



Study of The Clinico-Laboratory Profile of Sporadic Cases of Scrub Typhus

KEYWORDS

Scrub Typhus , Rickettsial , chiggers

Dr. Ravindra K. Shravasti

Professor in Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli - 416416

Dr. Vasant B. Jadhav

Associate Professor in Medicine Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli - 416416

Dr. Naman Mahesh Shah

Post-Graduate student Dept. of Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli - 416416

Dr. Akshay D. Shah

Post-Graduate student Dept. of Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli - 416416

Dr. Raghunath B. Kulkarni

Senior Resident Dept. of Medicine, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli - 416416

ABSTRACT *Scrub Typhus is a zoonotic disease characterized with acute febrile illness with multi-organ involvement caused by obligate intracellular gram negative bacteria. Human rickettsial disease is transmitted through the bite of trombiculidmites(chiggers).Our study is retrospective study of hospitalised patients with rickettsial infection during period 2012-2013. 8 patients above age of 18 with clinical features of rickettsiosis (fever,rash) with Weil-Felix positivity were included.All the patients responded well to treatment and there was no mortality. The purpose of this study was to show that though uncommon, sporadic cases of rickettsial diseases is prevalent in this region throughout the year. The disease is grossly underdiagnosed owing to the non-specific clinical presentation, lack of access to the specific diagnostic facilities and low index of suspicion by the clinician. Scrub typhus is one of the differential diagnoses (in addition to Leptospirosis , Malaria , Dengue fever) in patients presenting with fever, thrombocytopenia with maculo-papular rash.*

Introduction

Scrub typhus, caused by *Orientia* (formerly *Rickettsia*) *tsutsugamushi*, is an acute infectious disease of variable severity that is transmitted to humans by an arthropod vector of the *Trombiculidae* family. "Tsutsuga" means small and dangerous and "mushi" means insect or mite. It affects people of all ages including children. Humans are accidental hosts in this zoonotic disease. While scrub typhus is confined geographically to the Asia Pacific region, a billion people are at risk and nearly a million cases are reported every year¹. Scrub typhus was first described from Japan in 1899. It was a dreaded disease in pre-antibiotic era and a militarily important disease that affected thousands of soldiers in the far east during the second World War². The overall mortality varied from 7% to 9%, second only to malaria among infectious diseases. In India, scrub typhus broke out in an epidemic form in Assam and West Bengal during the Second World War. It is often acquired during occupational/agricultural exposures because active rice fields are an important reservoir for transmission.

The term "scrub" is used because of the type of vegetation (terrain between woods and clearings) that harbors the vector; however, the name is not entirely correct because certain endemic areas can also be sandy, semiarid and mountain deserts. The word "typhus" is derived from the Greek word "typhus", which means "fever with stupor" or smoke¹.

Epidemiology

Mortality rates in untreated patients range from 0-30% and tend to vary with the patient's age and region of infection. In the preantibiotic era, mortality rates in Japan averaged 30%. The mortality was 15% in patients aged

11-20 years, 20% in those aged 21-30 years, and 59% in those older than 60 years. In Taiwan, the overall mortality was estimated at 11% but was only 5% in children and 45% in the elderly. With appropriate treatment, mortality is quite rare³. However, mortality is still approximately 15% in some areas due to missed or delayed diagnosis. If severe complications such as adult respiratory distress syndrome (ARDS) arise, mortality may still be high.

Scrub typhus is endemic to a part of the 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 in the west⁴.

Indian Scenario

Scrub typhus is prevalent in many parts of India but specific data are not available. It is a re-emerging infectious disease in India⁵. There have been outbreaks in areas located in the sub-Himalayan belt, from Jammu to Nagaland. There were reports of scrub typhus outbreaks in Himachal Pradesh, Pondicherry, Tamil Nadu, Sikkim and Darjeeling^{6,7,8}. The seasonal occurrence of scrub typhus varies with the climate in different countries. The period of epidemic is influenced by the activities of the infected mite. It occurs more frequently during the rainy season. However, outbreaks have been reported during the cooler season in southern India⁹. Certain areas such as forest clearings, riverbanks and grassy regions provide optimal conditions for the infected mites to thrive.

Scrub typhus is difficult to recognize because the symptoms and signs are often nonspecific. The nonspecific presentation and lack of the characteristic eschar in 40-60% of patients lead to misdiagnosis and under-reporting.

On the other hand, diagnostic facilities are not available in all places. Therefore, the precise incidence of the disease is unknown. Mortality rates in untreated patients range from 0–30%¹⁰.

Materials and Methods

The study was conducted at Bharati Hospital, Sangli, a tertiary healthcare centre. We reviewed 8 patients with confirmed Scrub typhus (cases in whom all common causes like malaria/typhoid/dengue/UTI/leptospirosis were excluded) admitted in our hospital in 2013-2014. The cases were confirmed with Weil-Felix test (tube agglutination test) as other sensitive tests like Immunofluorescence antibody test or PCR were unavailable. Epidemiological variables included gender, age and residential address. Clinical manifestations were fever, rash, cough, anorexia, vomiting, pain in abdomen, headache, loose motions, weakness, drowsiness. Laboratory data included all routine biochemical tests.

Results

Table 1. Baseline characteristics of the patients

	Data	No. of cases	Percentage
1.	<u>Gender -</u>		
	Male	03	37.5
	Female	05	62.5
2.	<u>Age (in years)-</u>		
	18-40	02	25
	41-60	04	50
	>61	02	25
3.	<u>Occupation-</u>		
	Farmers	01	12.5
	Housewife	04	50
	Businessmen	03	37.5
4.	<u>Residence-</u>		
	Rural	06	75
	Urban	02	25

Table No. 2 Symptoms and signs

	Symptoms/Signs	No. of cases	Percentage
1.	<u>Fever duration-</u>		
	1-3days	01	12.5
	4-7days	01	12.5
	>7days	06	75
2.	Cough	02	25
3.	Breathlessness	01	12.5
4.	Headache	03	37.5
5.	Vomiting	03	37.5
6.	Pain in abdomen	02	25
7.	Loose motions	01	12.5
8.	Generalised weakness	03	37.5
9.	Loss of appetite	02	25
10.	Joint pain	01	12.5
11.	Altered mentation	02	25
12.	Maculopapular rash	04	50

13.	Eschar	02	25
14.	Jaundice	04	50
15.	Tachycardia	02	25
16.	Lymphadenopathy	02	25
17.	Hepato-splenomegaly	04	50
18.	Lung crepitations	03	37.5

Table No. 3 Laboratory Findings

	Laboratory Data	No. of Cases	Percentage
1.	Anemia	03	37.5
2.	Leucopenia	02	25
3.	Leukocytosis	03	37.5
4.	Platelets <1.5lakh/mm ³	07	87.5
5.	AST(SGOT) elevation	06	75
6.	ALT(SGPT) elevation	06	75
7.	ALP	03	37.5
8.	Sr. Creatinine	02	25
9.	CSF study (2pts)	Lymphocytosis in 1pt	50
10.	<u>USG(Abdomen & pelvis)</u>		
	Ascites with pleural effusion	01	12.5
	Bilateral pleural effusion	04	50
	Hepatosplenomegaly	01	12.5
11.	Chest X-Ray (Pneumonitis)	01	12.5
12.	ECG (Tachycardia)	02	25

Table No. 4 Organ involvement -

	Organ Involved	No. of cases	Percentage
1.	<u>Respiratory-</u>		
	Pneumonitis	01	12.5
	Pleural effusion	02	25
2.	CNS		
	Meningitis	01	12.5
3.	<u>CVS</u>		
	Tachycardia	02	25
4.	Renal Failure	02	25
5.	Hepatic dysfunction	06	75
6.	Hepato-splenomegaly	04	50
7.	Thrombocytopenia	07	87.5



Fig. No. 1 Eschar (seen on the trunk)



Fig. No 2 Maculopapular rash

A total of 8 patients were diagnosed with Scrub typhus from 2013 – 2014. All cases were positive for Weil-Felix test with significant titre. The demographic results are seen in Table 1. Both males (n=03) and females (n=05) were among identified cases.

Adults in the age group 18-40 constituted 25%, age 41-60 constituted 50% and age group above 60 constituted 25%. Almost 75% cases occurred in the rural population. This study done over a one year period showed equal distribution of cases in different seasons. It also showed no occupational association of cases as 50% of cases were found among housewives.

The clinical symptoms are shown in Table No. 2. All patients presented with fever, ranging from 1 to 14 days prior to hospital admission. Other symptoms included the presence of eschar (n=02) Fig No.1, skin rashes (n=04) Fig No.2, cough (n=02), breathlessness (n=01), loss of appetite (n=02), headache (n=03), vomiting (n=03), pain in abdomen (n=02), weakness (n=03), drowsiness (n=02), etc. Other signs included Jaundice (n=04), lymphadenopathy (n=02), Hepatosplenomegaly (n=04) and lung crepitations (n=03).

Several laboratory values were consistently elevated among cases, including white cell count (n=03), SGPT/SGOT (75% of the cases), etc. Other abnormalities like thrombocytopenia ($<1.5 \text{ lakh/mm}^3$), anemia and deranged renal function were noted in a few cases. Four cases (50%) had shown hepatosplenomegaly on USG and 2 cases showed pleural effusion with ascites. Lumbar puncture was done in just two cases who had shown altered mentation, one of them showed CSF leukocytosis with predominant

lymphocytes with normal protein and sugar whereas other study was normal. No mortalities occurred in the subjects.

Discussion

Scrub typhus, also known as tsutsugamushi disease, is an acute febrile illness caused by infection with *Orientia tsutsugamushi* and characterized by focal or disseminated vasculitis and perivasculitis, which may involve the lungs, heart, liver, spleen, and central nervous system^{11,12,13}. The symptoms are usually mild and the clinical course self limited, with spontaneous recovery after a few days. The diagnosis of scrub typhus is based on the patient's history of exposure, the clinical features, and the results of serologic testing^{14,15}. The article provides a review of the clinical features and the complications of scrub typhus.

There have been reports of the outbreaks of scrub typhus from various parts of the country in the recent past with serological evidence of widespread prevalence of spotted fevers and scrub typhus in the neighbouring states like Andhra Pradesh, Goa, etc¹⁶⁻²¹. Thus, there was a strong possibility of presence of rickettsial diseases in Western Maharashtra, but it had not been documented yet. All the 8 confirmed cases in the present study were the natives of Maharashtra. This proves the existence of the disease in the State.

Rickettsial diseases are common in the months of July to November particularly in the post monsoon period¹⁶⁻²¹. This is because, during the months of August to October, farmers are involved in the harvesting activity in the fields, where they are exposed to the bites of larval mites. Further, in the immediate post monsoon period (September to early months of the next year), there is growth of secondary scrub vegetation, which is the habitat for trombiculid mites (mite islands). But our study showed cases from different seasons too suggesting that sporadic cases can be found throughout the year.

Fever was the commonest clinical presentation in the present case series (100% cases). Previous studies from various authors reveal that in India the rash is generally not seen so commonly^{22,23} and it was the same in the present case series (50%). The painless chigger bite can occur on any part of the body but it is often located in areas that are hard to examine, such as the genital region or under the axilla. An eschar forms at the bite site in about half of the primary infections. It begins as a small papule, enlarges, undergoes central necrosis, and acquires a blackened crust to form a lesion resembling a cigarette burn²⁴. The reported percentages of eschar formation showed substantial variations across different studies ranging from 15–100%²⁵⁻²⁸. Eschars can be detected relatively frequently in white skinned individuals. However, it is relatively difficult to detect on dark-skinned individuals as in India²⁴. We noticed eschars in only two cases (25%). However, eschars have been described as the single most important diagnostic clue and therefore needs to be looked for in all febrile patients without localizing signs of the disease²⁹.

Though rash is considered as a hallmark of rickettsial disease, it is neither seen at presentation nor in all the patients^{30,31}. We found skin rashes only in 4 (50%) cases. Lymphadenopathy, rash, leucocytosis and organomegaly, which are features of the disease in South East Asian countries, were not prominent in the present study, a finding similar to earlier studies from India³². Gastrointestinal symptoms mainly in the form of pain abdomen, vomiting and loose stool were found in 25%, 37.5% and 12.5% cases, respec-

tively. This finding was consistent with the series by Liu YX et al who reported an overall 56% cases with gastrointestinal symptoms³³.

Similar to many other case series^{17,18} most patients had elevation of serum transaminases, even without any other evidence of multiorgan dysfunction. Our study showed 75% cases with hepatic dysfunction. Other laboratory findings noted were leukocytosis, thrombocytopenia, and deranged renal function tests. Non-specific lung infiltrates with predilection to the lower zone is described in scrub typhus³⁴ and was seen in 3 cases (37.5%) in the present series with both clinical and radiological findings.

Neurological complications in the form of meningitis were seen in 1 case (12.5%). Acute renal failure (ARF) has been described as a potential complication of scrub typhus cas-

es³⁵ and two cases of ARF was observed in the present case series that responded to conservative management.

All patients responded to the initial antibiotic therapy and no case of clinical drug resistance was found.

Treatment schedule for scrub typhus followed in our department. Failure to respond was defined as no defervescence within 72 h and no clinical improvement after treatment.

1. A 7-day course of doxycycline 4 mg/kg/day orally in patients with no complications and above 8 years of age.
2. A 7–14 day course of chloramphenicol 100 mg/kg/day intravenously in those patients with complications such as meningoencephalitis, septic shock or myocarditis.

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