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Research Article

Prevalence of Scrub typhus among Patients attending a Tertiary Care Hospital - A Prospective and Retrospective study

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I N F O

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A B S T R A C T

Background: Scrub typhus is an emerging acute febrile illness caused by a gram-negative obligate intracellular bacterium, *Orientia tsutsugamushi*. It is transmitted by a chigger mite that acts as a vector. This study was carried out to understand the prevalence, clinico-haematological profile and clinical outcome of patients who tested positive for scrub typhus (ST).

Materials and Methods: This study, both retrospective and prospective, was conducted in the Department of Microbiology, Chettinad Hospital and Research Institute, a tertiary care teaching hospital located in the suburbs of Chennai. The study period was from October 2019 to December 2022. Blood samples from clinically suspected scrub typhus patients were tested by the immunochromatographic test, a rapid card that detects both IgG and IgM antibodies for scrub typhus. The demographic, clinico-haematological parameters and disease outcome of the patients who tested positive for scrub typhus were analysed.

Results: 1021 patients who presented to the hospital with febrile illness and clinical suspicion of scrub typhus were tested for this disease. Of these patients, 93 were IgM-positive. Common haematological abnormalities observed were leucocytosis, thrombocytopenia, anaemia, lymphocytosis, and monocytosis, along with elevated c-reactive protein, hypoalbuminemia, raised transaminases and an increase in serum creatinine. Dengue co-infection was diagnosed in 5% of the patients and leptospirosis in 1% of the patients.

Conclusion: The serological prevalence of scrub typhus was found to be 9.1% and it should be regarded as an important aetiological agent in patients presenting with fever. As an eschar may not be detected in all patients, the diagnosis relies profoundly on prompt laboratory investigations which can aid in swift diagnosis and rapid initiation of therapy.

Keywords: Scrub Typhus, Laboratory Parameters, Rickettsia, Co-infection, Febrile Illness

Introduction

Scrub typhus is caused by *Orientia tsutsugamushi*, a gram-negative, obligate, intracellular bacterium. The vectors for scrub typhus are *Leptotrombidium akamushi* and *Leptotrombidium deliense.* These vectors called chigger mites, are seen worldwide, more commonly in South-East Asia. In countries like India, Indonesia, Thailand, Nepal, Sri Lanka, Maldives and Myanmar, scrub typhus remains endemic;[1] at least 30 serotypes have been recognised so far. The name "scrub" originated from the type of vegetation harboured by the vector and the name "typhus" is a Greek word meaning "fever with stupor" otherwise smoke.[1] "Tsutsuga" denotes dangerous and tiny and "mushi" means insect. The mite larva (chigger) which acts as the vector for scrub typhus is seen in the ecological niches of some rain forests in the equatorial region, terrains of subarctic Himalayan areas and semi-deserts. These ecological niches are often referred to as mite islands and the areas within the niche where intense transmission occurs are referred to as typhus islands.[2] The larval stages of these mites are called "chiggers" and they transmit the infection, as only these larval stages have a blood meal. The wild rats of the genus *Rattus* acts as natural hosts for the disease because the acarine hosts and other rodents are not susceptible to the disease.[3] The infective trombiculid mites transmit the infection to humans and rodents. After consuming a blood meal from the infected rodents and other small mammals, the vectors harbour the causative agent throughout their life.[4] Also, the infection is passed on to all the stages in the lifecycle of the vector that is from the egg to the larva and then to the adult. This is referred to as transstadial transmission. The scrub typhus lesion has a characteristic eschar at the site of chigger mite bite which is followed by an ulcer with a black central necrotic area along with regional lymph node swelling. A maculopapular rash that commences from the trunk and extends to the limbs is another symptom of the disease. This disease also affects various organ systems like the renal, cardiovascular, gastrointestinal, central nervous system, etc. The complications of the disease include acute renal failure, bleeding into the gastrointestinal tract, pneumonia, meningoencephalitis and leads to acute respiratory distress syndrome. Treatment is either doxycycline or chloramphenicol.

The clinical picture of scrub typhus presents with myriad manifestations involving various organs, based on the immunity of the patient. The goal of this study is to provide a detailed panel of clinical aspects of this disease and to create a better laboratory profile of this re-emerging disease which will enable clinical suspicion and early laboratory diagnosis.

Methods

This retrospective cum prospective descriptive cross-sectional study was carried out at Chettinad Hospital and Research Institute, a medical college hospital, located in Chengalpattu district, Tamil Nadu, South India. Patients admitted with scrub typhus (laboratory-confirmed) between October 2019 and December 2022, were included in this study irrespective of their age and gender. The study protocol was reviewed and approved by the Institutional Human Ethics Committee of Chettinad Hospital and Research Institute and informed consent was obtained from the study participants.

A total of 1021 patients who presented with febrile illness were included in this study. Data were collected based on the patient's demographics, clinical features, and laboratory parameters like complete blood counts, serum creatinine, liver function tests, c-reactive protein, etc. STANDARD Q Tsutsugamushi IgM/ IgG rapid immunochromatographic assay was used for the simultaneous detection of both IgM and IgG antibodies against *Orientia tsutsugamushi* present in serum, plasma and whole blood for the patients admitted with complaints of fever. The tsutsugamushi IgM/ IgG antibodies in the patient's serum react with the recombinant tsutsugamushi antigen conjugated with gold colloid and produce a violet-coloured band in the test line to give a positive result. Other co-infections like dengue, malaria, enteric fever, and leptospirosis were also studied in these patients. Dengue was confirmed by NS1, IgM and IgG ELISA, malaria by rapid antigen detection card test, leptospirosis by IgM ELISA and enteric fever by Widal test. Biochemical and haematological parameters for patients positive for scrub typhus were also studied. The data collected were analysed and descriptive statistics were used to analyse the demographic characteristics and laboratory parameters.

Results

Out of the 1021 patients with febrile illness tested for scrub typhus, 93 (9.1%) tested IgM positive. One patient tested positive for both scrub typhus IgG and IgM antibodies (Figure 1).

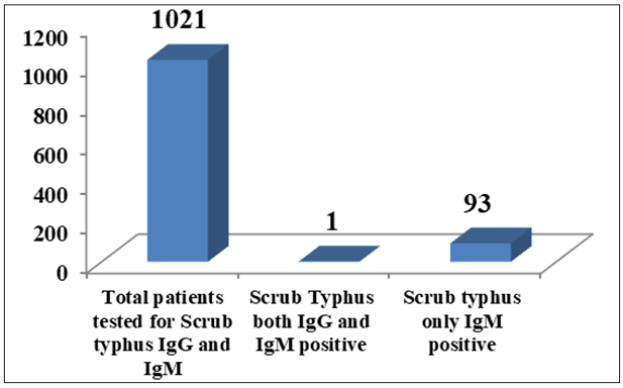

Figure 1.Results of Test for Scrub Typhus among the Participants

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The percentages of males and females included in the study were 42% (39) and 58% (54) respectively. Age-wise distribution of the patients showed that 37% (34) of the participants were 41-70 years old, 25% (23) were 19-40 years old, 33% (31) were 1-18 years old, and 5% (5) of the patients belonged to the age group of more than 70 years (Figures 2 and 3).

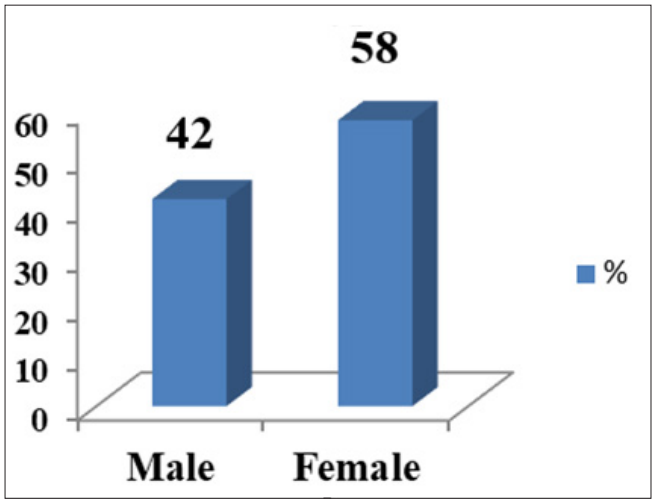

Figure 2.Genderwise Distribution of Participants Positive for Scrub Typhus

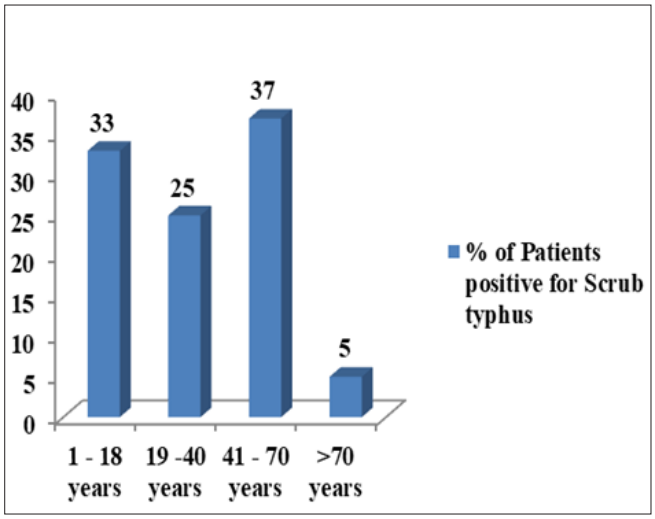

Figure 3.Agewise Distribution of Participants Positive for Scrub Typhus

Haematological parameters analysed in scrub typhus (ST)-positive patients have been tabulated in Table 1. 67% (62) of these participants had RBC counts in the range of 3.4-4.4 million/µL and 5% (5) had them in a range of 2.0 to 3.3 million/µL. 23% (21) of the patients showed haemoglobin levels of less than 10 g/dl. 20% (19), 11% (10), 4% (4) and 1% (1) of the ST-positive patients had leukocyte counts of 10000 to 13000 cells/µL, 13,000 to 15,000 cells/µL, 15,000 to 18,000 cells/µL, and more than 32000 cells/µL respectively. Neutrophilia was observed in 10% (9) of the individuals and neutropenia was observed in 13% of the patients. Lymphocytopenia was observed in 26% (24) of the patients and lymphocytosis was observed in 28% (26) of the individuals. Platelet count was found to be low in 32% (29) of ST-positive patients.

Table 1.Haematological Parameters of Scrub Typhus-positive Patients

Haematological Parameter Range	No. of Patients	% of Scrub Typhus-positive Patients
RBC (million/µL)		
2.0-3.3	5	5
3.4-4.4	62	67
> 4.5	26	28
Leukocyte (cells/µL)		
< 4,000	5	5
4,000-10,000	54	58
10,000-13000	19	20
13,000-15,000	10	11
15,000-18,000	4	4
> 32,000	1	1
Haemoglobin (g/dl)		
7-9	21	23
10-11	32	34
> 12	40	43
Platelet (lakhs/µL)		
< 1.	9	10
1.0-1.4	20	22
01.5-4.1	64	69
Neutrophils (%)		
< 40	12	13
40-80	72	77
> 80	9	10
Eosinophils (%)		
< 1	65	70
1-6	26	28
> 6	2	2
Basophils (%)		
0-0.9	90	97
1-2	3	3
Lymphocyte (%)		
< 10	4	4
10-20	20	22
20-40	44	47
41-60	22	24
> 60	4	4

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Monocyte (%)		
< 2	3	3
2-10	77	83
> 10-16	13	14

All (100%) ST-positive patients presented with fever. 34% (32) of the respondents presented with nausea/ vomiting, 46% (42) with headache, 38% (35) with cough, 32% (29) with breathlessness, and 6% (5) presented with altered sensorium. An eschar was noted in 33.3% of patients. Serum creatinine was elevated in 14% of the ST-positive patients (1.4-7.5 mg/dL) and hypoalbuminaemia was observed in 65% of the positive patients. Alanine transaminase was increased in 80% (74) of the patients. Aspartate aminotransferase was increased in 74% (69) of the respondents. 13% (12), 16% (15), 15% (14), and 11% (10) of the patients showed an increase in c-reactive protein of more than 200 mg/L, 100-200 mg/L, 50-100 mg/L, and less than 50 mg/L respectively. 5 (5.4%) patients had dengue and 1 (1%) had leptospirosis as co-infection.

Discussion

Patients with scrub typhus usually present with an acute undifferentiated fever. In our study, all the patients presented with fever which is found to be consistent with many studies. The current study showed that females were more affected as compared to males. This is concordant with the study done by Verma et al.[5] Our study showed patients belonging to the age group of 41-70 years were more affected (37%) followed by patients belonging to the age group of 1-18 years (33%). This correlates with a study done by George et al. where the age group of 51-60 years were affected more than other age groups.[6] The incubation period for scrub typhus fever ranges between 6 and 21 days from exposure. The causative agent *O. Tsutsugamushi* usually resides in the salivary glands of the larva (chigger) and they inject their mouthparts into the host when they feed. Patients pick up an infective larval mite accidentally while lying, sitting or walking on the infested ground most commonly during the monsoon period.[7] The initial sign in these patients is the appearance of a lesion that is vesicular at the site where the chigger mite has taken a blood meal and the lesion further develops into an eschar or an ulcer with marked regional lymphadenopathy.[8] Though the presence of eschar can be an evident sign for the diagnosis of scrub typhus, not all scrub typhus-positive patients are seen to have eschars. In our study, only 31 out of 93 (33%) positive patients had developed an eschar. Hence serological investigations play a major role in the diagnosis of scrub typhus. The severity of the disease depends on the immune status of the patients and the strain of the causative agent. The causative agent, *O. Tsutsugamushi*, invades the endothelial cells and results in disseminated perivascular inflammatory lesions and vasculitis leading to vascular leakage that further progresses to the injury of major organs like the lungs, heart, and kidney.[9] It was noted that this infection involved multiple organs predominantly the liver, spleen and lung among the admitted patients. In our study, the biochemical and haematological parameters were abnormal. We observed leucocytosis, thrombocytopenia, anaemia, lymphocytosis, monocytosis, increase in c-reactive protein, hypoalbuminaemia, raised transaminases and an increase in serum creatinine. These observations were found to be consistent with various studies.[5,6] Though the signs and symptoms of scrub typhus are common for many other infections like rickettsiosis and tularaemia, early diagnosis and treatment will bring down the in-patient burden in hospitals.[10] In our study, 5% of the patients had dengue as a co-infection. Few studies have reported dengue co-infection in scrub typhus-positive patients. Untreated dengue infection has a high mortality rate. Therefore a timely diagnosis of both scrub typhus and dengue infection will prevent the development of severe complications and will lower the mortality rate.[11] In our study, only one patient had leptospirosis as a co-infection.[12] Scrub typhus is now emerging in various parts of our country which is evidenced by studies reported from different parts of India, especially in south India.[13] Major outbreaks have been reported from Tamil Nadu, Himachal Pradesh, Nagaland, Meghalaya, and Puducherry.[14] In resource-poor healthcare centres, diagnoses are often missed, and a delay in diagnosis causes a delay in initiating treatment that further leads to adverse outcomes and increased mortality rate in immunosuppressed patients. Prompt and quick medical care and early diagnosis using accurate and affordable diagnostic tests help in the accurate identification of the disease and early initiation of treatment. Timely diagnosis using a rapid immunochromatographic test, especially in patients who come from rural areas with a history of fever, marked thrombocytopenia, and other organ dysfunction, and early treatment of the patients with doxycycline will reduce adverse outcomes and decrease mortality.

Thus, increasing awareness of scrub typhus infection among clinicians in endemic settings and improving reliable and rapid confirmatory methods will help to further reduce mortality.

Conclusion

As per the present study, the serological prevalence of scrub typhus was found to be 9.1% and considering its endemic nature, it should be regarded as an important aetiological agent in patients presenting with fever. Most of the scrub typhus-positive patients belonged to the age group of 41- 70 years, with female predominance. This study also gives an insight into the clinical settings and the geographical areas endemic to scrub typhus. The authors

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again reiterate that scrub typhus should be included in the differential diagnosis in patients presenting with fever and thrombocytopenia. Moreover, a strong clinical suspicion of scrub typhus is necessary for patients presenting with fever during the monsoon season. As an eschar may not be detected in all patients, the diagnosis relies profoundly on prompt laboratory investigations including appropriate serological tests, and haematological and biochemical parameters. This can lead to swift diagnosis and initiation of interventions that would reduce the morbidity and mortality due to scrub typhus.

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Conflict of Interest: None

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