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Original Research Article

Clinical and biochemical profile in patients of scrub typhus: an under reported disease-a tertiary care hospital based study in Uttarakhand, India

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ABSTRACT

Background: Scrub typhus is an emerging but neglected infectious diseases that generally results in acute febrile illness, with spectrum of diseases ranging from mild illness to multiorgan dysfunction. Hence we planned this study to know the demographic, clinical and biochemical profile of scrub typhus patients in hilly state of Uttarakhand.
Methods: This was a prospective observational study conducted from June 2020 to November 2020 in the Department of Internal Medicine, in a tertiary care institution located in state of Uttarakhand, India. All scrub typhus patients were evaluated by detailed history, examination and laboratory tests.
Results: Among 60 cases, the mean age of patients was 38.3±15.43 years, with majority of patients (70.2%) being young adults between the age 18-40 years. Majority of patients were females (60.0%) with (M:F-1:1.3). 53.3% patients reported from rural and 46.7% patients from urban area. Fever (100%), cough and breathlessness (40.0%), nausea and vomiting (20%), abdominal pain and diarrhoea (16.7%), headache (16.7%) and altered sensorium (8.3%) were the predominant clinical features. Hepatic dysfunction (51; 85.0%) and respiratory dysfunction (25; 41.6%) were the commonest findings followed by renal dysfunction (13; 21.7%).
Conclusions: Scrub typhus is often misdiagnosed or diagnosed late due to its wide clinical spectrum overlapping with clinical presentation of other commonly prevalent tropical diseases. An increasing awareness of this disease coupled with prompt management will go a long way in reducing both morbidity and mortality in this disease.

Keywords: Acute undifferentiated febrile illness, Adult respiratory distress syndrome, *Leptotrombidium* mites, *Orientia tsutsugamushi*

INTRODUCTION

Scrub typhus, caused by the bacteria *Orientia tsutsugamushi* and transmitted by *Leptotrombidium* mites, is responsible for a potentially fatal tropical infection which is a grossly under-recognized public health problem in India.[1,2] The disease is known to be endemic to the geographically confined area of the Asia-Pacific region termed as the 'tsutsugamushi triangle', which covers South and Southeast Asia, Northern Australia, and the islands of the Indian and Pacific Oceans.[1]

There has been a resurgence of scrub typhus across India in the recent years; and scrub typhus has re-emerged as a major cause of acute undifferentiated febrile illnesses

(AUFI) with high morbidity and mortality.[3,4] Scrub typhus commonly manifests with fever, breathlessness, cough, headache, nausea/vomiting, and altered sensorium. In some areas of the country, scrub typhus accounts for up to 35-50% of acute undifferentiated febrile illnesses requiring hospital admissions.[5,6] About a third of the scrub typhus cases requiring hospitalization have multi-organ dysfunction with pulmonary, hepatic, cardiac, neurological, or renal complications leading to high fatality rates.[4,7] Studies from India reveal that the case fatality rate (CFR) of scrub typhus ranges from 1.3% to 33.5% depending on the organ involvement and complications present.[8-10]

In view of resurgence in cases of scrub typhus in recent years in state of Uttarakhand, it is important to study the demographic, clinical and biochemical profile of patients of scrub typhus.

METHODS

This was a prospective observational study conducted in the Department of Internal Medicine, Shri Mahant Indiresh Hospital (SMIH) Dehradun, a tertiary care hospital in state of Uttarakhand, from June 2020 to November 2020. We enrolled a total of 60 patients for the study, who fulfilled the inclusion and exclusion criteria as mentioned below.

Inclusion criteria

Patients with pyrexia, age more than 18 years, and tested positive for IgM antibodies against *O. tsutsugamushi* by solid phase immunochromatographic assay were included.

Exclusion criteria

Patients who had other causes of fever like malaria, dengue, viral diseases, leptospirosis, typhoid fever, pneumonia, pleural effusion, urinary tract infections. Patients tested negative for IgM, IgG, antibodies against *O. tsutsugamushi* and patients who didn't gave their consent for the study were excluded.

Ethical approval was taken from institutional ethical committee. Written consent was taken from all the patients. All demographic data, detailed history, and complications were recorded. Area of residence, detailed clinical examination, presence or absence of eschar was noted. All patients admitted with history of fever were subjected to investigations to establish the cause of fever. Out of these, patients who were positive for IgM scrub typhus antibodies and needed indoor admission were enrolled for the study. Test for serum IgM for scrub typhus was done in the microbiology department of our hospital. A chest X-ray (CXR- PA view), arterial blood gas (ABG) analysis, electrocardiogram (ECG) were ordered as and when required. A CT scan of the brain and cerebrospinal fluid (CSF) analysis was done in selected patients with altered sensorium. All the patients were followed until discharge or death. The data was collected on Microsoft Excel spread sheet.

RESULTS

Age and sex distribution of the patients

Demographic data and clinical profile of the patients is depicted in Table 1. The mean age of the patients was 38.8±15.43 years. Most of the patients were young, with majority of patients (70.2%) were less than 40 year of age. Females were slightly more affected with male to female ratio of 1:1:3. 53.3% patients were from rural area which slightly outnumber the patients from urban area 46.7%.

Table 1: Distribution of demographic data and clinical profile of 60 patients of scrub typhus included in the study.

Variables	No. of cases	Percentage
Age (in years)		
18-30	16	26.7
31-40	26	43.5
41-50	12	20.0
> 50	06	10.0
Gender		
Female	36	60.0
Male	24	40.0
Duration of illness (days)		
< 7 days	16	26.7
8-14 days	40	66.7
> 14 days	4	6.6
Rural/urban		
Rural	32	53.3
Urban	28	46.7
Clinical features		
Symptoms		
Fever	60	100.0
Breathlessness	24	40.0
Nausea/vomiting	12	20.0
Headache	10	16.7
Abdominal pain & diarrhoea	10	16.7
Altered sensorium	5	8.3
Jaundice	11	18.9
Signs		
Pallor	13	21.7
Icterus	11	18.3
Hepatomegaly	11	18.3
Splenomegaly	13	21.7
Meningeal signs	5	8.3
Eschar	5	8.3

Distribution of clinical characteristics of patients with scrub typhus

All the patients presented with fever with a mean duration of 7.9±3 days. The fever was high grade, continuous and in majority of the patients (66.7%) the duration of fever was between 7-14 day. Cough and breathlessness was seen in (40.0%) patients followed by nausea and vomiting in 20.0% and headache in 16.7%. Other associated symptoms like abdominal pain and diarrhoea in 16.7%, altered sensorium in 8.3% and jaundice was seen in 20.0% patients. On examination, pallor in 21.7% was the most common finding followed by icterus 18.3%. Hepatomegaly was present in 11 (18.3%) and splenomegaly in 13 (21.7%) patients. Among patients presenting with altered sensorium, signs of meningeal irritation (neck rigidity and/or Kernig's sign) were present only in 5 patients (8.3%). Eschar was seen in 5 patients (8.3%).

Biochemical profile of patients with scrub typhus

The biochemical profile is depicted in Table 2. Complete blood count revealed anaemia in 13 (21.7%), leucocytosis in 22 (36.7%) and thrombocytopenia in 22 (36.7%) patients. Liver function test showed rise in SGOT and SGPT in 51 (85.0%) and 50 (83.3%) patients, respectively. The mean SGOT levels were 236 U/l compared with mean SGPT levels of 137 U/l. The rise in SGOT was more than SGPT with (SGOT/SGPT ratio >1) and hyperbilirubinemia (bilirubin >2mg/dL) in 11 (18.3%) patients. Acute kidney injury characterized by recent elevation of blood urea 34 (56.7%) and serum creatinine was seen in 13 (21.7%) patients.

Table 2: distribution of biochemical profile of the 60 patients of scrub typhus included in the study.

	Minimum	Maximum	Mean±Std deviation
Age (years)	20	68	38.3±15.43
Duration of illness (days)	3.0	16.0	7.9±3.06
Haemoglobin (gm/dl)	06	15.8	10.47±1.98
Total leucocyte count (TLC)	1900	26800	9964.17±5289.5
Neutrophil (n) %	40	94	68.08±13.69
Lymphocyte (l) %	5.0	56.0	27.95±13.65
Platelet count	40,000	2,23000	96000.15±10007.86
ESR	6.00	80.00	33.03±19.62
Bilirubin (mg/dl)	0.7	17.0	1.77±2.89
SGOT (U/l)	16.0	7014	236±895.36
SGPT (U/l)	5.0	3056	137.32±391.35
ALP (U/l)	59.00	831.00	193.05±146.92
GGT (U/l)	3.0	655.0	144.82±130.06
Albumin (g/dl)	1.6	5.7	3.00±0.76
Globulin (g/dl)	0.7	4.4	3.09±0.63
Urea (mg/dl)	8.0	199	46.62±32.91
Creatinine (mg/dl)	0.4	3.40	0.98±0.53
Sodium (Na) mmol/l	115	155	124.0±12.0
Potassium (K) mmol/l	2.8	6.4	3.8±1.8

Distribution of complication seen in patients of scrub typhus

The complications of scrub typhus in our patients are depicted in Table 3.

Acute hepatitis was the most common complication seen in our study. Hepatic dysfunction was seen in (51; 85.0%), was the commonest followed by respiratory dysfunction in (25; 41.6%) and renal dysfunction in (13; 21.7%) respectively. Among the 25 patients with respiratory dysfunction, pleural effusion (08, 13.3%) and pulmonary infiltrates on chest X-ray (08, 13.3%) were the commonest, followed by ARDS in (06; 10.0%) and pulmonary edema in (03, 5.0%) respectively.

Table 3: Distribution of complications of scrub typhus in patients included in study.

Characteristic	No of cases	Percentage
Hepatic dysfunction	51	85
Renal dysfunction	13	21.7
Pneumonia	8	13.3
Pleural effusion	8	13.3
ARDS	6	10.0
Acute encephalitis	5	8.3
Pulmonary edema	3	5.1

DISCUSSION

Scrub typhus is an under-reported rickettsial disease prevalent in India. In our study 60 patients were enrolled and followed during hospitalisation till discharge or death. Total 6 patients died out of the enrolled 60 patients.

The study was conducted from month of June- November 2020 for a period of 6 months. In Uttarkhand maximum rainfall occurs between July to September with humidity ranging from 60 to 85% and temperature around 15-30°C in lower altitudes. These conditions are conducive for the spread of vectors of scrub typhus (trombiculid mite) and maximum cases have been reported in monsoon and post monsoon season.

Most of the patients were young with mean age of 38 years with almost 70.2% patients were <40 years of age. Maximum number of patients were in age group of 31-40 year. Female were slightly more affected than male with M;F ratio of 1:1.3. Uttarakhand being a hilly state and young people especially females are actively involved in outdoor activies like agriculture, farming and collecting fooder for animals and wood for cooking which make them vulnerable to bite of mites (chigger). Sharma et al in their study also reported that 64% patients were < 40 year of age, almost same as in our study.[11]

Almost all patients presented with high grade continuous fever, which was relieved only with antipyretics. Most patients 93.4% reported in our study, had history of fever between 7-14 days with mean duration of 7.9±3 days. This study was conducted in a tertiary care centre and gets referrals from almost every corner of Uttarakhand, so most patients had a history of fever lasting >7 days. Lakshmi et al.[12] Also found that majority of the patients (58.6%) presented with 7–14 days of fever and 10.3% of them had prolonged pyrexia beyond 2 weeks. Similarly, Pathania et al reported mean duration of illness 9.8±4 days, which is almost same as found in our study.[13]

Hepatic dysfunction in the form of acute hepatitis with rise in SGOT and SGPT (51; 85.0%) was the most common complication in our study with SGOT/SGPT ratio >1. Hyperbilirubinemia was found in 11 (18.3%) patients. Hepatomegaly in 11 (18.3%) and splenomegaly in 13 (21.7%) patients. According to study done by Zhang et al, abnormal liver function test was the most common laboratory finding.[14] Elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) found in 75.0% and 80.3% of the patients, Lakshmi et al concluded that markers of severe disease include elevated aspartate amino transferase (AST) and serum creatinine and were seen in 82.7%, and 20.6% patients, respectively.[12]

Respiratory dysfunction (25; 41.6%) was seen in the form of pneumonia (8;13.3%), pleural effusion (8;13.3%), ARDS (6; 10.0%) and pulmonary edema (3;5.1%) . Renal dysfunction in the form of acute kidney injury (AKI) characterized by recent elevation of blood urea 34 (56.7%) and serum creatinine was seen in 13 (21.7%) patients. Pathania et al, Subbalaxmi et al and Griffith et al also reported 12% to 22% of AKI in their studies.[13,15,16] AKI was found in 18.7% cases in study done by Jayprakash et al.[17]

Biochemical findings which support the diagnosis of scrub typhus are anaemia, thrombocytopenia, leukocytosis, and elevated transaminases with SGOT/SGPT ratio >1. Similarly, study conducted by Varghese et al showed a combination of raised transaminases, thrombocytopenia and leucocytosis confers 80% specificity and 80% positive predictive value for scrub typhus diagnosis.[18]

CONCLUSION

Scrub typhus has become a leading infectious disease in northern India and an important cause of acute undifferentiated febrile illness. Early presentation of disease with duration of fever <7 days has better prognosis. Multiorgan failure, renal, liver and respiratory dysfunctions are the important life-threatening complications that lead to higher case fatality rates. Thus, in northern India, an increasing awareness about the disease presentation, clinical features, laboratory findings and prompt management will help in reducing both morbidity and mortality. Scrub typhus should be kept as one of the differential diagnoses of acute undifferentiated febrile illness.

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