

A Study of Clinico - Laboratory Profile of Scrub Typhus in a Tertiary Care Hospital in Telangana

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Abstract:

Introduction: Scrub typhus is a re-emerging infection caused by *Orientia tsutsugamushi* (formerly *Rickettsia*) and is transmitted to humans by an arthropod vector of the *Trombiculidae* family (*Leptotrombidium deliense* and *L. akamushi*).

Materials and Methods: The prospective study was conducted in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana. The study was conducted from November 2018 to November 2019. The aim of this study is to report the antibodies of scrub typhus and to assess the clinical features and outcomes of scrub typhus among the patients attending a tertiary care hospital.

Results: A total of 62 patients diagnosed as scrub typhus positive on the basis of eschar and specific tests were included in the study. They presented with subacute fever with eschar 18(29.03%), lymphadenopathy 41(66.12%), hepatomegaly 33(53.22%) and splenomegaly 37(59.67%).

Conclusion: Scrub typhus is exhibiting a resurgence in our region, which is evident by recent rise in reports from regions of India since last two decades. Scrub typhus cases were under diagnosed because of non specific clinical presentation, limited awareness in conjunction with lack of facilities in diagnosis. Other common infectious conditions that clinically mimic scrub typhus should be ruled out diagnostically. All the patients responded well to Azithromycin and Doxycycline, empirical therapy with these antimicrobial agents may be given among the suspected cases.

Key words: Scrub typhus, , *Orientia tsutsugamushi*, Enzyme Linked Immunosorbent Assay, Eschar, Doxycycline

Introduction:

Orientia tsutsugamushi is an, intracellular gram-negative bacteria bacteria that causes a zoonotic acute febrile illness the scrub typhus disease in humans. The genus *Orientia* belongs to the order Rickettsiales within the family Rickettsiaceae. In addition

to scrub typhus caused by *Orientia tsutsugamushi* and newly identified *Orientia* species *Candidatus Orientia chuto* and others, the rickettsial (spotted fever and typhus group), ehrlichial, and anaplasma diseases were also included within the order Rickettsiales. This is found only in areas with a suitable climate, plenty of moisture and scrub vegetation^{1,2}.

Scrub typhus is endemic in the geographical region which is known as “tsutsugamushi triangle” that extends from northern Japan and far-eastern Russia in the north, to the territories around the Solomon Sea into northern Australia in the south, and to Pakistan and Afghanistan in the west³. Several cases of scrub typhus were reported from India and the number of cases were being increasingly reported from southern region.⁴

The first case of scrub typhus was reported from India in 2009 from Kerala. The prevalence rate in India was not reported yet though it is reported widely all over the continent, but epidemics with scrub typhus have been reported from north, east and south India. The overall mortality varies from 7% to 30%, next only to malaria among infectious diseases. Due to lack of awareness among clinicians, lack of proper diagnostic and confirmatory facilities and the clinical symptoms mimicking other more prevalent diseases such as malaria, leptospirosis and dengue, scrub typhus is under-diagnosed in India, especially in Rajasthan.⁵ Scrub typhus is one of the differential diagnoses (in addition to enteric fever, leptospirosis, malaria or dengue fever) disease in patients with haemorrhagic fever, especially if associated with jaundice and/or renal failure.⁶

Scrub typhus may be mild or severe, having an incubation period of 6-21 days, the Rickettsiae proliferate within the site of the chigger bite to form a necrotic eschar with an erythematous rim among <50% of cases⁷. The observation of the eschar may often be missed and other signs and symptoms of the disease are not characteristic thus posing the problem of delay in diagnosis by the physician.⁴ The classical presentation of fever with eschar and accompanying constitutional symptoms such as myalgias and headache or with organ dysfunctions involving organs such as kidney (acute renal failure (ARF), liver (hepatitis), lungs (acute respiratory distress syndrome (ARDS), central nervous system (meningitis), or with circulatory collapse with haemorrhagic features.⁸⁻¹¹

The immunofluorescence assay (IFA) is considered to be a 'gold standard' in diagnosing the Rickettsial infections, however, but fluorescence microscope equipment is not easily available. Moreover, the test is expensive, requires an expert for it ideally requires cell culture facilities for sustaining Rickettsial antigens and often may require more than a week to get the results. Frequently used serological test in Rickettsial screening is the Weil-Felix test, but this test has poor sensitivity and specificity. Recent outbreaks are reported by detecting antigen-specific IgM or IgG antibodies by enzyme-linked immunosorbent assay.¹²

4. Materials and Methods

The prospective study was conducted in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana. The study was conducted from November 2018 to November 2019. Ethical approval was obtained from institutional committee. The samples were subjected for the detection of IgM antibodies for the diagnosis of scrub typhus by ELISA and Immunochromatography test. Simultaneously the samples were also tested for typhoid, dengue, leptospirosis, malaria and tuberculosis. We used In Bios International TM IgM ELISA for detection of IgM antibodies by ELISA. Immunochromatography method for

detection of IgM antibodies was done with SD Bioline tsutsugamushi, one-step scrub typhus antibody test.

5. Results

Among the 73 cases tested, 62 cases were diagnosed positive for Scrub typhus, all ages ranging from 8 - 64yrs were included in the study (Table:1). We excluded 11 cases as the patients presented other comorbidities like malaria, tuberculosis, chikungunya, dengue and typhoid, which endemic febrile diseases in our region, the Scrub typhus test may be positive because of cross reactivity with other coinfections. All cases were confirmed by both ELISA and Immunochromatographic method, the moto of this study is to determine morbidity pattern, and complications associated with scrub typhus and the clinical presentation. The diagnosis of scrub typhus was based on the presence of the characteristic Escher and / or positive ELISA and Immunochromatographic test. (Table: 2)

Table I: Age and Sex distribution.

S.No	Age wise distribution	No. of Patients
1	1-9	3(4.83%)
2	10 – 19	12(19.35%)
3	20 – 29	6 (9.67%)
4	30 – 39	15(24.19%)
5	40 – 49	8(12.90%)
6	50 – 59	14(22.58%)
7	60 – 69	4(6.45%)

Table II: Clinical presentation of patients.

S.No	Clinical Conditions	No. Of cases
1	Fever	62(100%)
2	Eschar	18(29.03%)
3	Lymphaedenopathy	41(66.12%)
4	Hepatomegaly	33(53.22%)
5	Splenomegaly	37(59.67%)
6	Jaundice	3(4.83%)
7	Rigor	22(35.48%)
8	Vomiting	36(58.06%)
9	Diarrhoea	4(6.45%)
10	Skin Rash	11(17.74%)
11	Pain Abdomen	14 (22.58%)
12	Icterus	3(4.83%)
13	Seizures	1(1.61%)
14	Cough	13(20.96%)

Fever is the commonly observed clinical manifestation (100%). Eschar was seen in seven patients and skin rash was seen in Eighteen patients over chest and abdomen. Skin rash was seen only in 17.74% of patients. Different laboratory investigations were given in the Table:III. There was 98.38% correlation between ELISA and rapid method, only one sample was negative by immunochromatographic method.

Table III: List of laboratory investigations.

S.No	Investigations	Number	Percentage
1	Leukocytosis	12	19.35%
2	↓Platelets	13	20.96%
3	↑Bilirubin >1.2mg/dl	7	11.29%
4	↑Creatinine	2	3.22%
5	↑ SGOT	18	29.03%
6	↑SGPT	12	19.35%
7	↑Alkaline Phosphate	16	26.9%
8	↓ Albumin	9	25.80%
9	↓Decreased Sodium	19	30.64%

Discussion

Scrub typhus is a re-emerging infectious disease, which clinically presents as an acute febrile illness with a generalized vasculitis that may involve the tissues of any organ system. The disease is transmitted to humans when an infected chigger bites them while feeding and inoculates *Orientia tsutsugamushi* pathogens. The organism multiplies at the site of inoculation with the formation of a papule that ulcerates and becomes necrotic, evolving into an eschar. Regional lymphadenopathy occurs that progresses to generalised lymphadenopathy within a few days.^{9,14}

Orientia tsutsugamushi, targets the endothelial cells in humans throughout the body and also the macrophages and cardiac myocytes. Rickettsial infection may cause a focal or disseminated vasculitis and perivasculitis with significant vascular leakage and end-organ injury to lung, liver, heart, spleen and central nervous system, thus leading to several clinical manifestations, such as respiratory distress syndrome (ARDS), hepatitis, myocarditis, acute, multiorgan dysfunction syndrome (MODS), disseminated intravascular clotting with shock and several neurological manifestations.⁶

In India this disease is grossly under-reported and under-diagnosed owing to the misconception that scrub typhus is only a concern in heavily forested areas. This study was planned to monitor the level of scrub typhus-specific antibodies among febrile cases in our hospital for which a rapid qualitative immunochromatographic assay (Standard Diagnostics, Korea) was introduced for the detection of IgM, IgG and IgA antibodies to *O. tsutsugamushi* from the serum of suspected febrile patients.

We identified maximum number of cases in the October. Similar findings were observed by Umesh G et.al, where highest numbers of cases 23% were observed during the month of September resembling autumn-winter type scrub typhus. Similar seasonal distribution was established by B.S.Kalal et.al.^{9,12}

Eschar was observed in 29.03% of cases in our study, the results were consistent and inconsistent with many studies from India, 50—70% of cases were reported by Radha Kumar et.al¹³ and Ira shah et al.,¹⁴ JasaShree Choudhury et.al,¹⁵ reported eschar in 50% of cases, 47.36% in a study by Dr.Neeraj Jain et.al,¹⁶ 43.5% in Narendra Rungta et al.,¹⁷ 17.5% in Sunil Dutt Sharma et.al study,¹⁸ In contrast A Ramyasree et al.,⁴ from Tirupati did not observed presence of eschar in their study.

Regional or generalized lymphadenopathy found to be a characteristic feature of Rickettsial infection. Present study shows lymphadenopathy was the most common complication seen in 41% of patients. Many studies reported similar findings a study by Richard Mariyo Lurshay et.al from Meghalaya reported 13%, Ajith Babu et.al., from Chidambaram 22%, Deepak Jain N et.al from North India observed 20.05%.^{19,5,}

Doxycycline is universally the drug of choice for treatment of scrub typhus irrespective of the day of presentation, other antibiotics of choice for Scrub typhus is Macrolides, Chloramphenicol and Tetracycline. We started treating all the cases with Doxycycline. All the patients responded well to therapy with antibiotics, In a study by Radha Kumar et al,¹³ from Chennai reported 94.1% and a study from Uttarakhand by Bhat NK et.al observed 90% patients became afebrile within 2days of treatment with Doxycycline^{16, 19}. 95.16% of patients became afebrile with in 48hrs of antimicrobial therapy. The prognosis and clinical course of the disease varies based on the type of strain and various host factors such as age, immune status and the co-morbidities.

Conclusion

Scrub typhus need to be included in the differential diagnosis of patients presenting with acute febrile illness even in the absence of characteristic eschar. Scrub typhus should be suspected as one of the differential diagnosis of high grade fever, with hepatosplenomegaly, lymphadenopathy. High index of clinical suspicion should be kept, particularly during viral outbreaks where the diagnosis can be missed. Timely diagnosis and appropriate management can prevent fatal outcomes associated with scrub typhus. Tests like IgM ELISA and Immunochromatographic tests should be performed for confirming the suspected cases. In the recent years number of studies has reported the resurgence of Scrub typhus from different parts of India, but there is paucity in community based data, more research is required on this entity with respect to epidemiology, pathogenesis, clinical findings in context of the Indian subcontinent.

Declarations

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Conflict of interest: Nil

Ethical approval: Approval taken

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