

Small Bites - Big Threats: Prevalence of scrub typhus among the pediatric population in a rural tertiary care hospital in South India

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Background: It is an acute, febrile, exanthematous illness with a high fatality rate. Scrub typhus is underdiagnosed in India due to its non-specific clinical presentation, limited awareness, and low index of suspicion among clinicians and lack of diagnostic facilities. **Objective:** This study was carried out to know the seroprevalence of scrub typhus in clinically suspected children and to compare a rapid test which is a simple and economic test with IgM ELISA for the diagnosis of scrub typhus. **Methods:** This cross-sectional analytical study was conducted from a period of three months. The study population comprised mainly 140 young children attending Pediatric OP and in patients admitted to a tertiary care teaching hospital with fever and related symptoms. A serum sample was tested for Weil Felix reaction, IgM ELISA, and rapid card test. **Results:** The mean age group of the study population is 7 to 9 years, of which seven cases were positive. The major predisposing factor for scrub typhus infection was vegetation around houses. The sensitivity and specificity of both card test and IgM ELISA was 100%. **Conclusion:** In this study, 5% of febrile children were positive for scrub typhus. Leptospirosis, Dengue, and Typhoid were the common co-infections found in scrub typhus, positive children. Scrub typhus should be included in the differential diagnosis of fever of unknown origin in children.

Keywords: Febrile children, Orientia tsutsugamushi, Scrub typhus

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Introduction

Scrub typhus, a mite borne Rickettsial disease caused by the *Orientia tsutsugamushi*, was once widely prevalent in the Tsutsugamushi triangle in the East Pacific region [1]. It is an acute, febrile, exanthematous illness with a high fatality rate. According to the World Health Organization, "Scrub typhus is probably one of the most under-diagnosed and under-reported febrile illnesses requiring hospitalization" [2]. Scrub typhus accounts for up to 23% of all febrile episodes, with an estimated 1 million cases occurring annually, in endemic areas.

Human beings get infected accidentally when they encroach upon mite-infested rural and suburban areas. It is often acquired during recreational, occupational, or agricultural exposure because crop fields are an important reservoir for transmission. It was considered a lethal disease in the pre-antibiotic era and continues to be a public health problem in South Asian and Western Pacific regions.

Four elements are essential to maintain *O. tsutsugamushi* in nature. Trombiculid mites, small mammals like the field, mice, rats, secondary scrub vegetations, and wet season (when mite lays eggs) [3].

The clinical spectrum of scrub typhus varies from mild to moderate severity. Acute fever is the most common manifestation later accompanied by headache, myalgia, and cough [4]. Eschar is a characteristic skin lesion usually observed in most of the scrub typhus patients. Severe complications include prominent encephalitis, interstitial pneumonia, and ARDS, circulatory collapse with hemorrhagic features. Mortality may be as high as 35 to 60% if diagnosis or appropriate therapy is delayed [5].

Several tests are available with their own advantages and limitations. Weil-Felix test is being the cheapest and easily available, shares antigens with other bacteria (members of *Enterobacteriaceae*). IgM ELISA has been evaluated and found to be satisfactory in diagnosis. Rapid test (Immunochromatography) which is economic and single tests can be carried out.

Scrub typhus is under-diagnosed in India due to its non-specific clinical presentation, limited awareness, and low index of suspicion among clinicians and lack of diagnostic facilities. Once diagnosed, treatment with Doxycycline is affordable and successful with a

Dramatic clinical response within 48 hours. In children, treatment with azithromycin for 3 days is recommended [3].

This study was carried out to know the seroprevalence of scrub typhus in clinically suspected children and to compare a rapid test which is a simple, and economic test with IgM ELISA for the diagnosis of scrub typhus.

Material and Methods

The setting of the study- The present study was conducted in a tertiary care teaching hospital to all young children attending Paediatric OP and in patients.

Duration and type of study- The present cross-sectional analytical study was conducted from the period of May to June 2019.

Sampling methods- Universal sampling was done and all children presenting with fever and related symptoms were included. There were a total of 140 children presenting with fever and related symptoms.

Sample size calculation: -The sample size was calculated from pre-existing studies in the literature with a prevalence rate of 23% in adults in the Pondicherry [3].

Inclusion criteria: All children presenting with acute febrile illness due to infectious etiology

Exclusion criteria: Children presenting with fever due to metabolic causes or other non-infectious etiology were excluded.

Data collection procedure- A structured proforma was utilized for the current study. The details like age, place where the child is residing, socio-economic status, educational qualification of the mother, source of drinking water, history of any vector bites, rodents near the houses, history regarding vaccination status of the child were obtained.

Under strict aseptic precautions, 3 to 5ml blood was collected from children using a sterile syringe. Complete hemogram, erythrocyte sedimentation rate, C-reactive protein (CRP), liver function tests, and renal function tests were also performed. In all cases, a peripheral smear and/or QBC test was performed to exclude malaria and Widal was put up to rule out the enteric fever. In cases of negative for malaria and enteric fever, the presence of leptospiral

Dengue, chikungunya infection was investigated by IgM ELISA for *Leptospira*, IgM antibody, and NS1 antigen ELISA (Panbio) for dengue and IgM ELISA (Panbio) for Chikungunya.

Finally, after all these investigations the serum sample was tested for Weil Felix reaction and scrub typhus IgM ELISA using the INBIOS kit. A rapid card test was done in addition to this. A single titer of $\geq 1:160$ or a four-fold rise in titer from two consecutive samples submitted a week apart is considered significant Rapid card test by SD Biotec Tsutsugamushi, rapid qualitative test for the detection of antibodies (IgG, IgM, and IgA) to *Orientia tsutsugamushi* was used.

Ethical consideration and permission- The purpose of the study was explained to the parents of the children presenting with fever and written informed consent was obtained before enrolling in the study. Institutional Ethics Clearance was obtained before starting the study (Ref. No: 636/TSRMMCH and RC/ ME-1/ 2019 – IEC No: 006 dated 17.07.2019).

Statistical analysis- The cases which were found to be positive with scrub typhus was noted. Co-infections are quite common, so if the child tests positive for either WIDAL or leptospirosis was taken and analyzed. The cases were evaluated with their habitat and any conclusive finding was noted. Statistical analysis was done using version Epi info version 7.2 Statistical software for windows.

Results

All the acute febrile illness of pediatric cases attending the hospital was taken into account. The current study observed about 140 cases. The age and gender analysis of the patients included in this study were depicted in Table 1.

Table-1: Age-wise prevalence of the study population.

Age (in years)	Male	Female	Number of cases(n=140)
4 to 6	24	14	38 (27.1)
7 to 9	38	17	55 (39.3)
10 to 12	25	22	47 (33.6)
	87 (62.1)	53 (37.9)	140 (100)

[Figure in parenthesis denoted percentages]

Gender wise analysis of the study population was recorded as 62.1 and 37.9% among males and females respectively. Of the 7 scrub typhus positive cases, 4 were male and 3 were female children.

The major factors of the predisposition of scrub typhus were analyzed and among 7 positive cases, 42.8% had vegetation around houses, 28.5% had the habit of frequent forest visiting, 28.5% used to defecate at open fields and 14.2% practice poor personal hygiene (Table 2).

Table 2: Predisposing factors to scrub typhus (n=7).

Predisposing factors	Number of patients (n=7)
Vegetation around houses	3 (42.8%)
Open field defaecation	2 (28.5%)
Forest visiting	2 (28.5%)
Poor personal hygiene	1 (14.2%)

The laboratory investigations of the positive scrub typhus were analyzed thereby leucocytosis, anemia was found among 5 and 2 cases respectively. Elevated transaminase levels were found among one child; increased bilirubin and urea/ creatinine also found among one case each and the detailed laboratory investigations are impregnated in table 3.

Table 3: Laboratory investigations of positive cases (n=7).

Lab investigations	Number of cases (n=7)
Total leucocyte count >11,000/cu.mm	5 (71.4%)
Anaemia (haemoglobin<10 g/dl)	2 (28.5%)
Elevated transaminase levels (normal 40/56 I.U)	1 (14.2%)
Increased bilirubin (normal 0.3–0.8 mg/dl)	1 (14.2%)
Increased urea/creatinine (normal 60/0.6–1.2 mg/dl)	1 (14.2%)

Other serological investigations were done. Of the 140 cases, WIDAL, ASO, CRP, leptospirosis, malaria, and dengue were found to be positive in 24, 16, 39, 4, 2, and 2 respectively (Table 4).

Table-4: Profile of serological investigations of the study population.

Investigations	Number of cases positive (n=140)	Scrub typhus positive (n=7)
C - reactive protein	39 (27.8)	2 (28.6)
ASO	16 (11.4)	-
typhoid	24 (17.1)	1 (14.2)
Malaria	2 (1.4)	-
Dengue	2 (1.4)	1 (14.2)
Leptospira	4 (2.8)	1 (14.2)
Scrub typhus	7 (5)	7 (100)
Non-reactive	49 (35)	-

[Figure in parenthesis denoted percentages]

Weil Felix test gave more false positive and false negative results in this study; sensitivity and specificity of the Weil-Felix test were to be found as 57.1% and 85.7% respectively. This implies that Weil-Felix is not a reliable diagnostic test when compared with the card test and IgM ELISA results.

The sensitivity and specificity related to the tests done for screening scrub typhus were done and tabulated (Table 5). Co-infections were found with *Leptospira* (14.2%), dengue (14.2%) and typhoid (14.2%) (Table 6).

Hence, the prevalence of scrub typhus with other co-infections is common.

Table 5: Screening and diagnostic tests for scrub typhus and results in the study population (n=140).

Tests	Number of cases positive for the test	Number of cases negative for the test	The sensitivity of the test (%)	The specificity of the test (%)
Weil Felix test	28	112	57.1	85.7
Card test	7	133	100	100
IgM ELISA	7	133	100	100

Table 6: Comparison of test results of scrub typhus positive cases (n=7).

Tests	Number of cases positive for the test	Number of cases negative for the test
Weil Felix test	4 (57.1)	3 (42.9)
Card test	7 (100)	-
IgM ELISA	7 (100)	-

[Figure in parenthesis denoted percentages]

Discussion

Scrub typhus, a long-forgotten and neglected infectious disease, with no licensed vaccines is undoubtedly a reemerging disease. With improvements in approaches to estimating the burden of febrile illnesses, it is important to reevaluate the burden of scrub typhus. A study done in Ludhiana in 2014 reported that out of 772 fever patients, 12.7% positive for scrub typhus [5].

Another study done in India [6] observed that 24% of patients presenting with unexplained febrile illness had scrub typhus. A study done in Goa during 2012 found that 34% of fever cases [7] were

Positive for IgM antibodies against *O. tsutsugamushi*.

The mean age group of the study population was 7 to 9 years (39.3%), which is similar reported [8]. Most of the study participants resided in the rural area (58.6%), thereby the proximity to mite friendly surroundings appears to be more. Studies have shown that rodents carrying the mites are transmitting the disease in the urban locales in India [9,10]. Urbanization, contaminated environment, and rodent population had made it suitable for the transmission of the disease in the urban setting.

The abnormalities in cell counts, and liver and renal functions in the present study were consistent with those reported in other studies [11,12]. Of the 140 cases, 7(5%) tested positive for scrub typhus in card test and IgM ELISA. Scrub typhus was diagnosed by Weil-Felix, card test, and IgM ELISA where sensitivity and specificity of the Weil-Felix test were 57.1 and 87.5% respectively.

The sensitivity and specificity of the card test and ELISA was 100%. An earlier study conducted in Thailand using SD Bioline ICT had reported sensitivity and specificity to be 66.7 and 98.4%, respectively [13]. On the contrary, it was reported that higher sensitivity (72.6%) of SD Bioline ICT in the Korean population [14].

Another ICT, ImmuneMed RDT was found to be more sensitive (98.6%) than SD Bioline RDT (84.8%) in the Korean population [15]. A comparative study to determine the sensitivity was found as 44 and 87% with Weil-Felix test and IgM ELISA respectively [16].

Of the scrub typhus positive cases, 14.2% of cases were co-infected with either *Leptospira* or dengue or typhoid. A study done in Odisha [17] supported the fact where 36.2% of cases were positive for malaria, dengue, or chikungunya. Similarly, a study done in Arunachal Pradesh [18], confirms the co-infection rate of scrub typhus and *Leptospira* being 25%. This may be due to greater exposure to mites/ mammals, in the field and to the rodents during household activities at home.

Limitations of the study

- The study is a single centered.
- A seasonal variation could not be studied.
- Entire population (Only Paediatric population) was not included; thereby full prevalence can't be detected

Conclusion

The study recommends that scrub typhus should be included in the differential diagnosis of fever of unknown origin along with leptospirosis and dengue fever which are other endemic diseases in this region, which will help in proper diagnosis, timely and adequate treatment and avoidance of the complications which are associated with high mortality.

What does the study add to the existing knowledge?

The study recommends that scrub typhus should be included in the differential diagnosis of fever of unknown origin along with leptospirosis and dengue fever which are other endemic diseases in this region, which will help in proper diagnosis, timely and adequate treatment and avoidance of the complications which are associated with high mortality.

Author's contribution

RajKumar B.: Planning the study,

Dr. Anupriya A.: Data collection and analysis

Dr. Uma A.: Statistical analysis

Dr. Prabhusaran N.: Manuscript preparation

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