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Epidemiology and clinico-laboratory manifestations of scrub typhus in Hadoti region of Rajasthan, India: A cross-sectional study

Pankaj Jain, Manoj Sharma, Manoj Seval[✉], Pramod Meena

Department of General Medicine, Govt. Medical College, Kota, India

ABSTRACT

Objective: To study epidemiology, clinical manifestations, and laboratory parameters of scrub typhus in Hadoti region of Rajasthan, India.

Methods: A cross-sectional study was conducted on 50 patients with scrub typhus between August 2022 and November 2022. Scrub typhus was diagnosed by ELISA IgM scrub typhus antibody. The data about demography, vital parameters, and lab investigations were collected and analyzed.

Results: Ninety-two percent of the patients were from a rural background (92%), 86% were farmers and the majority were females. Most patients were 40-60 years old. The major complaints were fever (100%), myalgia (100%), headache (82%), and body swelling (80%). Major complications were pneumonia (68%), multiple organ dysfunction syndrome (62%), hepatitis (44%), and acute kidney injury (42%). Triglyceride levels were >200 mg/dL in 80% of patients, albumin <3.5 g/dL in 98% and eschar mark was present in 24% of patients.

Conclusions: Scrub typhus is a serious acute febrile illness that can lead to multi-organ dysfunction and is associated with significant mortality. Increasing awareness regarding disease in endemic regions, early screening of patients, and treatment as early as possible could help prevent the patient from severe life-threatening complications.

KEYWORDS: Scrub typhus; Epidemiology; Eschar mark; Multiple organ dysfunction syndrome

1. Introduction

Scrub typhus is an acute febrile illness endemic to the 'tsutsugamushi triangle', which encompasses broad areas of south

and southeastern Asia, the Asian Pacific Rim, and northern Australia, with a population of over one billion people[1]. This infection is caused by *Orientia tsutsugamushi*, which is an obligate intracellular Gram-negative bacterium, transmitted to humans by the bite of the larval stage of trombiculid mites. It is a seasonal infectious disease occurring between August to December. A clear re-emergence of the disease has been documented in the southern part of India and some states of north India like Rajasthan[2], is more prevalent in Hadoti region of Rajasthan. As scrub typhus is more prevalent in this region of the state, we conducted a cross-sectional study to study epidemiology, clinical manifestations, and laboratory parameters of scrub typhus.

The disease mainly presented with fever, headache, myalgia, cough, breathlessness, generalized body swelling, seizures, and altered sensorium, in which fever is the most common presenting

Significance

There was delay in diagnosis of scrub typhus patients who presented with acute febrile illness in particular season. In our study it was observed that patients who were scrub typhus positive, presented with similar clinical presentation and laboratory findings. So based on these characteristic findings, scrub typhus patients can be diagnosed early and associated mortality and morbidity can be reduced.

[✉]To whom correspondence may be addressed. E-mail: drsevalm@gmail.com

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symptom. In a highly variable percentage (10%-92%) of patients an eschar mark can be found at the inoculation site[3]. The infection can range from a self-limiting disease to a fatal illness in 35%-50% of cases, with multiorgan dysfunction, if not promptly diagnosed and appropriately treated[4]. Complications including acute respiratory distress syndrome, hepatitis, renal failure, meningococcal meningitis, and myocarditis with circulatory collapse may present in a varying percentage of patients.

The disease is presented with various abnormal laboratory parameters including thrombocytopenia, deranged liver function test with transaminitis, reported in the majority of cases (66.7% to > 90%)[2,5,6], renal dysfunction as evidenced by elevated serum creatinine, most studies have reported it to be presented in 10%-20%[2,6], and hypoalbuminemia, increased triglyceride levels, increased lactate dehydrogenase (LDH), hypocalcemia in variable proportion.

2. Patients and methods

2.1. Study design

This cross-sectional study was conducted from August 2022 to November 2022. Patients over the age of 14 years with acute febrile illness, admitted to the Medicine Department of Government Medical College & Attached Hospitals, Kota were included in the study. The sample was collected using a nonprobability convenience sampling technique.

2.2. Methodology

During the time of admission, a structured questionnaire was administered to assess the demographic variable. Data were collected regarding demographics, occupation, clinical presentation, delay in presentation to hospital, complications, and laboratory data (complete blood counts, urine complete, blood urea, serum creatinine, liver function tests, lipid profile, serum LDH, creatine kinase isoenzyme, serum calcium), requirement of oxygen, ventilatory support, vasopressor support, duration of illness before hospital admission, and duration of hospital admission. All patients underwent complete history, general physical & systemic examination. Specific emphasis was given to patient's vitals and the presence of an eschar mark. The diagnosis was confirmed by serum IgM ELISA scrub typhus. The presence of an eschar mark provided supportive evidence.

2.3. Ethical statement

Ethical clearance was taken from Institutional ethical committee of GMC, Kota, India. Written informed consent was obtained for each patient before their enrollment in the study.

2.4. Statistical analysis

After initiating treatment, the primary outcomes were the number of days required for complete recovery of the patient and mortality. Data were presented as numbers and percentages and analyzed using Microsoft Excel.

3. Results

A total of 89 patients presented with acute febrile illness and were potentially eligible candidates for the study. Out of which 63 candidates were confirmed eligible as scrub typhus IgM was positive in these patients. Out of these 63 candidates, 9 patients lost to follow up and 4 patients did not consent for study. Finally 50 patients completed the follow up and all of them were included in the study (Figure 1).

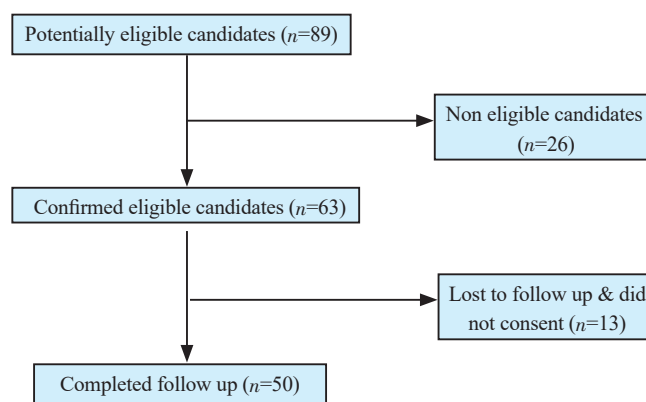


Figure 1. The study flow diagram.

Table 1. Demographic and basic characteristics (n=50).

Items	n	%
Age (years old)		
<20	3	6
21-40	15	30
41-60	20	40
61-80	12	24
Sex		
Male	20	40
Female	30	60
Occupation		
Farmers	43	86
Non farmers	7	14
Location		
Rural	46	92
Urban	4	8
Admission month		
August	7	14
September	22	44
October	15	30
November	6	12

3.1. Demographic and basic characteristics

Most of the patients were admitted in September 2022 and after September, there was a steep decline in the number of cases. Very few cases were reported in November 2022. Out of the total patients admitted, 92% of the patients were from a rural background, 86% were farmers, and the majority were females (female/male=6:4) (Table 1).

3.2. Clinical symptoms and complications

Out of the 50 patients included in the study, all of them complained of fever and myalgia. Majority of them had headache, nausea, vomiting, cough, shortness of breath, generalized body swelling. Few of them also developed seizures, altered sensorium, hepatosplenomegaly and eschar mark. Complications like pneumonia and multi organ dysfunction syndrome were seen in majority of patients and some of them developed hepatitis, acute kidney injury, and shock (Table 2).

3.3. Laboratory results

Anemia (<10 g/dL) was observed in 26% of patients and thrombocytopenia in 90% of patients, out of which 4 patients required packed cell volume transfusion and 7 patients required platelets transfusion. Bilirubin>2.5 mg/dL was seen in 32% of patients and serum glutamic-oxaloacetic transaminase/serum glutamic pyruvic transaminase more than 4 times of upper limit was seen in 38% of patients, creatinine \geq 1.5 mg/dL was seen in 42% of patients, triglyceride >200 mg/dL was in 80% of patients, high-density lipoprotein<30 mg/dL in 76% of patients, low-density lipoprotein (LDH)>480 IU/L in 90% of patients, albumin<3.5 g/dL in 98% of patients. Hypocalcemia (<8 mg/dL) was observed in 56% of patients (Table 3).

It was observed that in critically ill patients, triglyceride levels and LDH level was high while serum albumin and serum calcium levels were decreased. With the improvement in clinical status, levels of these indexes became near normal without any intervention.

3.4. Treatment and outcomes

The average duration of illness before hospital admission was 8 days and the average duration of hospital stay was 6.5 days. It was observed that patients who presented late in hospital during course of illness were found more critically ill and their hospital stay was also long.

Oxygen support was required in 64% of patients and they were put on either a simple oxygen mask or a nonbreathing face mask according to oxygen requirement. A total of 12% required invasive ventilatory support and 4% required non-invasive ventilatory support. Vasopressor support was required in 40% of patients and 56% of patients required ICU admission. Mortality was 18%.

Table 2. Clinical symptoms and complications (n=50).

Items	n	%
Symptoms		
Fever	50	100
Myalgia	50	100
Headache	41	82
Nausea/vomiting	31	62
Cough	34	68
Shortness of breath	30	60
Seizure	5	10
Altered sensorium	10	20
Body swelling	40	80
Hepatosplenomegaly	18	36
Eschar mark	12	24
Complications		
Meningoencephalitis	10	20
Pneumonia	34	68
Hepatitis	22	44
Acute kidney injury	21	42
MODS	31	62
Shock	20	40

MODS: Multiple organ dysfunction syndrome.

Table 3. Laboratory data (n=50).

Laboratory indexes	Normal range	Median (Q1, Q3)
Hemoglobin (g/dL)	13-18 (male)	9.4 (8.3, 10.4)
	11.5-16.5 (female)	
Platelet ($\times 10^4$ /L)	15-40	44.0 (28.0, 90.0)
Bilirubin (mg/dL)	0.3-1.3	1.3 (.70, 3.0)
SGOT (U/L)	12-38	121.0 (72.0, 195.50)
SGPT (U/L)	7-41	77.0 (49.7, 195.5)
Total protein (g/dL)	6.7-8.6	6.0 (5.2, 6.3)
Albumin (g/dL)	3.5-5.5	2.3 (2.0, 2.7)
Creatinine (mg/dL)	0.6-1.2	1.2 (0.8, 2.2)
Blood urea (mg/dL)	20-40	53.5 (38.5, 84.2)
Triglyceride (mg/dL)	< 160	297.5 (214.7, 368.2)
High-density lipoprotein (mg/dL)	> 60	16.5 (11.7, 26.0)
Serum calcium (mg/dL)	8.7-10.2	7.4 (6.8, 8.2)
Lactate dehydrogenase (U/L)	115-221	980.0 (687.5, 1200.0)

SGOT: serum glutamic-oxaloacetic transaminase. SGPT:serum glutamic pyruvic transaminase.

4. Discussion

Scrub typhus is a potentially fatal infection that affects about one million people every year[1]. In our study, most of the patients were from a rural area (92%), which is slightly higher compared to the study of Saha *et al*[7](78.6%). A total of 86% of patients were farmers or engaged in animal husbandry.

Patients were between 15 to 80 years old but most of the cases were between the age of 40 to 60 years old. More patients were female, which is similar to the study by Takhar *et al*[8]. It is because most of the work related to farming and husbandry is carried out by females in this region.

In this study, cases of scrub typhus occurred between August to November and more occurred in September, which is similar to other studies as well[8-10]. In this study, mean duration of illness before the

hospital visit was 8 days, and patients presented with fever (100%), myalgia (100%), headache (82%), nausea/vomiting (62%), cough (68%), shortness of breath (60%), seizure (10%), altered sensorium (20%), and body swelling (80%).

Skin lesion eschar mark was present in 24% of patients. The incidence varies from 10% to 70% in various studies[7,11]. The variation in the incidence of an eschar may represent the different geographic distribution of the various strain of the organism or inadequate search for the eschar; further research is warranted in this area[1].

In this study, pulmonary dysfunction was the most common complication (64%) and it varied from mild pneumonia to acute respiratory distress syndrome, in which 16% of patients required ventilatory support. In the study by Varghese *et al*[1], the most common complication was also pulmonary dysfunction and 69% of patients required ventilatory support. Other complications include shock (40%), hepatitis (44%), multiple organ dysfunction syndrome (62%), and acute renal failure (42%). The incidence of renal impairment is higher than the 18% reported by Varghese *et al*[1] and 23.2% reported by Attur *et al*[12], and 66.4% reported by Mahajan *et al*[2]. Higher mortality was seen in the patients who presented with acute respiratory distress syndrome and hypotension and required vasopressor support. In this study, thrombocytopenia was seen in 90%, increased triglyceride was seen in 80%, decreased albumin levels in 98%, and increased LDH in 90% of patients.

Fatality rate varies from 0% to 25% in various studies conducted in India[8,11,13], while in this study, it was 18%.

Scrub typhus is a serious acute febrile illness that can lead to multiorgan dysfunction and is associated with significant mortality. Mortality is significantly higher in a patient with pulmonary dysfunction or renal failure and in those who required vasopressor support for hypotension. Because of increasing awareness and early diagnosis, mortality is decreasing over several years. By increasing awareness regarding disease in endemic regions, early screening of patients, and treatment as early as possible we can prevent the patient from severe life-threatening complications.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

PJ developed the concept and design of the study. M Sharma contributed with literature search, data acquisition. Data analysis,

statistical analysis, manuscript preparation and editing was done by M Sharma and M Seval. PM and All authors have reviewed and approved the final version of the manuscript.

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