

Prediction of Scrub Typhus in Tertiary Care Centre of Northern Bihar

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Conflict of interest: Nil

Abstract

Objectives: This present study was to evaluate the severity of scrub typhus in various age group in tertiary care centre of northern Bihar.

Methods: ELISA for IgM antibody was performed to detect Scrub Typhus IgM by following instructions. The antigen used to coat the wells was a recombinant 56-kDa type-specific antigen. The absorbance was read at 450 nm and an optical density of > 0.5 was considered positive. A nested polymerase chain reaction (PCR) was also performed for scrub typhus. DNA was extracted from the whole blood, blood clot, or eschar material by the phenol–chloroform method, and was amplified to detect scrub typhus according to nested PCR protocol. The oligonucleotide primers used were based on the nucleotide sequences of a gene encoding for the 56-kDa antigen of a Gilliam strain of *O. tsutsugamushi*. The specific PCR products of size 484 base pairs were sequenced in a few representative samples to confirm the diagnosis.

Results: A total of 50 scrub typhus patients with age group 18 to 60 years were enrolled. Most of the cases 30(60%) were in age group of 40-60 years. Most of the cases 18(36%) were males. Most of the common symptoms 47(94%) of scrub typhus was high grade fever with chills and rigor followed by 41(82%) shortness of breath, 17(34%) jaundice, 15(30%) abdominal pain, 13(26%) headache. Most common signs of scrub typhus were 29(58%) hepatomegaly followed by 21(42%) splenomegaly, 15(30%) hypotension, 14(28%) pneumonitis, 11(22%) pallor, 9(18%) eschar. thrombocytopenia was the most common laboratory findings of scrub typhus patients followed by 32(64%) increased SGOT/SGPT ratio, 23(46%) hyperbilirubinemia, 29(58%) anemia.

Conclusions: Scrub typhus was more prone in middle age male population. High-grade fever with chills and rigor and shortness of breath, hepatomegaly and splenomegaly were the most common symptom and sign of scrub typhus. Thrombocytopenia and SGPT/SGOT (≥ 2 times normal) were the most common laboratory findings of scrub typhus patients.

Keywords: Scrub typhus, Signs, symptoms, Laboratory findings

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Introduction

Scrub typhus is a treatable disease but if not diagnosed and treated early may result in complications. These patients may have an eschar which is quite characteristic of this disease. In our study, 21.4% of the patients had eschar. Other studies have shown an eschar detection rate of 46%-86% [1].

The disease is caused by a Gram-negative bacterium, *Orientia tsutsugamushi*, and is transmitted by the larval stage of mites ("chiggers") in the family Trombiculidae. Scrub typhus has an expanding known distribution, with most disease occurring across South and East Asia and parts of the Pacific Rim [2]. The infection may be acquired in both rural and semi-urban environments and thus an enormous human population is to be at risk. In some areas of Southeast Asia, scrub typhus causes up to 23% of febrile hospital admissions [3,4]. In prospective studies in six countries across Asia, seroprevalence ranged from 9.3 to 27.9% with a median of 22.2% [5].

Symptoms of scrub typhus appear after 5–14 days of *Lepto-trombidium* bite with manifestations of infection such as fever, rash, myalgia, lymphadenopathy, nausea, vomiting, eschar (black spot arises at mite biting site), abdominal pain, and non-specific flu-like symptoms. This infection precedes to severe complications that event in multiorgan failure including jaundice, acute renal failure, and disseminated intravascular coagulation (DIC), acute respiratory distress syndrome, myocarditis, and meningoencephalitis (Xu et al. 2017a, b) [2]. Symptoms of scrub typhus concur with other co-endemic diseases such as leptospirosis, dengue, brucellosis, and typhoid, which makes it more troublesome to differentiate from others (Koh et al. 2010) [6]. The presence of eschar at mite biting site is a specific (98.9%) marker for clinical diagnosis of scrub typhus; however, the presence of

eschar can be varied extensively in patients from 7 to 97% (Saraswati et al. 2018) [7]. The presence of eschar in India and other Asian populations is meagre, which makes it an inappropriate method for the detection of *Orientia tsutsugamushi*, hence, the diagnosis relies upon laboratory tests (Shivalli 2016) [8]. The laboratory-based diagnosis of scrub typhus relies on serological assays like the Weil–Felix test, indirect Immunofluorescence assays, indirect immunoperoxidase assays, enzyme-linked immunosorbent assay (ELISA) and immunochromatographic tests (ICT), etc. Among all serological assays, IgM ELISA-based method is most reliable for the diagnosis of scrub typhus (Phetsouvanh 2013) [9]. Objectives of our study was to evaluate the assessment of severity of scrub typhus in children in tertiary care centre of northern Bihar.

Material & Methods

This present study was conducted in the department of Microbiology with the collaboration of the Department of Medicine, MGMC & LSK Hospital, Kishanganj, Bihar during a period from February 2022 to September 2022. Attendants of entire subject signed an informed consent approved by institutional ethical committee of MGMC, Kishanganj, Bihar was sought.

Patients with a positive diagnosis of severe scrub typhus were enrolled in this study. A total of 50 patients of scrub typhus were included.

Laboratory tests carried out were a complete hemogram, renal function tests, liver function tests, coagulation tests including international normalized ratio and activated partial thromboplastin time, serum electrolytes, calcium, and phosphorous.

For scrub typhus, ELISA for IgM antibody was performed to detect Scrub Typhus

IgM by following instructions:- The antigen used to coat the wells was a recombinant 56-kDa type-specific antigen. The absorbance was read at 450 nm and an optical density of > 0.5 was considered positive. A nested polymerase chain reaction (PCR) was also performed for scrub typhus. DNA was extracted from the whole blood, blood clot, or eschar material by the phenol-chloroform method, and was amplified to detect scrub typhus according to nested PCR protocol [10]. The oligonucleotide primers used were based on the nucleotide sequences of a

gene encoding for the 56-kDa antigen of a Gilliam strain of *O. tsutsugamushi*. The specific PCR products of size 484 base pairs were sequenced in a few representative samples to confirm the diagnosis.

Observations

In this present study, a total of 50 scrub typhus patients with age group 18 to 60 years were enrolled. Most of the cases 30(60%) were in age group of 40-60 years. Most of the cases 18(36%) were males.

Table.1. Age and gender wise distributions of scrub typhus.

Variables		No. of cases (N=50)	Percentage
Age (years)	18-39	4	8%
	40-60	30	60%
	>60	16	32%
Gender	Male	32	64%
	Female	18	36%
Socio-economic status	Low	29	58%
	Middle	15	30%
	High	6	12%

In this present study, most of the common symptoms 47(94%) of scrub typhus was high grade fever with chills and rigor followed by 41(82%) shortness of breath, 17(34%) jaundice, 15(30%) abdominal pain, 13(26%) headache, 11(22%) altered sensorium, 9(18%) cough and vomiting, 7(14%) myalgia, 5(10%) rashes and generalized body swelling, 4(8%) diarrhoea and 3(6%) seizure. Similarly, most common signs of scrub typhus were

29(58%) hepatomegaly followed by 21(42%) splenomegaly, 15(30%) hypotension, 14(28%) pneumonitis, 11(22%) pallor, 9(18%) eschar, 7(14%) lymphadenopathy, 6(12%) facial puffiness and pedal edema, 4(8%) ascites and neck stiffness. Most of scrub typhus cases were belonged in low income socioeconomic status. 15(30%) and 6(12%) scrub typhus cases were belonged in middle and high socioeconomic profile respectively.

Table.2. Distribution of signs and symptoms

Variables	No. of case (N=50)	Percentage
Symptoms		
Headache	13	26%
High-grade fever with chills and rigor	47	94%
Shortness of breath	41	82%
Abdominal pain	15	30%
Jaundice	17	34%
Altered sensorium	11	22%
Rash	5	10%
Cough	9	18%
Myalgia	7	14%

Diarrhoea	4	8%
Vomiting	9	18%
Seizure	3	6%
Generalized body swelling	5	10%
Signs		
Hypotension	15	30%
Splenomegaly	21	42%
Hepatomegaly	29	58%
Pneumonitis	14	28%
Pallor	11	22%
Pedal edema	6	12%
Eschar	9	18%
Lymphadenopathy	7	14%
Ascites	4	8%
Neck stiffness	4	8%
Facial puffiness	6	12%

In this present study, thrombocytopenia was the most common laboratory findings of scrub typhus patients followed by 32(64%) increased SGOT/SGPT ratio, 23(46%) hyperbilirubinemia, 29(58%) anemia, 9(18%) hyponatremia, 8(16%) hypoalbuminemia, 7(14%) hypokalemia, 5(10%) leukopenia and 3(6%) metabolic acidosis.

Table.3. Showing the laboratory findings of scrub typhus.

Laboratory parameters	No. of cases	Percentage
Hyperbilirubinemia (> 2.5 mg/dL)	23	46%
SGOT/SGPT (≥ 2 times normal)	32	64%
Thrombocytopenia ($< 1.0 \times 10^9 /\mu\text{L}$)	47	94%
Hypoalbuminemia (< 3 g/dL)	8	16%
Hyponatremia (< 135 mEq/L)	9	18%
Anemia (< 11 g/dL)	29	58%
Hypokalemia (< 3.2 mEq/L)	7	14%
Hyperkalemia (> 5.2 mEq/L)	6	12%
Leukopenia ($< 4,000/\mu\text{L}$)	5	10%
Hypernatremia (> 150 mEq/L)	4	8%
Metabolic acidosis (pH < 7.3)	3	6%

Discussions

Scrub typhus was recognized as a typhus-like fever in India in 1917 [11]. The widespread use of insecticides and empiric treatment of febrile illness as well as changes in lifestyle all contributed to the subsequent decrease in incidence [12]. However, scrub typhus is still an under-diagnosed disease in India [12]. Field epidemiology studies indicate that the disease occurs all over India, from South India to Northeast India and Northwest India. There were cases reported from

Maharashtra, Tamil Nadu, Karnataka, Kerala, Himachal Pradesh, Jammu and Kashmir, Uttaranchal, Rajasthan, West Bengal, Bihar, Meghalaya, and Nagaland [13,12,14,15,16]. The peak of the disease is between August and October. *Leptotrombidium deliense* is reported as the primary vector of *O. tsutsugamushi* [11]. Socioeconomic status and occupation are important risk factors for scrub typhus. Most scrub typhus patients in India are uneducated and live in rural areas [13,12].

This present study was conducted in northern area of Bihar. In this study we were seen a total of 50 patients of scrub typhus. Majority of cases were belonged from rural area and low socioeconomic status 29(58%). Majority of patients 30(60%) were in age group of 40-60 years. Most of the patients were males 32(64%).

Md. Jamil et al & Aroma Oberoi et al supported to our study. They were noted higher predilection of scrub typhus towards males [17,18].

In this present study, most of the common symptoms 47(94%) of scrub typhus was high grade fever with chills and rigor followed by 41(82%) shortness of breath, Similarly, most common signs of scrub typhus were 29(58%) hepatomegaly followed by 21(42%) splenomegaly. Eschar was presented in 9(18%) cases.

Most of the studies reported that fever or fever with headache as the most common feature [19, 17,20]. Studies have reported wide range in frequency of appearance of eschar ranging from 10% to 86.3 % [19,17,21,22].

In this present study, thrombocytopenia was the most common laboratory findings of scrub typhus patients followed by 32(64%) increased SGOT/SGPT ratio, 23(46%) hyperbilirubinemia, 29(58%) anemia.

A study done in South India observed thrombocytopenia in 60% of the subjects [1]. Leukocytosis i.e. WBC count >10,000 mm³ noted with severe scrub typhus infection in our study. Kim, et al., [23] and Lee, et al., [24] also observed leukocytosis in severe group suggesting serious infection. We observed anemia (hemoglobin >12 g/dl) to be a predictor of severe scrub typhus, which is in agreement to study done by Suman, et al., [25] and contrary to study done by Kim, et al., [23], who failed to demonstrate anemia as an independent risk factor. Serum creatinine of greater than 1.4 mg/dl was an independent predictor of severity as per a

study done in South India which is in agreement with the results of our study [26, 27].

Conclusions

This present study concluded that scrub typhus was more prone in middle age male population. High-grade fever with chills and rigor and shortness of breath, hepatomegaly and splenomegaly were the most common symptom and sign of scrub typhus. Thrombocytopenia and SGPT/SGOT (≥ 2 times normal) were the most common laboratory findings of scrub typhus patients.

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