

ORIGINAL ARTICLE

Socio-demographic and Clinico-Epidemiological Study of Scrub Typhus in Two Tertiary Care Hospitals of Kolkata

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Abstract

Background and Aims: Scrub typhus is the commonest of the rickettsial diseases in India and is difficult to diagnose. Untreated cases have fatality rates of 30-45%. Eschar is present in 7-97% cases. Pneumonia and acute respiratory distress syndrome (ARDS) are frequent complications. Serum immunoglobulin M capture ELISA is the most sensitive test. Doxycycline is the drug of choice. Our objectives were to study the socio-demographic and clinic-epidemiological profiles of scrub typhus cases in two tertiary care hospitals in Kolkata, India. This was the first study of scrub typhus in Southern West Bengal and its neighboring areas.

Methods: Study was conducted over 16 months and all fever cases of Tropical Medicine / Medicine outpatients' clinics were evaluated.

Results: Fourteen cases were diagnosed. 78.6% were from rural areas and 35.7% were farmers. Headache and fever were the commonest presenting complaints while eschar was found in only 21.4%. Serum IgM scrub typhus antibody was positive in all cases

Conclusion : Scrub typhus should be a differential diagnosis in acute febrile illness cases, as early diagnosis and therapy prevents complications.

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 the commonest occurring rickettsial infection in India. It is caused by *Orientia tsutsugamushi*. Scrub typhus is endemic in a part of the world known as the Tsutsugamushi triangle (after the name *O. tsutsugamushi*). This extends from northern Japan and eastern Russia in the north, to the regions around the Solomon Sea in Pacific Ocean into northern Australia in the south, and to Pakistan and Afghanistan in the west.

Scrub typhus is transmitted through the larval mites or "chiggers" belonging to the family *Trombiculidae*. Only the larval stages take blood meal. A number

of small rodents particularly wild rats of subgenus *Rattus* are natural hosts for scrub typhus. The field rodent and vector mites act as reservoir and between the two the infection perpetuates in nature. The vector mite is known to be present in diverse ecological niches such as equatorial rain forests, semi deserts and Alpine subarctic terrains in the Himalayan regions. Endemic foci are usually associated with specific habitats such as abandoned plantations, gardens or rice fields, overgrown forest clearings, shrubby fringes of fields and forests, river banks and grassy fields. These ecological patches which attract the natural host of mite vectors are called "mite islands".² Scrub typhus can occur in areas where scrub vegetation-consisting of low lying trees and bushes

is encountered, and also in habitats as diverse as banks of rivers, rice fields, poorly maintained kitchen gardens, grassy lawns which can all be inhabited by chiggers. The chiggers, too small to be seen by the naked eye, feed usually on rodents and accidentally on humans, and transmit the infection during the prolonged feeding which can last 1-3 days. Incidence of scrub typhus is higher among rural population.¹ Cases are more likely to have exposure to rodents at home or at work, and to occupational (farming) or recreational activities which expose them to the risk of encountering chiggers sitting in grass blades, bushes, shrubs. The disease is seasonal.¹ The incubation period of scrub typhus is about 5 to 20 days (median, 10-12 days). Vertical transmission has been reported and few evidences show possibility of blood borne transmissions.²

Rickettsial infections are generally incapacitating and difficult to diagnose; untreated cases have case fatality rates as high as 30-45% with multiple organ dysfunction, if not promptly diagnosed and appropriately treated.⁴ Acute fever is the most common presenting symptom often associated with breathlessness, cough, nausea, vomiting, myalgia and headache.⁵⁻⁶ In another study⁷ it was found that the most common presenting complaints were headache (64.2%), nausea/vomiting (60%), altered sensorium (53.7%) and seizures (22.1%). Although they also found a high C.S.F white blood cell count, high protein and low sugar in scrub typhus meningitis/meningo-encephalitis, only a high CSF protein level was found to be a

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Table 1: Socio-demographic profile of the patients diagnosed as scrub typhus (n=14)

Characteristic	Number of patients (%)
Sex	
Male	10 (71.4)
Female	4 (28.6)
Age groups	
Below 10 years	2 (14.3)
10-19 years	1 (7.1)
20-29 years	4 (28.6)
30-39 years	2 (14.3)
40-49 years	3 (21.4)
50 years and above	2 (14.3)
Residence	
Rural	11 (78.6)
Urban	3 (21.4)
Religion	
Hinduism	9 (64.3)
Muslim	5 (35.7)
Occupation	
Agricultural and other workers	5 (35.7)
Housewife and unemployed	4 (28.6)
Having a business	3 (21.4)
Student	2 (14.3)

predictor of mortality. 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%.⁸ Eschars are painless ulcers upto 1 cm in size, with a black necrotic centre (resembling the mark of a cigarette burn). Usually a single eschar is found on the neck, axillae, chest, abdomen and groin, but multiple eschars have also been documented.⁸ Though rash is considered as the hallmark of rickettsial disease, it is neither seen at presentation nor is it found in all patients. Presence of rash is common in spotted fever and extremely rare in scrub typhus. Rash usually becomes apparent after 3-5 days of onset of symptoms. Initially rash is in the form of pink, blanching, discrete macule which subsequently becomes maculopapular, petechial or hemorrhagic.⁹

Pneumonia is one of the most frequent complications of scrub typhus which manifests as a non-productive cough and breathlessness and leads to ARDS which could be life-threatening. Severe complications besides acute respiratory distress syndrome (ARDS) include hepatitis, renal failure, meningo-encephalitis and myocarditis with shock may occur in varying proportions of patients.¹⁰

ELISA techniques, particularly

Table 2: Clinical features of the patients diagnosed with scrub typhus

Symptoms	Patients No. (%)	Signs	Patients No. (%)
Fever less than 1 week	1 (7.1)	Hypotension	13 (92.9)
Fever of 1 to 2 weeks	7 (50.0)	Icterus	3 (21.4)
Fever of 2 to 3 weeks	4 (28.6)	Pedal oedema	4 (28.6)
Fever more than 3 weeks	2 (14.3)	Conjunctival congestion	3 (21.4)
Headache	6 (42.9)	Subconjunctival haemorrhage	1 (7.1)
Nausea / vomiting	5 (35.7)	Lymphadenopathy	3 (21.4)
Weakness	5 (35.7)	Eschar	3 (21.4)
Gastrointestinal symptoms	4 (28.6)	Crepitations	5 (35.7)
Shortness of breath	4 (28.6)	Hepatomegaly	5 (35.7)
Urinary symptoms	3 (21.4)	Splenomegaly	3 (21.4)
		Pleural effusion	5 (35.7)

immunoglobulin M (IgM) capture assays for serum, are probably the most sensitive tests. In cases of infection with *O. tsutsugamushi*, a significant IgM antibody titre is observed at the end of 1st week, whereas IgG antibodies appear at the end of 2nd week. PCR is a rapid and specific test for diagnosis. It can be used to detect rickettsial DNA in whole blood and eschar samples. The PCR is targeted at the gene encoding the major 56 Kda and/or 47 Kda surface antigen gene. PCR from eschar material is more sensitive than that from blood.¹¹ The results are best within first week for blood samples because of presence of rickettsemia in first 7-10 days. Filter paper Immunofluorescence Assay (IFA) is a reference serological method for diagnosis of Rickettsial Diseases and is considered serological 'gold standard'. Because filter paper blood samples do not require sophisticated and expensive storage and transport, they may be an appropriate specimen collection technique for the diagnosis of rickettsial disease in the rural tropics.¹³ Indirect Immunoperoxidase Assay (IPA) gives comparable result as IFA. Weil Felix (heterophile antibody test) is based on sharing of the antigens between rickettsia and Proteus. Though this test lacks high sensitivity and specificity but still serves as a useful and inexpensive diagnostic tool for laboratory diagnosis of rickettsial disease. This test should be carried out only after 5-7 days of onset of fever. Titre of 1:80 is to be considered possible infection. However, baseline titres need to be standardized for each region.¹

Prompt antibiotic therapy, shortens the course of the disease, lowers the risk of complications and reduces morbidity and mortality due to rickettsial diseases. Currently, doxycycline is the drug of choice.⁹ Azithromycin and chloramphenicol are effective alternatives. Azithromycin is also

the drug of choice in children and in pregnant women. In resistant serotypes, rifampicin added as a supplemental therapy to azithromycin or doxycycline is effective. Weekly doxycycline is effective for chemoprophylaxis.¹³ This was the first study of scrub typhus in Southern West Bengal and its neighboring areas.

Objective

To study the socio-demographic as well as epidemiological pattern, clinical features and complications of scrub typhus in two tertiary care hospitals in Kolkata.

Material and Methods

The study was conducted in two tertiary care hospitals – one Government and one private in the city of Kolkata. All consecutive patients presenting in Tropical Medicine/Medicine OPD with febrile illness were evaluated. Total study duration was 16 months i.e. from September 2014 to December 2015. Informed consent was taken from all the patients who participated in the study.

Differential diagnoses such as malaria, dengue, chikungunya, enteric fever, urinary tract infection (UTI), respiratory tract infection (RTI), leptospirosis were ruled out by history, clinical examination and appropriate laboratory investigations. The patients were subjected to a series of investigations such as complete blood count including platelet count, serum electrolytes, urine analysis, renal function tests (Urea and Creatinine), liver function tests, smear and rapid antigen tests for malarial parasite, serology for leptospirosis (IgM) serology for dengue (NS1 antigen or IgM as applicable), serology for chikungunya (IgM), Widal test, Prothrombin time (PT), Activated plasma thromboplastin time (APTT), blood and urine culture. They were also subjected to IgM for

Table 3: Laboratory findings of the patients diagnosed as scrub typhus (n=14)

Laboratory findings	Patients No. (%)
Leucocytosis (>11000/cmm)	5 (35.7)
Thrombocytopenia (<150000/cmm)	1 (7.1)
Raised ESR (>40 mm in 1st hr)	12 (85.7)
Raised AST (>50 IU/l)	14 (100)
Raised ALT (>50 IU/l)	13 (92.9)
Decreased serum albumin (<3 g/dl)	6 (42.9)
Increased serum bilirubin (>2 mg/dl)	3 (21.4)
Serum creatinine (>1.5 mg/dl)	1 (7.1)
Urinary albumin (1+ or more)	5 (35.7)
Presence of RBC in urine	1 (7.1)
Presence of pus cells in urine (>4/hpf)	4 (28.6)
Serum IgM for scrub typhus	14 (100)

scrub typhus as well as Weil-Felix Test with titre. The patients also underwent Ultrasonography of abdomen, Chest X-ray, CT scan of brain and CSF study as and when necessary.

The patients having IgM antibodies against *Orientia tsutsugamushi* in their serum were diagnosed as having scrub typhus. Some patients also underwent Weil-Felix test. The patients were admitted for necessary management. Various complications such as acute renal failure, hepatitis, Acute Respiratory Distress Syndrome (ARDS), meningitis, myocarditis, etc. were also looked for.

The collected data were compiled using Microsoft Excel 2010 and then analysed using statistical software Epi Info 7.1.5. The results were expressed in percentages and proportions.

Results

Among the 14 patients diagnosed as scrub typhus, 10 were male and 4 were female. Four of these 14 patients belonged to 20 to 29 years age group. Two patients were below 10 years of age and the oldest was aged 55 years. Eleven of them were from rural areas. Six patients were from South 24 Parganas district, 2 were from Howrah district, one each from Hooghly, North 24 Parganas, Kolkata, PurbaMedinipur and Malda districts, while one was referred from the neighbouring state of Bihar. All other socio-demographic characteristics are detailed in Table 1.

The common symptoms of these patients were fever, headache, nausea, vomiting, weakness followed by respiratory symptoms, gastrointestinal complaints such as abdominal pain and loose motions and urinary complaints. Eschar, the pathognomic feature,

was seen in only 3 patients (21.4%). 3 patients had lymphadenopathy. Crepitations in chest were found in 5 (35.7%) patients. Five (35.7%) patients developed pleural effusion, out of which three were bilateral. One of the patients had ascites. One patient had symptoms of meningism. The clinical features of these patients are summarized in Table 2.

Five (35.7%) patients had leucocytosis. All the patients had raised transaminase (AST or ALT) levels with a mean AST of 248.3 units and mean ALT of 125.7 units. Twelve patients had serum albumin less than 3.5g/dl with an overall mean of 2.9 g/dl. One patient had symptoms of meningism; CSF showed 20 cells, 95% lymphocytes and 5% neutrophil, elevated protein and reduced sugar. Four patients had low sodium levels. Weil Felix test was positive (>1:80)¹¹ in 2 out of three patients who underwent the test, while IgM antibody against scrub typhus was detected in all the 14 patients tested. The laboratory findings are summarized in Table 3.

One of the patients developed ARDS and was put on mechanical ventilation in critical care unit. All, except one, of the patients were administered Doxycycline 100mg twice daily for 10 to 14 days along with supportive management. One patient was allergic to Doxycycline and was given Azithromycin 500 mg for 6 days. All the patients were cured with this therapy.

Discussion

In our study majority of the patients were from rural areas (78.6%). This is in congruence with data published by the, Indian Council of Medical Research¹ and also with a study from Manipal, India. Most common occupation of our patients was agriculture and related works and the age-group of 20-29 years contributed 28.6% of patients to our cohort. Both these observations were similar to those found in the study¹⁵ from Manipal, India. These may be due to the fact that scrub typhus occurs more among persons who engage in occupational or recreational behavior that brings them into contact with mite-infested habitats such as brush and grass.

Eschar, which is very helpful in diagnosing scrub typhus was found in only 3 of the 14 patients (21.4%).

Various other studies found prevalence of eschars to vary from 7-97%.⁸ The incidence of eschar in a study conducted in South India by Verghese GM et al. was 55%.¹⁶ Apart from high fever, the most common presenting symptom of our patients was headache followed by nausea vomiting and weakness (same observations were published in the paper by Zhang Z, et al.) Meningism was found in just one of the patients with headache. Cerebrospinal fluid (CSF) analysis of the patient with meningism revealed lymphocytic pleocytosis with elevated protein as was described by Zhang et al.⁷ Lymphadenopathy was observed in 3 patients. Hepatomegaly was seen in 35.7% of the patients while splenomegaly was seen in 21.4%. 3 out of 14 patients had hepatosplenomegaly. Hepatosplenomegaly as well as lymphadenopathy were found to be common in various other studies.¹⁷⁻¹⁸

Acute respiratory distress syndrome (ARDS) is a well known complication of scrub typhus.¹⁵ One of our patients developed ARDS and required mechanical ventilation. Thus incidence of ARDS was not very common among our patients. Peripheral blood polymorphonuclear leucocytosis was seen in 35.7% of our patients and all of these patients had features of sepsis which is another common complication of scrub typhus fever. Elevated liver enzymes which is a well known¹⁸ feature of the disease was seen in all of our patients. Another complication of scrub typhus is proteinuria,¹⁹ it was seen in 35.7% of our patients.

Weil Felix test was done in only 3 of our patients and was found to be positive (>1:80) in two of them. All of our patients had Ig M scrub typhus antibody positive by ELISA. Weil Felix test is said to have poor sensitivity.²⁰

13 of our patients were treated with Doxycycline and one with Azithromycin. All of our patients recovered. Time to recovery varied from 5-14 days according to the complications that developed.

6 of our cases were from the South 24 Parganas district, 2 from Howrah district and 1 each from Maldah, Hooghly, North 24 Parganas, Kolkata and East Midnapore districts of West Bengal. One was from the state of Bihar.

Conclusion

Scrub typhus is seen in various parts of West Bengal and India. Clinicians

should be aware of the disease. When a patient presents with short term fever of about a week's duration scrub typhus should be considered as a possibility after malaria, dengue, chikungunya, typhoid, UTI, RTI, leptospirosis etc. An empirical therapy with doxycycline should be started if there is high index of suspicion. An early diagnosis and timely antibiotic therapy may prevent further complications.

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