Clinical Profile and Complications of Scrub Typhus: Hospital-Based Study in Sub-Himalayan Region

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Abstract

Background: Scrub typhus is a documented disease in Himachal Pradesh, but there have been no clinico-epidemiological studies in this area. The present study is done with IgM ELISA as a diagnostic test which has higher sensitivity and specificity as most of previous studies had used Weil Felix test as a diagnostic test.

Methodology: This was a prospective observational study. All the patients more than 18 years of age with positive IgM ELISA for scrub typhus with or without eschar were included. The clinical profile was observed. IgM scrub typhus was done by kit method manufactured by InBios International, Inc.

Results: Total 330 patients were observed. Maximum patients were observed in August, September, and October. Fever was the most common presenting complaint. Eschar was present in 40.61% patients. Complications were seen in 71.2%.

Conclusion: The general physicians should be sensitized for the early diagnosis to reduce mortality.

Introduction

Scrub typhus is an acute febrile, infectious illness caused by rickettsia O. tsutsugamushi. It was first described in detail by Hashimoto from Japan in 1810.¹ Scrub typhus is endemic to a part of world known as the “tsutsugamushi triangle” which extends from northern Japan and far-eastern Russia in the north, to northern Australia in the south, and to Pakistan and Afghanistan in the west.² In India rickettsial infections have been documented from the states of Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Rajasthan, Assam, West Bengal, Maharashtra, Kerala and Tamil Nadu³. Himachal Pradesh is a mountainous state in northern India, with the altitude of 350-7000 meters above mean sea level. During the rainy seasons, areas at lower altitudes experience average temperature between 20 to 35°C which is suitable for the spread of arthropod vector⁴. Scrub typhus is a zoonosis and human are accidental hosts. The incubation period ranges from 6 to 21 days. The onset of disease is characterized by high fever (104-105°F), headache, myalgia, cough, conjunctival suffusion and gastrointestinal symptoms. An eschar at the site of chigger bite, regional lymphadenopathy and a maculopapular rash may provide a clue to diagnosis. Mortality rates in untreated patients range from 0-30% and tend to vary with the patient’s age and region of infection and if severe complications such as ARDS arise, mortality may still be higher. Scrub typhus is a documented disease in Himachal Pradesh, but there have been no clinico-epidemiological studies in this area, so this study was planned to provide the knowledge regarding various aspects of scrub typhus in adult age group. The present study is done with IgM ELISA as a diagnostic test which has higher sensitivity and specificity as most of previous studies had used Weil Felix test as a diagnostic test.

Methodology

This was a prospective observational study done in the
department of Medicine and Microbiology IGMC, Shimla from July 2012 to June 2013. All the patients more than 18 years of age admitted with febrile illness with positive IgM ELISA for scrub typhus with or without eschar were included in the study. The clinical profile was observed using a detailed history of symptoms, travel, recreation, agricultural activities, treatment record prior to admission and a detailed examination and the treatment outcome was noted. Fever workup including cultures, CXR, CSF analysis, serology for scrub was done. IgM scrub typhus was done by kit method manufactured by InBios International, Inc. This was qualitative ELISA for the detection of IgM antibodies to O. tsutsugamushi in serum. Statistical analysis was done using EPI info 2000 (Centre Of Disease Control And Prevention, Atlanta, GA, USA) and SPSS student version 16.0 (SPSS inc, Chicago, US).

**Results**

This study included a total number of 330 patients of proven scrub typhus, admitted in the Medicine ward in Indira Gandhi Medical College, Shimla between July 2012 to June 2013. Only those patients who tested positive for IgM ELISA for scrub typhus were included and observed. Out of the 330 patients 250 were females (75.75%) and 80 were males (24.24%). Mean age at presentation was 40.12 ± 14.65 years with range of 18-74 years. Maximum number of patients (94) was in age group of 18-29 years as this age group is mostly engaged in farming. Majority of the patients were farmers 295 (89.40%) and only 33 (10%) patients had other profession but indirectly they were also involved in agricultural activities. 319 (96.66%) patients belonged to rural areas and 11 (3.33%) to urban areas in the study. Demographic profile of the patients has been tabulated in Table 1.

In our study the number of cases started rising in August 17(5.20%), peaked in September 156(47.30%), October 141(42.70%) declined thereafter. 314(95%) of all our cases occurred in three months of peak rainy season and only 5% cases occurred during rest of year which is statistically significant (p=.000). Fever was the main complaint, present in 329 (99.99%) patients followed by headache 196 (59%), myalgia 170 (51%), shortness of breath 150 (45.50%), abdominal pain 103(31.20%), vomiting 93(28.20%), cough 72(21.80%), altered sensorium 57(17.70%), loose stool 35 (11.20%), facial puffiness 27(8.20%), decreased urine output 19(5.80%), sore throat 18 (5.50%), decreased hearing 1(3.80%), swelling feet 6(1.80%) and seizures 4 (1.20%). At the time of admission clinical signs noted were temperature > 100°F in 317 (96.10%) patients, tachycardia 317 (96.90%), hypotension 123 (37.80%), congested eyes 152 (46.10%), tachypnea 134 (40.60%), pallor 110 (33.3%), icterus 81 (24.50%), eschar 134(40.61%), lymphadenopathy 58 (17.50%), skin rash 48 (14.54%), cyanosis 8 (2.40%), edema 6 (1.80%), raised JVP 5 (1.50%) patients (Table 2). Eschar was most commonly seen in inguinal 38 (29%) followed by abdomen 27 (20.6%), axilla 24% (18.32%), lower limbs lower limbs 15 (11.2). Lymphadenopathy was present in 55 (16.6%) of patients and was tender. It was present in axilla 26(47.27%), cervical 17 (30.9%), inguinal 4 (7.2%) and multiple sites 8 (14.52%) (Table 2).

Complications rates were also quite high with 71.2% of patients having hepatic dysfunction, 69% patients having features of sepsis and 42% patients having renal dysfunction (Table 3). We analysed patients for individual system manifestations and abnormalities and tabulated in Table 4. Mortality rate was 8.5% and these patients had > 7 days of febrile illness, and had multiple more severe complications at presentation.

**Discussion**

We observed total 330 patients confirmed by IgM ELISA for scrub typhus. Out of the 330 patients 250 were females (75.75%) and 80 were males (24.24%) with the ratio of 3.12: 1. The higher incidence in female may be associated, with conventional working behaviour in hilly states where females actively participate in the farming work and tend to work in a squatting position, whereas male tend to work in a standing position, with tools. Similar observations had been made in a Korean and other Indian studies.\(^{5-7}\) Mean age at presentation was 40.12 ± 14.65 years with range of 18-74 years. Maximum number of patients (94) was in age group of 18-29 years as this age group is mostly engaged in farming. Majority of the patients were farmers 295 (89.40%) and only 33 (10%) patients had other profession but indirectly they were also involved in agricultural activities. 319 (96.66%) patients belonged to rural areas and 11 (3.33%) to urban areas in the study. Participation in outdoor agricultural and farming activities form most important factor in both urban and rural inhabitants determining the occurrence of scrub typhus. This correlation had been observed in 34.4% to 100% in medical literature.\(^{8-10}\) In our study the number of cases started rising in August 17(5.20%), peaked in September 156(47.30%), October 141(42.70%) declined thereafter. 314(95%) of all our cases occurred in three months of peak rainy season and only 5% cases occurred during rest of year which is statistically significant. In Himachal heavy rainfall occurs between July to September with humidity ranging from 65 to 85% and temperature around 15-30°C in lower altitudes. These conditions are conducive for spread of vector of the scrub typhus.\(^{5,11,12}\) Fever was the main symptom of presentation present in 99.9% patients accompanied by
generalised symptom of myalgias, headache, pain abdomen. An eschar at the site of mite is single most useful diagnostic clue. In our study the eschar was found in 134 (40.61%) of the patients which was similar to 41.7%, 46% from studies done by Dass et al at Meghalaya and M. Vivekanandan et al study at Pondicherry, while most studies of the Oriental countries had eschar in 60-70% patients. The probable explanation for the less frequency
of eschar in South East Asia is variation in cutaneous immunity as well as dark skin of the patients. Active search must be carried out to find the eschar at unusual locations as these are painless lesions. Lymphadenopathy was present in 55(17.50%). Patients usually feel lymph node swelling or tenderness in the draining lymph nodes. Quite a large number of patients presented with complications (70%). This high percentage of complications was most probably observed because maximum patients were referred cases and their treatment was delayed. Maximum number of patients 230 had hepatic dysfunction followed by renal dysfunction in 140 and septic shock in 73 patients. Patients had mild anaemia with leukocytosis with predominant lymphocytic response in 101 patients and neutrophilic reaction in 51 patients. Only 2 patients had leukopenia. We analysed the data for each system manifestations and found that in GIT/ hepatobiliary system abdominal pain was the most common symptom with icterus being the most common sign followed by splenomegaly. Quite substantial number of patients (20) developed acalculus cholecystitis and only 2 patients had pancreatitis. In our study, ascites was present in 27(8.18%) patients. Plasma leakage due to diffuse vasculitis and increased vascular permeability may cause low serum albumin leading to ascites and is a transient process. Upper gastrointestinal endoscopy findings in patients of upper gastrointestinal bleed were petechiae, superficial hemorrhage and erosive ulcers. The differentiating point for endoscopic findings in scrub typhus compared to other causes was that the stomach lesions were more frequent and severe than duodenal lesions. The central pathophysiology for derangement was widespread vasculitis due to multiplication of organisms in endothelial cells lining of the small blood vessels and the microangiopathy involving gastrointestinal tract can lead to gastrointestinal hemorrhage. Raised level of SGOT (>40IU) was present in 235 (71.12%) patients with range of 15-6732 IU (mean of 173.90±388.48 IU), raised level of SGPT (>30IU) was present in 234 (71%) of patients with range of 11-4294 IU (mean of 127.57±258.37 IU). Hypoalbuminemia (<3g/dl) was found in 167 (50.60%) of patients (mean of 2.90±6.6g/dl). Similar to our study Mahajan et al13 and Jim et al16 had also observed raised transaminase levels in 66.67% of patients. In our study 57 (17.20%) patients had presented with altered sensorium with Glasgow Coma scale less than 15. Other neurological feature were cerebellar signs in 5 (1.50%), meningeal signs in 10 (3.60%) and seizure in 4 (1.2%) patients. Similar findings were seen in Vivekanandan12 and Vikrant et al13 studies. Cranial nerve involvement in the form of bilateral papilloedema, 3rd nerve palsy, and 6th nerve palsy was present in 1 patient each, 7th nerve palsy in 2 patients and 8th nerve palsy in 3 patients. In a study conducted by George M. Varghese et al20 at Christian Medical College Vellore has reported meningitis or meningencephalitis in 19.2% similar to our study. Kim et al21 had described 6th and 7th nerve palsy. There were three patients of hearing loss in our study. Deafness has been described as a clue to the diagnosis of scrub typhus; awareness of this symptom facilitates early diagnosis. Acute hearing loss or hearing impairment in a febrile patient should arouse strong suspicion of scrub typhus. CSF analysis done in 30 patients revealed WBC with range of 4-300 with WBC mean 25.90±62.93, and lymphocytes in 12 (40%) patients with range of 4-200 with mean of 19.90±41 and raised protein in 20 (66%) and low sugar in 8 (26%). ADA was raised (>10 IU) in 5. IgM ELISA test to diagnose scrub typhus may give false positive result in tubercular meningitis. In our study shortness of breath was presenting complaints in 150 (45.50%) patients. Tachypnea (respiratory rate >24) present in 134 (30.60%) was suggestive of more severe respiratory involvement. Out of 60 patients 15 (25%) patients required ventilatory support. The incidence of the chest radiographic abnormalities for patients with scrub typhus varies from 67.7-78%. Literature reported interstitial pneumonia, cardiomegaly, pulmonary edema, pleural effusion, hilar adenopathy, and focal atelectasis as frequent pathologies. 1st degree heart block was observed in 3 (9%) patients, complete heart block in 1 (3%) patient, atrial fibrillation and flutter in 6 (1.8%) patients and congestive heart failure in 5 (1.5%) patients. Other ECG findings sinus tachycardia and nonspecific T wave changes were present in 86 (24.80%) Echocardiography was done in patients presenting with ECG changes showed minimal pericardial effusion in 7 patients with normal myocardial function and ejection fraction. All patients responded to treatment of scrub typhus and changes reverted. Endothelial cells invasion by rickettsia causes vasculitis and responsible for myocarditis and pericardial effusion. In our study acute kidney injury, hypokalemia and hyperkalemia were present in 140 (42%), 135 (40%), 23 (6.9%) which was similar to 44%, 35%, and 6% in study conducted by Vikrant et al.13 Only 2 patients required hemodialysis support. The presumed causes could be renal hypoperfusion resulting from shock or volume depletion, vasculitis, rhabdomyolysis, acute interstitial nephritis and direct micro invasion of the renal tubules causing acute tubular necrosis.

**Conclusion**

Scrub typhus is endemic in Himachal Pradesh and all cases of febrile illness during this period should be evaluated for scrub
typhus. The general physicians should be sensitized regarding symptoms, signs and management of Rickettsial disease and there should be a media campaign for the public, regarding the prevention of this disease with onset of monsoon, to reduce the morbidity and mortality associated with the disease.

References