

Original Article

Myriad of Presentation of Scrub Typhus in a Tertiary Care Hospital in North Eastern India — A Prospective study

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Background and Objectives : Among the Rickettsial Diseases caused in human, the most wide spread is Scrub Typhus. Scrub Typhus is a re-emerging infectious disease that generally causes Acute Febrile Illness, with disease spectrum ranging from mild illness to multi organ dysfunction. The study was aimed at documenting the demographic characteristics, clinical profile and complications associated with Scrub Typhus.

Materials and Methods : This is a prospective study, done at a Tertiary Care Hospital including patients presenting with Acute Febrile Illness who were found positive for scrub typhus on IgM ELISA.

Results : The most common age group affected is 20-40 years. Majority were from Rural background with male predominance. Apart from fever, which was present in all the patients considered in this study, the other common presenting complaints were pain abdomen in 48.3%, cough in 43.1% and vomiting in 36.2%. Headache was present in 32.8% and altered mental state in 8.6% patients. Findings on physical examination were eschar in 27.5%, hepatomegaly in 15.5% patients. The common laboratory abnormalities were hypo-natremia in 89.7%, elevated liver enzymes, SGOT in 72.4%, SGPT in 65.5% and hypo-albuminemia in 68.9% cases.

Conclusion : Scrub typhus is an important cause of Acute Febrile Illness, with varied presentations and far reaching complications. With the presence of fever with abdominal, respiratory symptoms and supportive findings of eschar, hypo-natremia, hypo-albuminemia in this part of the country, scrub typhus should be kept in the differentials of Acute Undifferentiated Fever, which can help in grabbing the diagnosis early and thus limit the multi-system involvement and complications of scrub typhus.

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Key words : Scrub typhus, Rickettsial diseases, Hyponatremia, Hypo-albuminemia.

Scrub typhus, an Acute Febrile Illness, is one of the most common Rickettsial infections in the Indian subcontinent¹. The disease is caused by a parasite known as *Orientia tsutsugamushi*, which belongs to the family Rickettsiaceae. Hashimoto from Japan first described Scrub typhus in 1899². Scrub typhus is endemic over a wide geographical area in Afghanistan, Pakistan, India, China, South East Asia, Japan, Korea, Russia and Australia. In India, it is distributed primarily over the forests and Rural areas where endemic pockets have been established and seasonal outbreaks occur on regular basis. It is transmitted by larval form of trombiculid mite, which is a parasite of rodents. The larval stage serves both as reservoir and vector by infecting humans and rodents. The adult mite lives in decaying ground- vegetation where it lays its eggs but does not feed on vertebrate hosts^{3,4}.

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Editor's Comment :

- In a tropical country like India, fever is the most common presentation of patients with infectious diseases.
- Scrub typhus is also a common but most often overlooked cause of acute fever associated with a variety of clinical features, which if left untreated, can have serious complications. Herein comes the importance of including Scrub Typhus in the differential diagnosis of acute undifferentiated fever in patients residing in or having recent travel history to places with dense scrub vegetation, mainly in the rainy season, and supportive evidence of an eschar, hyponatremia, elevated hepatic transaminases etc. At a time when drugs against scrub typhus are so readily available, developing a high clinical suspicion regarding this disease can go a long way in preventing morbidity and mortality.

The incubation period of Scrub Typhus infection varies from 6-21 days. The infected human host may present with a variety of symptoms like fever, headache, pain-abdomen, vomiting, myalgia, rashes and/or features suggestive of other organ system involvement. At the site of bite, a papule appears which subsequently evolves in to a painless eschar with an erythematous outer rim. The myriad of non-specific clinical features which overlap with other common

tropical features, make the diagnosis challenging, owing to which many patients land up in life threatening complications. Hence, early recognition of the disease from the clinical presentation, meticulous clinical examination and abnormal laboratory parameters may help in early administration of the highly efficacious drugs. This, in turn, may significantly reduce the disease duration, morbidity and mortality associated with Scrub Typhus. In the North-eastern region of India, although Scrub Typhus is not uncommon, yet not enough studies are available on the dynamic spectrum of the disease. So this study has been undertaken with an aim to understand the demographic characteristics, clinical profile and complications associated with the disease.

MATERIALS AND METHODS

This was a prospective study, done on patients presenting with Acute Febrile Illness who were admitted in the department of General Medicine, Silchar Medical College and Hospital. The study comprised of 58 patients presenting with Acute Febrile Illness with IgM ELISA positive Scrub typhus and was done over a period of 1 year and 1 month, ie, from 1st January, 2019 to 31st January 2020.

Inclusion criteria :

- Inpatients admitted with Acute Febrile Illness for a duration more than 5 days and are found to be positive on serum IgM ELISA Scrub typhus test
- Age > 12 years

Exclusion criteria:

- Patients who did not give consent for participation in the study
- Cases with an established cause of Acute Febrile Illness such as Malaria, Enteric fever, Dengue, Leptospirosis, Viral hepatitis, Urinary tract infection, Respiratory tract infection, Acute gastroenteritis, Meningitis, Encephalitis or other infections and chronic diseases such as Chronic liver disease, Chronic kidney disease, Tuberculosis.

Serological test for detection of IgM antibodies against the causative agent *Orientia tsutsugamushi* was done in the Department of Microbiology of the Institute using ELISA kit.

Organ dysfunction which occurred as a complication of Scrub Typhus in the study cases has been defined as:

Acute Kidney Injury (AKI) : As per the Kidney Disease Improving Global Outcome (KDIGO) criteria⁵.

Hepatic Dysfunction : Elevation of serum transaminases level (SGOT and SGPT) more than two folds of the upper normal limits

Acute Respiratory Distress Syndrome (ARDS) :

A clinical syndrome of severe dyspnea of rapid onset, hypoxemia ($\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg) and diffuse pulmonary infiltrates leading to respiratory failure⁶.

Statistical data analysis was done with the help of Microsoft EXCEL 2010.

OBSERVATIONS AND RESULTS

Demographic Indices:

The mean age of the patients was observed to be 37.8 ± 14.5 years, of which maximum number of patients was in the age group of 20-40 years followed by 40-60 years. Most of the affected individuals were male with a male-to-female ratio of 2.2:1. More than 84% patients were from Rural background and most of them were either farmers or worked in open fields/ jungles. Among the study subjects, most of the patients were admitted in the month of October and November. The demographic indices have been summarized in the Table 1.

Clinical profile :

A total of 58 cases were recruited in the study and all of them had fever at the time of presentation. The duration of fever at the time of hospitalization varied from 6 days to 13 days with a mean of 8.1 ± 2.1 days. Other common symptoms were pain abdomen in 28 patients (48.3%), vomiting in 21 patients (36.2%), loose stools in 10 patients (17.2%), cough in 25 patients (43.1%) and dyspnea in 10 patients (17.2%). Headache and altered mental status were present in 19 (32.8%) and 5 (8.6%) patients respectively. Dysuria was seen in 4 patients (6.9%).

Findings on physical examination revealed eschar in 16 patients (27.5%), Pedal edema in 10 (17.2%), Hepatomegaly in 9 (15.5%), Splenomegaly in 2 (3.4%), abdominal tenderness in 12 patients (20.7%), signs of ARDS and Pneumonia were found in 6 (10.3%) and 8 (13.8%) patients respectively. Signs of Meningitis were detected in 4 patients (6.9%). In the present series, eschar was found in most cases in well covered

Table 1 — Summarizing the demographic indices of the study subjects

Variables	Number of cases	Percentage
Gender :		
Male	38	65.5
Female	20	34.5
Age groups		
< 20 Years	7	12.1
20-40 Years	29	50
40-60 Years	18	31
>60 Years	4	6.9
Address		
Rural	48	82.8
Urban	10	17.2

areas like the medial aspect of thigh, perineum, abdomen, armpit, blouse clad part of upper back, etc. Furthermore, owing to its painless and non-itchy character, these eschars remain undetected most of the time. Bar diagrams depicting the presenting symptoms and signs of the cases has been shown in the Figs 1 & 2 respectively.



Fig 1 — An eschar on the anterolateral aspect of right knee



Fig 2 — Eschar on the anterior part of arm

Cerebrospinal Fluid (CSF) analysis was done on 5 patients, in 3 patients (5.2%) there was elevated CSF protein with lymphocytic predominance and the other two patients had normal CSF findings. The laboratory abnormalities in the study subjects have been summarized in the Figs 3-5.

Laboratory and Radiological Findings :

The profile of laboratory finding of Scrub Typhus cases are depicted below.

Hematological profile :

Leucocytosis was observed in 25 patients (43.1%), Thrombocytopenia and Leucopenia in 11 (18.9%) and 8 (13.8%) patients respectively on the day of admission.

Biochemical profile :

Biochemically, commonest abnormality was found to be hyponatremia in 52 patients (89.7%) with a mean \pm SD of 129.2 ± 4.5 mmol/dl. Other abnormalities include elevated liver enzymes, SGOT in 42 (72.4%) and SGPT in 38 (65.5%), where SGOT (159.3 ± 59.6 U/L) was observed to be more raised than SGPT (112.6 ± 33.8 U/L), hypo-albuminemia in 40 (68.9%) with mean \pm SD of 3.0 ± 0.33 g/dl. Raised Serum creatinine was observed in 8 patients (13.8%). Abnormal Urine routine examination was observed in 4 patients (6.9%).

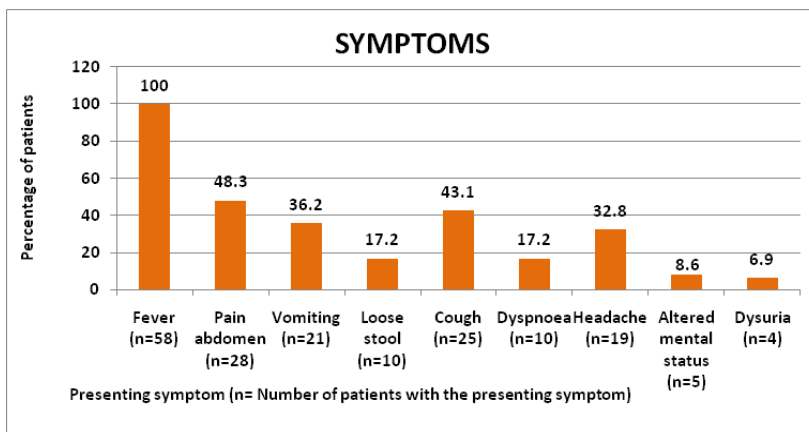


Fig 3 — Bar diagram depicting the presenting symptoms of the cases

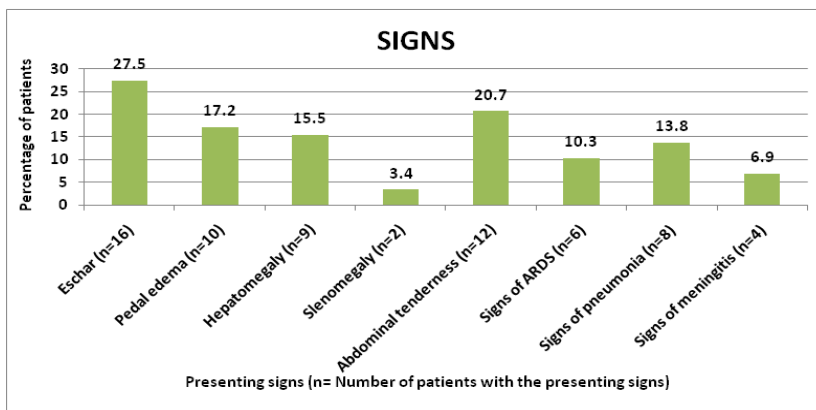


Fig 4 — Bar diagram summarizing the signs observed in the study subjects

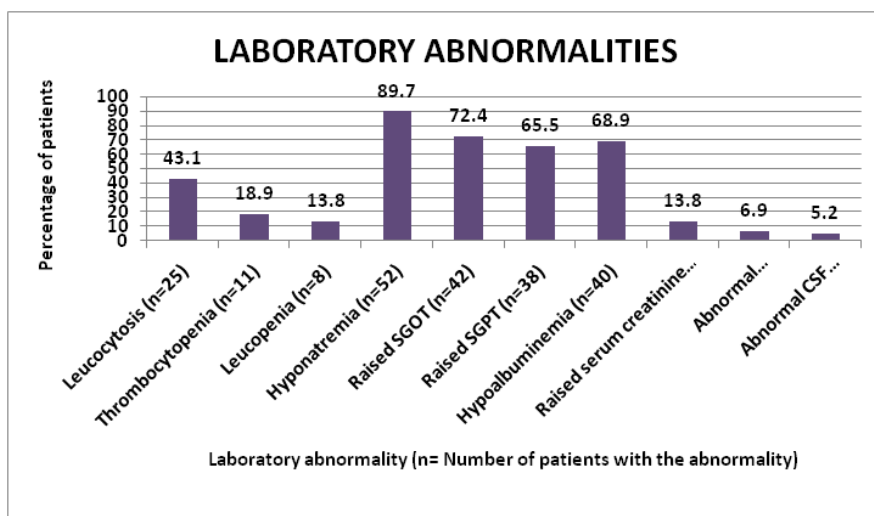


Fig 5 — Bar diagram showing the laboratory abnormalities in the study subjects

In this study, the disease was found to be predominant in the postmonsoon months with maximum cases being reported in the months of October and November. This is the period when ground vegetation is seen to grow more leading to more exposure to scrub infection. This finding tallies with the finding from other studies.

The patients presented with wide variety of clinical features and in general GI symptoms were found to be much more common in the present series which includes pain abdomen in 48.3%, nausea/ vomiting in 36.2%, loose

Radiological findings:

Chest X-ray postero-anterior view showed non-homogenous opacity in bilateral lung fields in 6 patients (10.3%) and signs of consolidation in 3 patients (5.2%).

Ultrasonography of whole abdomen revealed hepatomegaly in 12 patients (20.7%) and mild splenomegaly in 2 patients (3.4%).

DISCUSSION

The results of the present study were compared with the results from other studies done in the Indian subcontinent as well as some studies from other Asian countries. Results of this study showed that the commonest age group of affected patients ranged between 20 to 40 years, as also seen with the study by Pathania *et al*⁷. Males were found to be more commonly affected than females. Factors responsible might be that this constitutes the main working force in the local population who engage in agrarian activities, go to forests to collect firewood and spend more time outdoors, as is often seen among the rural folk. This is in contrast to the study by Pathania *et al*⁷, where female pre-ponderance was seen to be higher.

stools in 17.2%, hepatomegaly in 15.5%, splenomegaly in 3.4%, which is consistent with the findings of Sivarajan *et al*⁸, in Meghalaya, where they observed pain abdomen in 26.7%, nausea/ vomiting in

	Pathania <i>et al</i> ⁷	Subbalaxmi <i>et al</i> ⁸	Sivarajan <i>et al</i> ⁸	This study
Place (India)	Uttarakhand	Andhra Pradesh	Meghalaya	Barak Valley, Assam
Sample size	54	176	90	58
Clinical features :				
Fever	54 (100%)	176 (100%)	75(83.3%)	58(100%)
Pain abdomen	39(79.22%)	NA	24(26.7%)	28 (48.3%)
Nausea/vomiting	29 (53.7%)	NA	21(23.3%)	21 (36.2%)
Loose stools	5 (9.25%)	28 (15.9%)	NA	10 (17.2%)
Cough	28(51.85%)	94 (53.4%)	21(23.3%)	25 (43.1%)
Dyspnoea	NA	NA	NA	10 (17.2%)
Headache	45(83.33%)	92 (52.8%)	24(26.7%)	19 (32.8%)
Altered mental status	14(25.92%)	23 (13.1%)	5(19%)	5 (8.6%)
Dysuria	NA	NA	NA	4 (6.9%)
Eschar	7 (12.96%)	23 (13.1%)	10(11.1%)	16 (27.5%)
Pedal edema	NA	NA	NA	10 (17.2%)
Hepatomegaly	10 (18%)	51(28.9%)	24(26.7%)	9 (15.5%)
Splenomegaly	4 (7.4%)	51 (28.9%)	NA	2 (3.4%)
Abdominal tenderness	29 (53.7%)	NA	NA	12 (20.7%)
Complication :				
Hyponatremia	NA	NA	NA	52(89.7%)
Hypo-albuminemia	NA	NA	NA	40(68.9%)
Pneumonia	1(1.87%)	NA	NA	8 (13.8%)
ARDS	4(7.4%)	NA	NA	6 (10.3%)
Meningitis	11(20.3%)	NA	NA	4 (6.9%)
Renal failure	2(3.70%)	49(27.8%)	11(12.2%)	8 (13.8%)
Leukocytosis	16(29.62%)	18(10.2%)	23(25%)	25 (43.1%)
Leukopenia	1(1.87%)	42(23.9%)	11(12%)	8 (13.8%)
Thrombo-cytopenia	7(12.9%)	53(30.1%)	18(20%)	11 (18.9%)
Elevated transaminases	40(74.07%)	153(86.9%)	SGOT 90(100%) SGPT 85(94%)	SGOT 42(72.4%) SGPT 38(65.5%)
NA - not available				

23.3% and cough in 23.3%. Cough as a presenting feature was found in this study in 43.1% patients which is less than that found in the studies by Kun Ming Wu *et al*¹⁰ (52.5%) and Subbalaxmi *et al*⁸ (53.4%) and is higher than what was reported by Sivarajan *et al*⁹ (23.3%). CNS involvement in scrub typhus may result in altered sensorium, seizures, meningitis etc. Headache (32.8%), altered mental status (8.6%), meningitis (6.9%) were found to be less common in this study than in the other studies.

In this series, another observation was the presence of pedal edema in 17.2%, which is in contrast to the study by Pathania *et al*⁷ where facial puffiness, upper eyelid edema (74.07%) were also observed along with pedal edema. Among other symptoms, dysuria was present in 6.9% patients at admission where as in the study by Premraj *et al*¹⁴ dysuria was present in 24%.

The presence of eschar as a clue to diagnosing scrub typhus was seen in 27.5% of the cases in the present study, as compared to 11.1%, 13.1%, 12.9% which were seen in the studies conducted by Sivarajan *et al*⁹, Subbalaxmi *et al*⁸, Pathania *et al*⁷ respectively.

A high level of suspicion and a meticulous clinical examination preferably with clothes removed after proper consent can yield an early diagnosis.

Among lab parameters, the most common ones were hypo-natremia (89.7%), elevated transaminase (SGOT in 72.4%, SGPT in 65.5%), which are consistent with the findings by Pathania *et al*⁷. This depicts that scrub typhus can be a very important differential in cases of Acute Febrile Illness being evaluated for Anicteric Hepatitis. This finding of elevation of SGOT more than SGPT found here is suggestive of multi system involvement in these cases. Hypo-albuminemia was observed in 68.9% of the study subjects, which is probably a result of increased vascular permeability. Other findings were Leukocytosis in 43.1%, Leukopenia in 13.8%

and Thrombocytopenia in 18.9% which is in contrast to the findings of Subbalaxmi *et al*⁸ and Zhang *et al*¹¹. In resource poor areas where confirmatory tests for scrub typhus may not be present, these lab parameters can raise high degree of suspicion.

Among the complications encountered in an infected patient, Pneumonia (13.8%), ARDS (10.3%), renal failure (13.8%) have been found in this study with their incidence more than that found by Pathania *et al*⁷ 1.87%, 7.4%, 3.70% respectively. Whereas Subbalaxmi *et al*⁸ found 27.8% of renal failure as a complication of the disease. This might be owing to a more virulent strain here, less immunity, less awareness, or delay in seeking medical help among the general population. Comparisons made between this study and few other studies done in different regions of India and few other countries of Asia have been summarized in the Tables 2 and 3 respectively.

CONCLUSION

Scrub typhus is an important cause of Acute Febrile Illness that can have a wide range of clinical

Table 3 — A table of comparison between this study and few other studies done in other Asian countries

	Kun Ming Wu <i>et al</i> ¹⁰	Zhang <i>et al</i> ¹¹	Brummaier <i>et al</i> ¹²	This study
Place	Taiwan	Shandong	North-Western Thailand	Barak Valley, Assam, India
Sample size	136	102	422	58
Clinical features				
Fever	134 (98.5%)	102 (100%)	378 (89.6%)	58(100%)
Pain abdomen	NA	NA	NA	28 (48.3%)
Vomiting	NA	28 (27.4%)	116 (27.5%)	21 (36.2%)
Loose stools	NA	NA	NA	10 (17.2%)
Cough	71 (52.5%)	14 (13.7%)	115 (27.3%)	25 (43.1%)
Dyspnea	NA	NA	NA	10 (17.2%)
Headache	85 (62.5%)	64 (62.7%)	224 (53.1%)	19 (32.8%)
Altered mental status	NA	NA	7 (1.7%)	5 (8.6%)
Dysuria	NA	NA	NA	4 (6.9%)
Eschar	82 (60.3%)	88 (86.3%)	38 (%)	16 (27.5%)
Pedal edema	NA	NA	NA	10 (17.2%)
Hepatomegaly	NA	7 (6.9%)	NA	9 (15.5%)
Splenomegaly	NA	14 (13.7%)	NA	2 (3.4%)
Abdominal tenderness	42 (30.9%)	17 (16.7%)	98 (23.2%)	12 (20.7%)
Complication				
Hyponatremia	NA	NA	NA	52 (89.7%)
Hypoalbuminemia	NA	NA	NA	40 (68.9%)
Pneumonia	13 (20.6%)	22 (21.6%)	30 (9.9%)	8 (13.8%)
ARDS	4 (6.3%)	NA	NA	6 (10.3%)
Meningitis	NA	0	4 (1.3%)	4 (6.9%)
Renal failure	9 (6.8%)	0	8 (2.6%)	8 (13.8%)
Leukocytosis	39 (29.8%)	(13.5%)	NA	25 (43.1%)
Leukopenia	NA	(4.1%)	NA	8 (13.8%)
Thrombo-cytopenia	NA	(25.4%)	NA	11 (18.9%)
Elevated transaminases	109/127 (85.8%)	SGOT (75%) SGPT (80.3%)	NA	SGOT 42(72.4%) SGPT 38(65.5%)
NA - not available				

manifestations and thus, should be included unfailingly in the differentials of acute undifferentiated fever. Due to a myriad of presentation that may vary significantly from case to case and a low degree of suspicion on the part of the physician, these cases are often overlooked and under diagnosed. Scrub typhus as such, can have far reaching complications if left untreated. Particularly in this part of the country, presence of fever with abdominal, respiratory symptoms with supportive findings of eschar, hyponatremia, hypo-albuminemia can help in grabbing the diagnosis early and thus limit the multi-system involvement and complications of Scrub Typhus.

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REFERENCES

- 1 Chang WH — Current status of tsutsugamushi disease in Korea. *J Korean Med Sci* 1995; **10**: 227-38. doi: 10.3346/jkms.1995.10.4.227.
- 2 Mahajan SK — Scrub Typhus. *JAPI* 2005; **53**: 954-58.
- 3 Lai CH, Huang CK, Chen YH — Epidemiology of acute Q Fever, scrub typhus, and murine typhus, and identification of their clinical characteristics compared to patients with acute febrile illness in southern Taiwan. *J Formos Med Assoc* 2009; **108**(5): 367-76.
- 4 Suputtamongkol Y, Suttinont C, Niwatayakul K — Epidemiology and clinical aspects of rickettsioses in Thailand. *Ann N Y Acad Sci* 2009; **1166**: 172-9.
- 5 <https://www.medscape.com/answers/1925597-112195/what-are-the-kdigo-criteria-of-acute-kidney-injury-aki>.
- 6 The ARDS Definition Task Force — Acute respiratory distress syndrome: The Berlin definition. *JAMA* 2012; **307**(23): 2526-33. doi:10.1001/jama.2012.5669.
- 7 Pathania M, Amisha, Malik P, Rathaur VK — Scrub typhus: Overview of demographic variables, clinical profile, and diagnostic issues in the sub-Himalayan region of India and its comparison to other Indian and Asian studies. *J Family Med Prim Care* 2019; **8**: 1189-95.
- 8 Subbalaxmi MVS, Chandra N, Teja VD, Lakshmi V, Rao MN, Raju YSN — Scrub typhus – Experience from a South Indian tertiary care hospital. *BMC Infect Dis* 2012; **12**: 77.
- 9 Sivarajan S, Shivalli S, Bhuyan D, Mawlong M, Barman R — Clinical and paraclinical profile, and predictors of outcome in 90 cases of scrub typhus, Meghalaya, India. *Infect Dis Poverty* 2016; **5**: 91. doi: 10.1186/s40249 016 0186.
- 10 Wu KM, Wu ZW, Peng G, Wu JL, Yilee S — Radiologic pulmonary findings, clinical manifestations and serious complications in scrub typhus: Experiences from a teaching Hospital in Eastern Taiwan. *Int J Gerontol* 2009; **3**: 223 32.
- 11 Zhang M, Zhao ZT, Wang XJ, Li Z, Ding L, Ding SJ — Scrub typhus: Surveillance, clinical profile and diagnostic issues in Shangdong, China. *Am J Trop Med Hyg* 2012; **87**: 1099 104. doi: 10.4269/ajtmh. 2012.12 0306.
- 12 Brummaier T, Kittittrakul C, Choovichian V, Lawpoolsri S, Namaik I, Wattanagoon Y — Clinical manifestations and treatment outcomes of scrub typhus in a rural health care facility on the Thailand Myanmar border. *J Infect Dev Ctries* 2017; **11**: 407 13. doi: <https://doi.org/10.3855/jidc.8912>.
- 13 Pathania M, Amisha, Malik P, Rathaur VK — Scrub typhus: Overview of demographic variables, clinical profile, and diagnostic issues in the sub-Himalayan region of India and its comparison to other Indian and Asian studies. *J Family Med Prim Care* 2019; **8**: 1189-95.
- 14 Premraj SS, Mayilanthi K, Krishnan D, Padmanabhan K, Rajasekaran D — Clinical profile and risk factors associated with severe scrub typhus infection among non-ICU patients in semi-urban south india. *J Vector Borne Dis* 2018; **55**(3): 47-51.