definition as per DHR-ICMR guideline attending Assam Medical College & Hospital during the study period of March 2014 to February 2016. Serum samples were tested for Scrub typhus IgM antibodies by ELISA method.

**Results:** A total of 802 no of cases were included in the study. Of them 124 (15.46 %) were positive for Scrub typhus. Cases were presented with fever, headache, myalgia, nausea and vomiting, joint pain, seizure, altered mental status, unconsciousness, retro-orbital pain, lymphadenopathy, maculo-papular rash etc. Eschar was seen in two patients. Hepatosplenomegaly was observed in 13.71% patients. The study showed no significant association of the disease with the age and sex of the patient ( $p>0.05$ ). Most of the cases were found in June- February. 90.32 % cases were reported from

rural area and the association was statistically significant. ( $p<0.001$ )

**Conclusion:** It is recommended to include Scrub typhus in the differential diagnosis of acute febrile illness in this region which will help in proper diagnosis, timely and adequate treatment and avoidance of the complications and mortality.

**Key words:** Eschar, Lymphadenopathy, *Orientia tsutsugamushi*, Scrub typhus.

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### INTRODUCTION

Scrub typhus is an acute febrile infectious illness also known as tsutsugamushi disease, caused by *Orientia tsutsugamushi* [Japanese word tsutsuga (“dangerous”), mushi (“bug”)], which is a small Gram-negative, obligate intracellular organism. It is transmitted to humans by the bite of the larva of trombiculid mites (chiggers) which are almost microscopic, often red colored. Infected chiggers are found particularly in areas of heavy scrub vegetation during the wet season, (therefore this disease has also been called river/flood fever)<sup>1</sup> when mites lay eggs<sup>2</sup> usually June through November<sup>3</sup>. Scrub typhus is endemic to a part of the world known as the “tsutsugamushi triangle.” This extends from Japan, Taiwan, China, South Korea, Nepal, Northern Pakistan, Papua New Guinea and the Australian states of Queensland and Northern New South Wales<sup>4,5</sup>. In India, the presence of scrub typhus has been known for several years. The disease is widely spread all over the country, and was reported in several states - Haryana, Jammu and Kashmir, Himachal Pradesh, Uttaranchal, West Bengal, Assam, Maharashtra, Kerala and Tamilnadu<sup>6</sup>. Scrub typhus outbreaks among military troops were reported during World War II in Assam and West Bengal, in 1965 Indo-Pak war in the Jammu - Sialkot sectors and in 1971 Indo-Pak conflict in the northwestern border. There was a resurgence of the disease in 1990, in the scrub type jungle on the northwestern border of India<sup>7</sup>.

Upper Assam experiences heavy rainfall and flood every year hence the climate is suitable for the breeding of the vector mite. Therefore study was undertaken to know the seroprevalence of Scrub typhus among clinically suspected cases in this area and also to find out the association of different parameters like age, gender, geographical location, season etc. with the disease.

### MATERIALS AND METHODS

This prospective cross-sectional hospital based study was carried out in the Department of Microbiology, Assam Medical College & Hospital, Dibrugarh, Assam. The period of study was from March 2014 to February 2016.

All consecutive non repetitive clinically suspected cases attending to the institution during the study period were included in the study. Clinical and demographic findings were recorded on a pre-designed Performa. Patients of all age groups and both sexes were included in the study.

Cases satisfying the case definition as per DHR-ICMR guideline for diagnosis and management of Rickettsial diseases in India were included in the study. According to the guideline, acute undifferentiated febrile illness of 5 days or more with or without eschar should be suspected as a case of Rickettsial infection. (If eschar is present, fever of less than 5 days duration should be considered as scrub typhus.) Other presenting features may be

headache and rash (rash more often seen in fair persons), lymphadenopathy, multi-organ involvement like liver, lung and kidney involvement<sup>8</sup>. Patients with established causes of fever were excluded from this study. Serum samples were collected from the selected subjects. Samples were kept at 4-8°C if testing is done within 48hrs, for short and long term storage kept in a deep freezer at -20°C and at -80°C respectively. Scrub typhus IgM ELISA test was performed using Scrub Typhus Detect™ IgM

ELISA System kit (In Bios International, Inc.) strictly following the kit protocol. Samples with optical density value above cut off were considered to be reactive and samples below this criterion were considered to be non-reactive. Each reactive sample was retested to verify the result. Values near cut-off were considered as doubtful and the assay was repeated in triplicate.

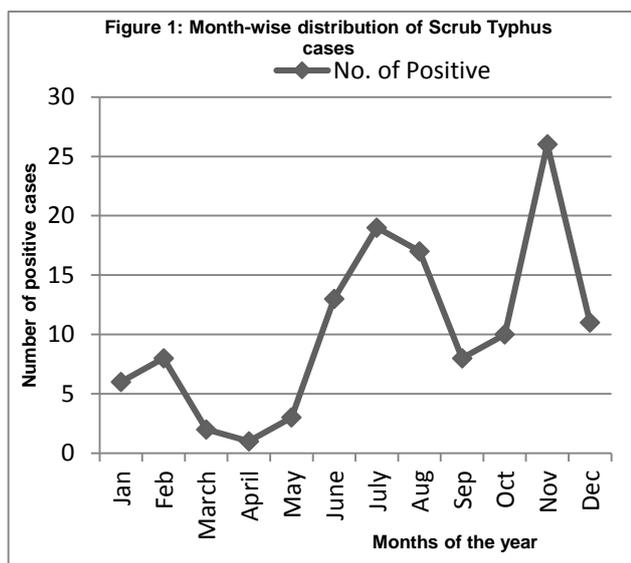
The data were analyzed by using Chi-Square test to determine statistical significance using Epi Info7 software.

**Table 1: Distribution of Scrub typhus cases according to age, gender and geographical location**

Characteristics		Positive (%)	Negative (%)	P-value
<b>Age Group (years)</b>	0-10	5 (18.52)	22 (81.48)	0.35
	11-20	17 (12.41)	120 (87.59)	
	21-30	37 (17.70)	172 (82.30)	
	31-40	32 (20.38)	125 (79.62)	
	41-50	15 (12)	110 (88)	
	51-60	10 (13.89)	62 (86.11)	
	61-70	4 (8.89)	41 (91.11)	
	>70	4 (13.33)	26(86.67)	
<b>Gender</b>	Female	38 (15.38)	209 (84.62)	0.97
	Male	86 (15.50)	469 (84.50)	
<b>Geographical location</b>	Rural	112 (19.48)	463 (80.52)	<0.001
	Urban	12 (5.29)	215 (94.71)	

**Table 2: Clinical presentations of Scrub Typhus cases**

Symptoms	Total cases with the symptom n=802 (%)	Positive cases with the symptom n= 124 (%)
Fever	802(100.00)	124(100.00)
Headache	659 (82.17)	97(78.23)
Myalgia	659 (82.17)	95 (76.61)
Nausea & Vomiting	272 (33.92)	76 (61.29)
Joint pain	423 (52.74)	37 (29.84)
Seizure	239 (29.80)	37 (29.84)
Change in mental status	133 (16.58)	23 (18.55)
Unconsciousness	122 (15.21)	19 (15.32)
Retro orbital pain	57 (7.12)	10 (8.06)
Lymphadenopathy	21 (2.62)	06 (4.84)
Maculopapular rash	28 (3.49)	04 (3.23)
Eschar	2 (0.25)	02 (1.61)



**RESULTS**

A total of 802 cases satisfying the inclusion criteria were included in the present study. Of them 124 (15.46 %) were positive for Scrub typhus.

**Baseline characteristics of study population:** Mean age of the study population was 37 (±17.2) years. There were 555 (69.2%) males and 247 (30.8%) females in our study. Most of the patients were from rural background with history of working in open fields. 746(93.02%) patients were from the different districts of upper Assam and 56 (6.98%) patients were from neighboring state Arunachal Pradesh.

**Age and sex distribution of the positive cases:** Most of the cases were found to be young adults mainly in 21-50 year age group (67.74% of total positive). But the study showed no significant association of Scrub typhus cases with the age of the patient (p>0.05). (Table 1) We found a similar type of distribution of the disease among both sexes (15.38% and 15.5% positivity in

female and male respectively) and the association was not significant. ( $p > 0.05$ ) (Table 1)

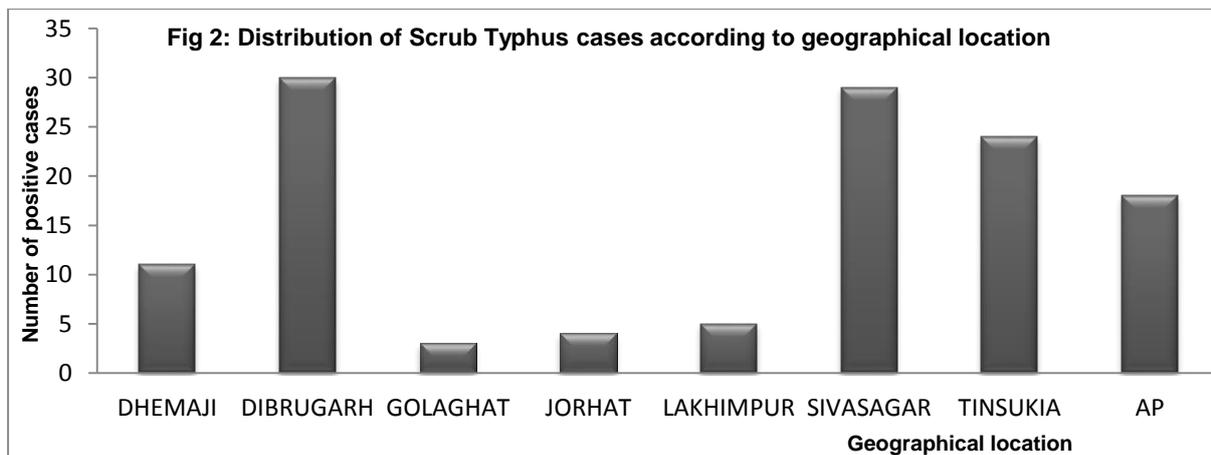
**Month wise distribution of positive cases:** The seasonal variation of Scrub Typhus was significant ( $p < 0.05$ ) with peak occurrence during rainy and post rainy cooler season i.e. June to February of next year (Fig 1).

**Geographical distribution of positive cases:** We received Scrub cases from different districts of Upper Assam including Dibrugarh, Sivasagar, Tinsukia etc and also from neighboring state Arunachal Pradesh (Fig 2). 90.32% of total positive cases were reported from rural area and the association of the disease with the geographical location was found to be statistically significant. ( $p < 0.001$ ) (Table 1)

**Clinical presentations of positive cases:** All patients presented

with fever and the average duration was 8.57 days (range 1 to 30 days). Next common symptoms were headache (78.23%), myalgia (76.61%) and nausea and vomiting, (61.29%). Seizure was present in 29.84% patients and one patient presented with status epilepticus. Joint pain was seen in 29.84%, retro-orbital pain in 8.06%, lymphadenopathy in 4.84% and unconsciousness in 15.32% patients. Maculo papular rash and eschar was seen in 4 (3.23%) and 2(1.61%) patients respectively. 18.55% patients had altered mental status. The other sign of organ involvement observed was hepato-splenomegaly which was present in 17 (13.71%) patients. (Table 2)

**Travel history of the positive cases:** Of 124 positive cases 9 cases had the history of visit to Arunachal Pradesh, 2 cases to Bihar, 3 cases to West Bengal.



## DISCUSSION AND CONCLUSIONS

15.46% cases were found to be Scrub Typhus positive in the present study which was comparable with Khan et al from Uttarakhand (19.4%)<sup>9</sup>. The positivity was observed to be higher in the reports of Munilakshmi et al (41.7%) and Ramyasree et al (39%) from Andhra Pradesh<sup>10,11</sup>, Narvencar et al from Goa (34%)<sup>12</sup>, Bithu et al (49.1%) from Rajasthan<sup>13</sup>. This low positivity in this region may be attributed to the variable and non-specific presentation of the disease, absence of eschar and lack of proper diagnostic facilities.

The clinical presentation of Scrub typhus varies from mild and self-limiting to fatal disease<sup>2</sup>. After an incubation period of 6-21 days, onset is characterized by fever, headache, myalgia and gastrointestinal symptoms<sup>1</sup>. The classic case description includes a primary papular lesion (where the chigger has fed and can occur anywhere on the body), which enlarges, undergoes central necrosis, and crusts to form a flat black eschar. This is associated with regional and later generalized tender lymphadenopathy<sup>5</sup>. In the present study fever was the commonest presentation and was present in all cases similar to other studies<sup>11,12</sup>. It is followed by headache, myalgia, nausea and vomiting, seizure, joint pain, change in mental status, unconsciousness, retro-orbital pain etc. Hepatosplenomegaly was reported in 17(13.71%) patients. However much higher percentages of patients with hepatosplenomegaly were reported from Chennai (80%)<sup>14</sup> and Uttarakhand (42%)<sup>9</sup>.

Though eschar is pathognomonic of Scrub typhus infection but it has a variable occurrence (7-97%)<sup>15</sup> and has to be differentiated from anthrax and other Rickettsial infections. It was reported to be more frequent in primary infections and less often seen in secondary infections<sup>16</sup>. Eschar was reported by Subbalaxmi et al in 13.1%<sup>17</sup>

and Vivekanandan et al in 46%<sup>18</sup> of cases. No eschar was reported by Ramyasree et al<sup>11</sup> and very few patients with eschar and lymphadenopathy were reported by Narvencar et al and Singh et al<sup>12,19</sup>. In the study we received only 2 cases with eschar, 4 cases with maculopapular rash and 6 cases with lymphadenopathy. None of these clinical symptoms and signs including eschar is diagnostic of Rickettsial disease. Therefore epidemiological factors pertaining to geographical area, habitat, occupation, movement of the subject (vocational or recreational) could assist in reaching a diagnosis of Rickettsial disease with certainty and initiating treatment in time<sup>8</sup>. In the study 14 positive cases had travel history.

Although cases were reported throughout the year, most of them were seen from June to February of next year. This duration was observed to be longer than other states as monsoon comes earlier and winter season last longer in this area. This monsoon and post- monsoon seasonal distribution of cases were also observed in the studies from different states of the country i.e August – October in Uttarakhand<sup>9</sup>, July - November in Goa<sup>12</sup>, September - October in Rajasthan<sup>13</sup>, August- October in Andhra Pradesh<sup>17</sup> and July - October in Manipur<sup>19</sup>. During the monsoon season mites lay their eggs<sup>2</sup>, further, in the immediate post monsoon period i.e. in cooler season (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>20</sup>. Farmers are mostly involved in the harvesting activity in the fields during these months, where they are more exposed to the bites of larval mites.

In this study, cases were seen from 1 to 86 years of age and the highest numbers of cases were from 21 to 50 years age group similar to Subbalaxmi et al<sup>17</sup>. As this young and active population is mainly involved in outdoor occupational activities, the risk of the

disease is higher. Different authors reported Scrub cases in different age groups e.g. Girija et al in 13-71 years<sup>16</sup>, Ramiyasree et al in 16- 30year<sup>11</sup>, Bithu et al in 46-60 years<sup>13</sup> and Singh et al in 15-65years<sup>19</sup>. Cases were mainly reported in males from Andhra Pradesh by Subblaxmi et al<sup>17</sup> and in females from Tamilnadu and Rajasthan by Girija et al<sup>16</sup> and Bithu et al<sup>13</sup> respectively. But no sex difference in the occurrence was observed in the present study ( $p= 0.97$ ) as people of both sexes were involved equally in outdoor activities. This observation was similar to a report from Thailand<sup>21</sup>. Most of the cases in present study were from rural background living near to forest and involved in outdoor activity like agriculture, collecting of firewood from jungle, rearing poultry etc. Same was reported by other authors also<sup>16,17,22</sup>.

The limitations of the present study were: 1. It was a hospital based study so it could not show the actual burden of the disease in the community. 2. IgM ELISA was used for serological diagnosis of cases because the indirect immune-fluorescence assay for Scrub typhus, the gold standard confirmatory test is not yet available in our setup.

In conclusion, the present study provided an evidence for the seropositivity of scrub typhus in Upper Assam. It is recommended to include Scrub typhus in the differential diagnosis of acute febrile illness in this region which will help in proper diagnosis, timely and adequate treatment and avoidance of the complications and mortality. There is need of establishment of comprehensive diagnostic services for Rickettsial diseases in Upper Assam. We propose a number of public health recommendations to prevent the infection, firstly, education of the population regarding safe living and working environment. Secondly, promotion of protective measures like wearing fully covered cloths during outdoor activities and use of repellents may reduce individual risks. There is a need of a proper national and state level surveillance system for Scrub typhus in India.

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## REFERENCES

- Hornick RB. Rickettsial Diseases. In: Bennett JC, Plum F, editors. Goldman: Cecil Textbook of Medicine. 21st ed. Philadelphia, USA: WB Saunders Company; 2000. pp. 1911–2.
- Walker DH, Dumler JS, Marrie T. Rickettsial Diseases. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's Principle of Internal Medicine. 18th ed. USA: The McGraw-Hill Companies; 2012. pp. 1064–5.
- Dumler JS, Siberry GK. Scrub Typhus (Orientia Tsutsugamushi). In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, editors. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: Saunders, Elsevier; 2007. pp. 1295–6.
- Chang WH. Current status of tsutsugamushi disease in Korea. J Korean Med Sci. 1995; 10: 227–38.
- Mahajan SK. Scrub typhus. J Assoc Physicians India. 2005; 53: 954–8.
- Mahajan SK, Kashyap R, Kanga A, Sharma V, Prasher BS, Pal LS. Relevance of Weil-Felix test in diagnosis of scrub typhus in India. J Assoc Physicians India. 2006; 54:619–21.

- Singh LCP. Scrub typhus, a case report: Military and regional significance. Med J Armed Forces India. 2004;60: 89–90.
- Indian Council of Medical Research, Department of health research. Guideline for Diagnosis and management of Rickettsial diseases in India, 2015. (Accessed on 24.09.2015) Available from URL: www.pharmabiz.com/NewsDetails.aspx?aid=88318&sid=1
- Khan F, Mittal G, Agarwal R K, Ahmed S , Gupta S, Shadab M. Prevalence of Scrub Typhus - A Cause of concern in Uttarakhand Region, India. Int.J.Curr.Microbiol.App.Sci.2015; Special Issue-1: 101-9.
- Munilakshmi P, Krishna MV, John MS, Deepa T, Avinash G, Reddy PS. FUO Cases Showing Prevalence of Scrub Typhus: A Comparative Study by ELISA and Rapid Test in a Tertiary Care Hospital in Andhra Pradesh, India. Int J Curr Microbiol App Sci. 2015; 4(2): 632-40.
- Ramiyasree A, Kalawat U, Rani ND, Chaudhury A. Seroprevalence of Scrub typhus at a tertiary care hospital in Andhra Pradesh. Indian J. Med. Microbiol. 2015; 33(1): 68-72.
- Narvencar KPS, Rodrigues S, Nevrekar RP, Dias L, Dias A, Vaz M et al. Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa. Indian J Med Res. 2012 Dec; 136: 1020-24.
- Bithu R, Kanodia V, Maheshwari RK. Possibility of scrub typhus in fever of unknown origin (FUO) cases: An experience from Rajasthan. Indian J. Med. Microbiol. 2014; 32(4): 387-90.
- Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. Indian J Pediatr. 2012 Nov; 79(11):1459-62.
- Paris D H, Shelite T R, Day N P, Walker D H. Unresolved Problems related to scrub typhus: A seriously neglected life-threatening disease. Am J Trop. Med. Hyg. 2013; 89 (2): 301- 07.
- Girija S, Rajan A, Sathiyarayanan J, Mangaiyarkarasi T, Saban P, Sunil S et al. Scrub typhus- An emerging disease in South India. IJRRMS. 2013 Oct-Dec; 3(4):11-3.
- Subbalaxmi MVS, Madisetty MK, PrasadAK, TejaVD, Swaroopa K, Chandra N et al. Outbreak of Scrub Typhus in Andhra Pradesh – Experience at a Tertiary Care Hospital, J Assoc Physicians India. 2014 Jun; 62: 490-6.
- Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S, Purty S. Outbreak of scrub typhus in Pondicherry. J Assoc Physicians India. 2010; 58:24-8.
- SinghSK, Ram R, Marangmei L, Chakma G. Case Series on Scrub Typhus from a tertiary care hospital of North East India. IOSR-JDMS. 2014 Nov; 13(11): 62-4.
- Saah AJ. Orientia tsutsugamushi (scrub typhus). In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Disease. 5th ed. Philadelphia: Churchill Livingstone; 2000. Pp.2056–7.
- Chanyasaha C, Kaeburong K, Chenchittikul M, Sujirarat D. Seroprevalence of scrub typhus infection in patients with pyrexia at some malaria clinics in three western provinces of Thailand. Asian Pac J Allergy Immunol. 1998; 16:119-25.
- Jamil M, Lyngrah KG, Lyngdoh M, Hussain M. Clinical Manifestations and Complications of Scrub Typhus: A Hospital Based Study from North Eastern India. J Assoc Physicians India. 2014 Dec; 62: 19-23.

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