

Hepatic dysfunction in Scrub typhus patients treated at tertiary care institute: A retrospective study

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Abstract

Introduction: Scrub typhus is endemic in a part of the world known as the Tsutsugamushi triangle and the most common rickettsial infection in the Indian subcontinent. Early diagnosis is important because there is usually an excellent response to treatment and timely anti-microbial therapy may help prevent complications.

Objective: To assess liver dysfunction in scrub typhus patients and to find association of morbidity and mortality with de-arranged liver function.

Material and method: A retrospective study was carried out on scrub typhus patients. A predesigned semi-structured questionnaire was used for collection of data. Data such as patient demographic details, clinical features, vital parameters and laboratory findings were collected from case records available at Medical Record Department (MRD) of the institute. The collected data were compiled and tabulated using MS Excel 2010. Results: Most of scrub typhus patients were in between age of 30 to 49 years of age. Fever (93.88%) was most common symptoms present in patients followed by headache (86.39%) and generalized weakness (69.39%). Eschar was present only in 38.09% of patients. Elevated liver enzyme such

as SGOT, SGPT and alkaline phosphatase was found in 85.71%, 87.76% and 59.86% patients respectively. Morbidity was significantly higher in patients having liver dysfunction.

Conclusion: The study reveals the wide range of clinical manifestations and complications of scrub typhus. Liver enzymes were elevated in majorities of the cases. Study emphasizes that when a patient presents with fever and elevated liver enzymes, scrub typhus should be considered as differential diagnosis.

Keywords: Scrub Typhus, Eschar, Liver Enzyme, SGOT, SGPT, Alkaline Phosphatase.

Introduction

Rickettsial diseases are considered some of the most covert emerging and re-emerging diseases and are being increasingly recognized in India. Among the major groups of rickettsioses, commonly reported diseases in India are scrub typhus, murine flea-borne typhus, Indian tick typhus and Q fever.¹

Scrub typhus is endemic in a part of the world known as the Tsutsugamushi triangle and the most common rickettsial infection in the Indian subcontinent. It is a zoonotic illness caused after the bite of a trombiculid mite larva carrying *Orientia tsutsugamushi*, an obligate intracytosolic bacterium. “Tsutsuga” means small and

dangerous and “mushi” means insect or mite. The mites use rodents as hosts.²

In India, the first case of scrub typhus was reported in 2009 from Kerala.³ Epidemics of scrub typhus have been reported in many parts of India, including the sub-Himalayan region.^{4,5} The common presentation of scrub typhus is fever, headache, myalgia, lymphadenopathy, hepato-splenomegaly with varying involvement of the major organs.^{6,7} *O. tsutsugamushi* infects the endothelium of the small blood vessels and causes vasculitis which may result in severe complications such as acute respiratory distress syndrome, hepatitis, renal failure, meningo-encephalitis, myocarditis and shock.^{7,8} An eschar at the site of chigger bite can be seen in early disease and is useful diagnostic clue in scrub typhus, though its frequency varies from 7-97%.⁹ The diagnosis is confirmed by serological testing.

Early diagnosis is important because there is usually an excellent response to treatment and timely anti-microbial therapy may help prevent complications. Mortality rates in untreated patients range from 0% to 30% and tend to vary with different geographical regions.^{6,8} Due to lack of awareness, nonspecific presentation, a low index of suspicion among clinicians, paucity of confirmatory diagnostic resources and clinical symptoms mimicking other more prevalent diseases such as dengue, malaria and leptospirosis, scrub typhus is under diagnosed in India, especially in Rajasthan.¹⁰

Scrub typhus may cause mild symptoms, serious complications, or even death. The aim of this retrospective study was to provide a detailed panel of clinical and laboratory profile with special reference to hepatic dysfunction of this re-emerging disease in order to prevent serious complication and better

understanding of clinician in management of scrub typhus.

Objectives

1. To assess liver dysfunction in scrub typhus patients.
2. To find association of morbidity and mortality with de-arranged liver function.

Methodology

A retrospective study was carried out on 154 cases (aged ≥ 18 years old) with scrub typhus who were admitted in IPD of Department of General Medicine, SRG Hospital attached with Jhalawar Medical College, Jhalawar, Rajasthan between July 2017 and June 2019. The patients having IgM antibodies against *Orientia tsutsugamushi* in their serum, diagnosed as having scrub typhus and admitted during study period in various units of medicine department were included. Total 07 patients having co-morbid condition like chronic renal failure, chronic liver disease, patient with known neoplastic disease and patients co-infected with dengue, malaria and typhoid fever were excluded from the study. A predesigned semi-structured questionnaire was used for collection of data. Data were collected from case records available at Medical Record Department (MRD) of SRG hospital such as patient demographic details, clinical features and vital parameters. Laboratory findings such as complete blood count including platelet count, liver function tests, renal function tests, serum electrolytes and protein were recorded as such. Various complications such as acute renal failure, hepatitis, Acute Respiratory Distress Syndrome, meningitis, myocarditis, etc. were also recorded.

Ethical Approval

Ethical approval was taken from institutional ethic committee of Jhalawar Medical College, Jhalawar before the study.

Statistical Analysis:- The collected data were compiled and tabulated using MS Excel 2010 and analyzed using statistical software SPSS trial version 20. Appropriated tables and figures were generated. The results were expressed in percentages. Chi-square test was applied to determine association. P value < 0.05 was considered as statistically significant.

Results

During the study period total 154 patients of scrub typhus were treated at SRG hospital. Records of all scrub typhus patients were assessed. Out of 154 patients, 07 were found to have co-morbid condition such cirrhosis etc were excluded from study and rest 147 patients were assessed for clinical and laboratory parameters.

Table 1: Socio-demographic characteristic of Scrub typhus patients. (n= 147)

Characteristic	Number of patients (%)
Age	
18 – 29	29(19.73%)
30 - 39	42(28.57%)
40 - 49	39(26.53%)
≥ 50	37(25.17%)
Gender	
Male	86 (58.50%)
Female	61(41.50%)
Residence	
Rural	114(77.55%)
Urban	33(22.45%)
Religion	
Hindu	93(63.26%)

Muslim	52(35.38%)
Others	02(1.36%)
Occupation	
Agricultural or related work	109(74.15%)
Others	38(25.85%)

Socio-demographic characteristic of scrub typhus patients are depicted in table 1. Most of scrub typhus patients were in between age of 30 to 49 years of age (55.10%) followed by ≥ 50 years of age (25.17%). Scrub typhus was predominant in male (58.50%) with male to female ratio of 1.40:1. More than 75% patients belonged to rural area and most were related to agriculture or related labor work (74.15%). 63.26% patient were Hindus followed by Muslims (35.38%) and only 02 patient belonged to other religions.

Table 2: Clinical feature of Scrub typhus patients. (n=147)

Clinical features	Number of patients(%)
Duration of symptoms	
<7 days	23(15.64%)
7 – 14 days	98(66.67%)
>14 days	26(17.69%)
Symptoms	
Fever	138(93.88%)
Chills	112(76.19%)
Headache	127(86.39%)
Abdominal pain	43(29.25%)
Nausea/ vomiting	28(19.04%)
Cough	69(46.94%)
Breathlessness	33 (22.45%)
Haemoptysis	04(2.72%)
Skin rash	17(11.56%)
Diarrhea	19(12.93%)

Altered sensorium	07(4.76%)
Generalized weakness	102(69.39%)
Other	113(76.87%)
Signs	
Icterus	31(21.08%)
Oedema	25 (17.01%)
Lymphadenopathy	16(10.88%)
Hepato-splenomegaly	52(35.37%)
Eschar	56(38.09%)

Table 2 depicts clinical feature of scrub typhus patients. Majority of patients (84.35%) were having symptoms since 7 or more days when they present first time to medicine OPD at SRG hospital. Fever (93.88%) was most common symptoms present in patients followed by headache (86.39%) and generalized weakness (69.39%). Fever was associated with chills in 76.19% patients. On examination of these patients, icterus, oedema and lymphadenopathy was found in 21.08%, 17.01% and 10.88% patients respectively. On abdominal examination, hepato-splenomegaly was present in 35.37% patient. Pathognomic feature of scrub typhus, eschar was present only in 38.09% of patients.

Table 3: Laboratory findings of Scrub typhus patients. (n=147)

Laboratory findings	Number of patients(%)
Anaemia	71(48.29%)
Leucopenia	20(13.61%)
Leucoctosis	42(28.57%)
Platelet <1.5 lakh/cu mm	74(50.34%)
Platelet <50,000 /cu mm	12 (08.16%)
S. bilirubin>2 gm %	38(25.85%)
SGOT	126(85.71%)
SGPT	129(87.76%)
Increased alkaline	88 (59.86%)

phosphatase	
S. creatinine	26(17.69%)
Decrease serum albumin <3.5 gm/dl	103(70.06%)

Table 3 depicts laboratory finding of scrub typhus patients. Anaemia was found in 48.29% of patients. WBC count was high in 28.57% and low in 13.61% patients. Platelet count below 1.5 lakh was in 58.50% of patients and among them 08.16% having counts below 50,000. On examination, icterus was found in 21.08% of patients although bilirubin >2 gm% was found in 25.85% cases. Elevated liver enzyme such as SGOT, SGPT and alkaline phosphatase was found in 85.71%, 87.76% and 59.86% patients respectively. Serum creatinine was high in 17.69% of cases. Decrease serum albumin <3.5 gm/dl was present in 70.06% cases.

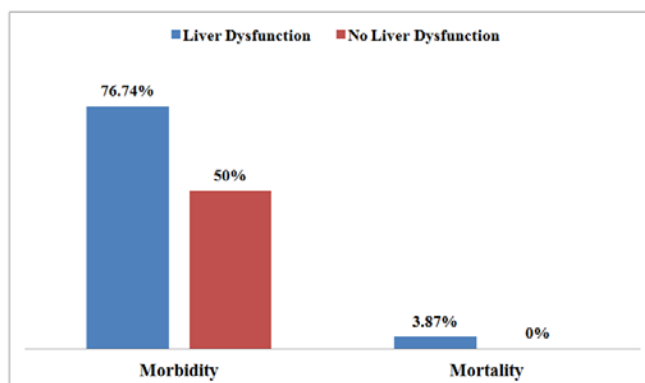


Figure 1: Morbidity and Mortality among Scrub typhus patients associated with Liver dysfunction.

Morbidity and mortality among Scrub typhus patients associated with liver dysfunction is illustrated in figure 1. Out of 129 scrub typhus patients having liver dysfunction, morbidity in form of shock, pneumonia, ascites, pleural effusion, acute renal failure etc was encountered in 76.74% of cases. Morbidity was significantly higher in patients having liver dysfunction (p=0.016). All patients (05) died during treatment were

having liver dysfunction although association was not statistically significant ($p=0.39$).

Discussion

In present study, 147 scrub typhus patients were assessed for clinical and laboratory parameters. Most of patients (55.10%) were in age group of 30 to 49 years and most (74.15%) were related to agriculture or related labor work. These findings are in consistent with study by Bibhuti Sahaet al¹¹ and Imandar S et al¹². These findings can be explained with the fact that scrub typhus occurs more among those people who used to engage in occupational or recreational behavior that brings them into contact with mite-infested habitats such as brush and grass. As Hindu religion is preponderance in our study area, 63.26% patients were Hindus followed by Muslims (35.38%) in our study.

In present study, Scrub typhus was predominant in males (58.50%). This is in accordance to study by Bibhuti Sahaet al¹¹. There was nearly equal incidence of scrub typhus among female and male population with slight preponderance to females (51%) in study by James Philomena et al¹³.

More than 75% patients belonged to rural area in present study. Similar to our study, 78.6% patients were from rural area in study by Bibhuti Sahaet al¹¹.

Fever was the most common symptoms (93.88%) present in patients in our study. These finding was consistent with other studies who also reported fever as the commonest presenting feature.^{14,15}. Apart from Fever, headache (86.39%) and generalized weakness (69.39%) were the other symptoms reported by patients.

Lymphadenopathy was found in 10.88% patients in our study. On abdominal examination, liver and spleen were found palpable in 35.37% patient. Hepato-

splenomegaly as well as lymphadenopathy were found to be common in various other studies.^{11,16,17}

In scrub typhus, usually an eschar of approximately 5-20 mm in diameter is formed at the site bitten by trombiculid mites¹⁸. In our study, pathognomic feature of scrub typhus, eschar was present only in 38.09% of patients similar to a study done by James Philomena et al¹³ and Varghese GM et al⁸. Eschar was found in only 3 of the 14 patients (21.4%) in study by Bibhuti Sahaet al¹¹. Various other studies found prevalence of eschars to vary from 7-97%.⁹

In our study, Leukocytosis was found in 28.57% and Thrombocytopenia was in 58.50% of patients similar to the study done by James Philomena et al¹³. Increased serum bilirubin (>2 gm%) was found in 25.85% cases in our study which is in accordance to study by Bibhuti Sahaet al¹¹.

In our study, elevated liver enzyme such as SGOT, SGPT and alkaline phosphatase was found in 85.71%, 87.76% and 59.86% patients respectively. The mechanism of this characteristic hepatocellular-patterned dysfunction is not clear, but is speculated pathologically. The infection of *Orientia tsutsugamushi* is pathologically characterized by focal or disseminated vasculitis and perivasculitis on the affected organs. Thus, scrub typhus infected in liver is speculated to cause mild focal inflammation due to intrahepatic sinusoidal endothelial vasculitis and to increase the levels of aminotransferases due to direct cytopathic liver damage.^{19,20,21}. Similar findings have been observed in other studies also.^{11,12}. Elevated liver enzymes was present in only 26% of cases in study by Kumar R et al.⁴

In our study, out of 129 scrub typhus patients having liver dysfunction, morbidity in form of shock, pneumonia, ascites, pleural effusion, acute renal failure

etc. was encountered in 76.74% of cases. Morbidity was significantly higher in patients having liver dysfunction ($p < 0.05$). In a study published by Palanivel et al²² pleural effusion, ascites, shock and respiratory failure were seen in 61%, 47%, 45%, 34% cases, respectively. Acute kidney injury, hepatic failure, multiorgan dysfunction syndrome (MODS), meningoencephalitis and acute respiratory distress syndrome (ARDS) were seen in 10%, 10%, 7%, 6% and 4% cases, respectively.

This study highlights the need for increased awareness of rickettsial infections in north-western India. The diagnosis of scrub typhus should be largely based on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation. Use of empirical treatment may also be considered to decrease the high morbidity and mortality associated with the disease.

Conclusion

The study reveals the wide range of clinical manifestations and complications of scrub typhus. Liver enzymes were elevated in majorities of the cases. Morbidity was significantly higher in patients having liver dysfunction. Though eschar is pathognomonic of the disease, its absence does not rule out scrub typhus. Study emphasizes that when a patient presents with fever and elevated liver enzymes, scrub typhus should be considered as differential diagnosis and an empirical treatment should be started if there is high index of suspicion to prevent the complications.

Reference

1. Guidelines for diagnosis and management of rickettsial diseases in India. New Delhi: Department of Health Research Director General, Indian Council of Medical Research; 2015 February. 20p.

2. Mahajan SK. Scrub typhus. J Assoc Physicians India 2005;53:954-8.
3. Ittyachen AM. Emerging infections in Kerala: A case of scrub typhus. Natl Med J India 2009;22:333-4.
4. Kumar R, Thakur S, Bhawani R, Kanga A, Ranjan A. Clinical profile and complications of scrub typhus: Hospital-based study in sub-Himalayan region. J Assoc Physicians India 2016;64:30-4.
5. Mahajan SK, Rolain JM, Kashyap R, Bakshi D, Sharma V, Prasher BS, et al. Scrub typhus in Himalayas. Emerg Infect Dis 2006;12:1590-2.
6. Scrub typhus. Available at www.apiindia.org/medicine_update_2013/chap_06.pdf. Accessed on 12 July 2019.
7. Sankhyan N, Saptharishi LG, Sasidharan K, Kanga A, Singhi SC. Clinical profile of scrub typhus in children and its association with hemophagocytic lymphohistiocytosis. Indian Pediatr. 2014;15:651-3.
8. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, Abraham OC, Kavitha ML. Clinical profile and improving mortality trend of scrub typhus in South India. Int J Infect Dis. 2014;23:39-43
9. Kaushik RM, Kaushik R, Bhargava A. Multiple eschars in scrub typhus. Tropical Medicine and Health [serial on the Internet]. 2014
10. Isaac R, Varghese GM, Mathai E, Manjula J, Joseph I. Scrub typhus: Prevalence and diagnostic issues in rural southern India. Clin Infect Dis 2004;39:1395-6.
11. SahaB, ChatterjiS, MitraK, GhoshS, NaskarA, Ghosh MK et al. Socio demographic and Clinico-Epidemiological Study of Scrub Typhus in Two Tertiary Care Hospitals of Kolkata. Journal of

- The Association of Physicians of India 2018;66:22-25.
12. Imandar S, Thunga G, Acharya R, et al. Study of Clinical Characteristics and Treatment Pattern of Scrub Typhus in Tertiary Care Hospital. *J Pharmaceut Sci Res* 2013; 5:107–110.
 13. Philomena J, Rangaswami M, Prathiba P. A study on demographic, clinical profile and outcome of scrub typhus. *Int J Adv Med* 2016;3:586-90.
 14. Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S. Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India*. 2010;58:24-8.
 15. Somasekar HR, Prabhakar DM, Sreeja P, Elizabeth M, Didier R, Jean MR. Magnitude and features of scrub typhus and spotted fever in children in India. *J Trop Pediatr*. 2006;52:22.
 16. Fiang YF, Kim S, Wook YD, et al. Scrub Typhus: Clinical, Pathologic, and Imaging Findings. *Radio Graphics* 2007; 27:161–172.
 17. Aung-Thu, Supanaranond W, Phumiratanaprapin W, et al. Gastrointestinal manifestations of septic patients with scrub typhus in Maharat Nakhon Ratchasima Hospital. *Southeast Asian J Trop Med Public Health* 2004; 35:845-51.
 18. Chogle AR. Diagnosis and treatment of scrub typhus-the Indian scenario. *J Assoc Physicians India* 2010;58:11-12.
 19. Kanno A, Yamada M, Murakami K, Torinuki W. Liver involvement in Tsutsugamushi disease. *Tohoku J Exp Med*. 1996;179(3):213-217.
 20. Watanabe H, Saito T, Misawa K, Suzuki A, Sanjo M, Okumoto K, et al. Direct cytopathic liver injury and acute respiratory distress syndrome associated with Gilliam type tsutsugamushi disease. *J GastroenterolHepatol*. 2005;20(6):969-971.
 21. Chung JH, Lim SC, Yun NR, Shin SH, Kim CM, Kim DM. Scrub typhus hepatitis confirmed by immunohistochemical staining. *World J Gastroenterol*. 2012;18(36):5138-5141.
 22. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. *Indian J Pediatr*. 2012;79(11):1459-62.