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Seroprevalence of Scrub Typhus and Clinical Profile of Children with Scrub Typhus Presenting to a Tertiary Care Hospital in a Rural Setting

JUDY VERONICA J*, RAJAKUMAR PG†, JAISHREE V‡, VIKRAM R#

ABSTRACT

Introduction: Rickettsial infections were commonly recognized as an important cause of fever and central nervous system infections throughout Southeast Asia. Only in the recent years, it has been recognized to be an important cause of morbidity and mortality. **Objective:** To know the seroprevalence and clinical profile of children with scrub typhus presenting to a tertiary care hospital. **Methodology:** It was a cross-sectional study conducted in a tertiary health care center over a period of 1 year. Children presenting with fever for 5 days or more who were diagnosed negative for other causes of fever, like malaria and enteric fever, were considered as study population. A positive immunoglobulin M (IgM) ELISA (enzyme-linked immunosorbent assay) for scrub typhus was considered as primary outcome variable. Age, gender parameters were primary explanatory variables. Institutional ethical clearance was obtained. IBM SPSS version 22 was used for statistical analysis. **Results:** A total of 340 subjects were included in the final analysis. Among the study population, 241 (70.88%) children were aged >48 months. Male participants were 187 (55%) and remaining 153 (45%) were females. Out of 340 subjects, 48 (14.12%) participants were positive for scrub typhus. The common clinical features seen were fever, abdominal pain, cough, vomiting and hepatosplenomegaly in the decreasing order of frequency. **Conclusion:** The seroprevalence of scrub typhus rickettsial infection was 14.12%, which was quite high. Fever and abdominal pain were the prominent clinical features observed. Knowledge about scrub typhus fever may help in its early diagnosis and treatment and prevention of adverse outcome.

Keywords: Scrub typhus, prevalence, IgM ELISA

The infection caused due to Rickettsia normally presents as fever and is considered as one of the most significant central nervous system infections throughout Southeast Asia. Rickettsial infections are zoonotic infections. The transmission of rickettsial diseases is mainly through bites of arthropods like fleas, mites, etc. Rickettsia has three main serological groups of agents; scrub typhus is one of them. They are caused due to the serogroup *Orientia tsutsugamushi* and now there is newly discovered *Orientia chuto*, which is also known to cause scrub typhus fever. Scrub typhus is infectious in nature and trombiculid mites or chigger mites are mostly known for its transmission. The prevalence of scrub typhus infections is seen in areas of dense scrub vegetation. Hence, the name "scrub typhus" came into existence. Scrub typhus is endemic and is mainly found in the geographical region known as "tsutsugamushi triangle". The region majorly lies in Asia, Australia, islands in the Indian and Pacific Oceans. The triangle runs from northern part of Japan via Russia in the north, to Pakistan and Afghanistan in the west, and via the territories around India into northern Australia in the south. However, currently, the scrub typhus is widespread and is occurring in locations that were not previously thought to be endemic.

The typical characteristic feature that differentiates scrub typhus fever from other infections is the necrotic black lesion called "eschar", which is seen at the site of the mite bites. This helps in diagnosis of scrub typhus. The other signs and symptoms that are observed in scrub typhus cases include fever, chills, myalgia, headache,

*Post Graduate
†Professor and Head
‡Professor
#Assistant Professor
Dept. of Pediatrics
Shri Sathya Sai Medical College and Research Institute, Kanchipuram, Tamil Nadu
Address for correspondence
Dr Judy Veronica J
Post Graduate
Dept. of Pediatrics
Shri Sathya Sai Medical College and Research Institute, Ammapettai
Kanchipuram, Tamil Nadu
E-mail: judy.veronicaj@gmail.com

vomiting, diarrhea and rash. The complications may lead to acute renal failure, hepatitis, acute respiratory distress syndrome, meningitis, circulatory collapse and multiple organ dysfunctions.

Scrub typhus represents a major cause of treatable febrile illness across Asia. The prevalence of scrub typhus has been reported worldwide but the true incidence of the disease is still unknown. The extent of the disease is mainly seen in East and Southeast Asia such as Japan, Taiwan, China, South Korea, Nepal, Indonesia and Australia. A study by Balaji et al showed that 40% fever cases were positive for scrub typhus in Tamil Nadu and in another study, S Kanagasabai et al noted that 15% of the study subjects were positive for scrub typhus. The data on the prevalence of scrub typhus is scarce.

Scrub typhus with considerable morbidity and mortality has now been well-documented in several states in India and neighboring countries. Most studies in India are retrospective in nature or based on adult population. Hence, this study was carried out to know the seroprevalence and clinical profile of children with scrub typhus presenting to a tertiary care hospital in a rural Indian setting.

MATERIAL AND METHODS

Study Site

This study was conducted at the Dept. of Pediatrics of a tertiary care teaching hospital in a rural setting.

Study Population

Children up to 18 years of age, presenting with fever for 5 days or more and diagnosed negative for other causes of fever, like malaria and enteric fever, were considered as study population.

Study Design

The current study was a prospective cross-sectional study.

Sample Size

Sample size was calculated by assuming the expected prevalence of scrub typhus among the suspected cases as 56.42%, as per the previous published literature. The other parameters considered for sample size calculation included 10% absolute precision and 95% confidence level.

Sampling Method

All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size was reached.

Study Duration

The data collection for the study was done for 1-year period between July 2017 and June 2018.

Inclusion Criteria

Children aged less than 18 years, presenting with fever for 5 days or more.

Exclusion Criteria

- Adults aged above 18 years.
- Confirmed cases of malaria, enteric fever, leptospirosis.

Data Collection Tools

All the relevant parameters were documented in a structured study proforma.

Methodology

Statistical Methods

Scrub typhus immunoglobulin M (IgM) status was considered as primary outcome variable. Age, gender parameters were considered as primary explanatory variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.

The association between age, gender and scrub typhus IgM status was assessed by cross tabulation and comparison of percentages. Chi-square test was used to test statistical significance.

P value of <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

OBSERVATIONS AND RESULTS

A total of 340 subjects were included in the final analysis. Among the study population, 11 (3.24%) children were aged up to 12 months, 21 (6.18%) children were aged 13-24 months, 67 (19.71%) children were aged 25-48 months and 241 (70.88%) children were aged >48 months. Out of 340 children, male participants were 187 (55%) and remaining 153 (45%) were females.

Among the study population, 48 (14.12%) participants had positive results (Table 1).

Out of 11 participants aged up to 12 months, 1 (9.090%) participant had positive result; of 21 participants aged

Table 1. Seropositivity (IgM by ELISA) in Study Population (n = 340)

Result	Frequency	Percentage (%)
Positive	48	14.12
Negative	292	85.88

Table 2. Comparison of Scrub Typhus Positivity with Age of the Study Population (n = 340)

Age group (in months)	Result		Chi-square	P value
	Positive	Negative		
Up to 12 (n = 11)	1 (9.090%)	10 (90.90%)	3.337	0.343
13-24 (n = 21)	1 (4.761%)	20 (95.23%)		
25-48 (n = 67)	7 (10.44%)	60 (89.55%)		
>48 (n = 241)	39 (16.18%)	202 (83.81%)		

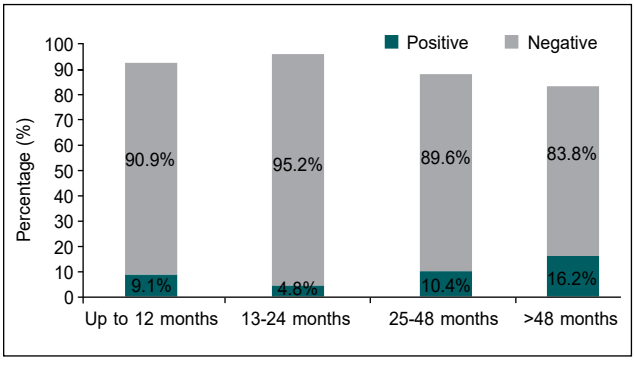

Figure 1. Stacked bar chart of scrub typhus positivity with age of the study population (n = 340).

13-24 months, 1 (4.761%) participant had positive result. Out of 67 participants aged 25-48 months, 7 (10.44%) participants had positive result and among 241 participants aged >48 months, 39 (16.18%) participants had positive result (Table 2 and Fig. 1). The difference in the proportion of results across different age groups was statistically not significant (p value 0.343).

The majority of participants had fever. The proportion of patients with abdominal pain and cough was 79.17% each, and for vomiting, hepatosplenomegaly (HSM), headache and myalgia was 47.92%, 39.58%, 31.25% and 31.25% (Table 3). Among the study population, 85 (25%) participants had fever up to 5 days and 255 (75%) participants had fever >5 days.

Table 3. Descriptive Analysis of Clinical Features in Study Population

Clinical Features	Frequency	Percentage (%)
Fever	48	100
Abdominal pain	38	79.17
Cough	38	79.17
Vomiting	23	47.92
HSM	19	39.58
Headache	15	31.25
Myalgia	15	31.25
Hepatomegaly	12	25.00
Poor appetite	10	20.83
Nausea	10	20.83
Rashes	9	18.75
Lymphadenopathy	9	18.75
Cool peripheries	8	16.67
Breathing difficulties	8	16.67
CRT >3 SEC	6	12.50
Conjunctival congestion	5	10.4
Splenomegaly	4	8.33
Jaundice	4	8.33
Seizure - I episode GTCS lasted for about 5 minutes	4	8.33
Melena	4	8.33
Oliguria	4	8.33
Cardiovascular dysfunction (shock)	4	8.33
Eschar	8	16.67
Crepts and crackles	2	4.17
Petechiae	2	4.17
Neck stiffness	2	4.17
High-colored urine	2	4.17
Hematemesis	2	4.17

DISCUSSION

In the current study, a total of 340 subjects were included in the final analysis. The study population varied in different studies. A study done in 2017 included only 96 participants, while a study done in 2018 had 964 patients.

Age

In the current study, 11 (3.24%) children were aged up to 12 months, 21 (6.18%) children were aged 13-24

months, 67 (19.71%) children were aged 25-48 months, 241 (70.88%) children were aged >48 months. In one study, the age ranged from 1 day to 18 years with the maximum number of children aged between 1 and 5 years (49.7%). In a study conducted in 2016, 13 (37%) subjects were aged between 1 and 5 years, 21 (60%) were aged >5-10 years and 6% were >10 years old. Various other studies reported the mean age as 8.97 ± 65.17, 7.3 ± 3.9, 3.2 ± 2.5 and 5.6 years.

In the current study population, 48 (14.12%) participants had positive results and 292 (85.88%) were negative for scrub typhus. The seroprevalence in our study was found to be 14.12%. The seroprevalence varied from 0.63% to 9.2% in various Indian studies.

Clinical Features in Study Population

A study in 2017 found that all the patients had fever. Other findings were also in accordance with our study where 56% of the participants had myalgia and 50.5% children experienced vomiting. Pallor was present in 48% of children, abdominal pain in 26% of the participants, headache in 28% children, facial puffiness in 15% participants and seizures in 8.7% participants. Other common signs were hepatomegaly in 29%, splenomegaly in 28%, hypotension in 24%, edema in 21%, oliguria in 17%, maculopapular rash in 10%, meningeal signs in 10.4% and conjunctivitis in 3% of the participants. Thrombocytopenia was seen in 67% participants, anemia in 51%, pleural effusion in 23%, shock in 16%, hepatitis in 23%, acute kidney injury in 17%, meningoencephalitis in 10%, myocarditis in 7% and acute respiratory distress syndrome in 7%.

A study done in 2009 found that the primary clinical symptoms included fever (100%), cough (50%), eschar (50%), rash (35.7%), poor appetite (42.9%), lymphadenopathy (42.9%), headache (39.3%) and hepatomegaly (35.7%). All these were in accordance with our study.

Eschar

In the current study, eschar in axilla was seen in 14.4%. In another study, eschars were often on the axilla/groin in 24.9% participants, followed by 23.4% in the abdominal region and waist area and 18.3% in the head and neck region.

Fever (in Days)

Among the study population, 85 (25%) participants had fever up to 5 days and 255 (75%) participants had fever for >5 days. In a study, 18 (27%) patients had fever <7 days, 39 (59%) had fever for 7-14 days and 9 (14%) had fever for >14 days. A study done in 2017 reported the mean days of fever to be 8.856 ± 3.18.

LIMITATIONS

- The present study was conducted only in pediatric population and was conducted at a single center. Hence, the study cannot be generalized to the rest of the population.
- Purposive sampling technique was employed for the study which is not a true representation of the general population. This may lead to selection bias.
- The study was hospital-based leading to Berksonian bias.

RECOMMENDATIONS

Given that there was high prevalence of scrub typhus rickettsiosis in our study, the clinicians and general practitioners must be aware of the clinical profile related to scrub typhus fever. Rickettsial fever must be considered when the symptoms don't fit into the profile of any other diseases causing fever (dengue, malaria, etc.). Timely recognition of complications may help prevent the adverse outcome.

It is recommended to conduct a large multicentric population-based study to know the true prevalence of scrub typhus.

CONCLUSION

The seroprevalence in our study was found to be 14.12% which was quite high when compared to previous studies.

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Blood Pressure Control Reduces Dementia Risk in Mid-life AF Patients

Dementia risk in mid-life patients with atrial fibrillation (AF) can be reduced by controlling high BP, according to a study presented at EHRA 2019, a congress of the European Society of Cardiology (ESC). The study also found that lowering BP in patients older than 70 years old may not have as big of an impact on dementia risk.

No Evidence that Calcium Increases Risk of AMD, Says Study

Eating a calcium-rich diet or taking calcium supplements does not appear to increase the risk of age-related macular degeneration (AMD), according to the findings of a retrospective analysis of data from the Age-Related Eye Disease Study (AREDS) published in *JAMA Ophthalmology*.