

## Original Research Article

# Clinical profile and complications: scrub typhus in children at a tertiary hospital in south India, Nellore

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**Received:** 04 February 2021

**Accepted:** 16 February 2021

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### ABSTRACT

**Background:** Rickettsial diseases, including scrub typhus, are emerging across the Asia-Pacific region as a significant source of acute undifferentiated febrile disease. The purpose of the research is to study the clinical profile, symptoms, and results of cases of scrub typhus admitted to rural medical colleges.

**Methods:** From November 2019 to August 2020, this prospective descriptive research was performed at Narayana Medical College, Nellore, Andhra Pradesh, India. Children who were scrub typhus-positive by immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) were tested.

**Results:** 164 children (more than 40 percent of fever cases) were scrub typhus-positive during the study time. Many of the children had a fever. 84.15 percent, 49.40 percent, 37.20 percent, 56.10 percent, and 25 percent respectively saw high-grade fever, chills, vomiting, cough, and headache. In 63.41 percent of children, Eschar was shown. The typical findings were lymphadenopathy (68.30 percent) and hepatomegaly (more than 57 percent). In 47.56 percent, 25.60 percent, 39.63 percent, and 37.19 percent, shock, respiratory failure, pleural effusion, and ascites were observed. Popular lab results were anemia (70.12 percent) and thrombocytopenia (74.40 percent). Complications were recorded in shock (47.56 percent), ARDS (10.36 percent), meningoencephalitis (7.32 percent), and MODS (1.22 percent). The complications were treated with doxycycline (51.21 percent), azithromycin (12.80 percent), and both drugs (35.97 percent) were used to treat the complications.

**Conclusions:** When a child presents with acute febrile illness, hepatosplenomegaly, lymphadenopathy, anemia with thrombocytopenia, and features suggestive of capillary leak diagnosis of scrub typhus must be considered. Doxycycline or azithromycin, proper fluid boluses, inotropes, and O<sub>2</sub> through Jackson-Rees circuit are life-saving for scrub typhus and its complications.

**Keywords:** Scrub typhus, Jackson-Rees circuit, Rickettsial diseases

### INTRODUCTION

In the Asia Pacific region, including India, scrub typhus is becoming a major cause of acute undifferentiated febrile disease. Rickettsial inflammation, or rickettsiosis, is a zoonotic acute febrile disease caused by *Rickettsia*, *Orientia*, *Ehrlichia*, *Neorickettsia*, and *Anaplasma* obligatory intracellular, gram-negative bacteria.<sup>2</sup> Rickettsiosis is transmitted by the bites of ticks or mites. There are records of rickettsial infections in different parts

of the world.<sup>3,4</sup> The most widely recorded rickettsial infection in India, like Andhra Pradesh and Telangana, is scrub typhus, which is caused by *Orientia tsutsugamushi*. Most research in India and other areas of the world on rickettsial infections are focused on adult populations.<sup>5</sup> There is a shortage of research in children from the Indian subcontinent on the prevalence and clinical profile of scrub typhus and most reported studies are observational studies or intermittent case reports.<sup>6-10</sup> To research the clinical characteristics and therapeutic effects of pediatric scrub

typhus, we performed a prospective retrospective study at a tertiary hospital in Nellore, southern India. The goal of the study was to decide whether the profile of children with scrub typhus at our institution differed from that previously reported. This research aimed to assess the clinical profile, complications, and outcomes of serologically confirmed cases of scrub typhus admitted to a rural medical college in South India.

## METHODS

### Study design

This is a prospective descriptive study.

### Study place

The study was conducted at the pediatric department, Narayana Medical College, Nellore, Andhra Pradesh, India.

### Study period

The study period was from November 2019 to August 2020.

### Inclusive criteria

The children less than 12 years with signs and symptoms suggestive of scrub typhus with serological confirmation were included in this study.

### Serological kit used

IgM ELISA technique by using INBIOS kit for scrub typhus<sup>11,12</sup>. It is 91% sensitive and 100% specific.

The children admitted with fever in the pediatric department were evaluated. The serological study was done after 5 to 7 days of illness.

Clinical presentation, laboratory findings, complications, and outcome of these children were taken for analysis.

Data analysis was done using Microsoft Excel software. Mean and proportions of outcomes of interest were arrived at as applicable. Informed consent from parents of children and institutional ethical committee clearance was obtained.

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For the study, the clinical presentation, experimental findings, complications, and outcomes of these children were taken.

Using Stata Software (OriginPro 8.5.), data processing was performed. The mean and proportion of interest outcomes is achieved as appropriate. Informed consent was received from parents of children and clearance from the educational ethics committee.

## RESULTS

The 408 fever cases were tested for scrub typhus during the study time. Of 408 (40.20 percent) fever cases, 164 were male-positive scrub typhus: gender ratio of 1.10:1. Most of the 112 cases (68.30 percent) were reported from September to December.

The majority of children [92 children (56.10 percent)] were in the 1-6 age range. 16 children (9.76 percent) were under 1 year of age and 56 (34.14 percent) were over 6 years of age. The recorded lowest age was 9 months. 124 children (75.60 percent) were from rural areas and 40 children (24.40 percent) were from urban areas (Table 1).

**Table 1: Clinical profile of scrub typhus (n=164).**

Clinical profile	Number of children	%
<b>Sex distribution</b>		
Male	86	52.44
Female	78	47.56
<b>Age distribution (years)</b>		
<1	16	9.76
1-6	92	56.10
6-12	56	34.14
<b>Locality distribution</b>		
Rural	124	75.60
Urban	40	24.40
<b>Symptoms</b>		
High-grade fever	138	84.15
Chills	81	49.40
Vomiting	61	37.20
Cough and cold	92	56.10
Lethargy	91	55.50
Headache	41	25
Myalgia	52	31.70
GI bleed	24	16.64
Abdominal pain	33	20.12
Diarrhoea	21	12.80
Altered sensorium	17	10.36
Seizures with posturing	17	10.36
Oliguria	12	7.32
Incessant cry	7	4.27
<b>Signs</b>		
Lymphadenopathy	112	68.30
Eschar	104	63.41
Hepatomegaly	96	58.53
Splenomegaly	88	53.66
Anasarca	29	17.68
Rash	24	14.63

Fever in all 164 children ranged from 5 days to 3 weeks, with a median of one week. Fever was elevated in many infants [138 (84.15 percent)] and was correlated with chills [81 (49.40 percent)]. The main signs were cough, cold [92 (56.10 percent)] and vomiting [61 (37.20 percent)]. In 91 (55.50 percent), 41 (25 percent), 52 (31.70 percent), 33 (20.12 percent), 21 (12.80 percent), 17 (10.36 percent), and 7 (4.27 percent) children respectively, lethargy, headache, myalgia, stomach pain, diarrhoea, convulsions, and incessant cries were recorded.

The key clinical results of scrub typhus positive children were lymphadenopathy (68.30 percent), Eschar (63.41 percent), hepatomegaly (58.53 percent), and Splenomegaly (53.66 percent) (Figure 1).



**Figure 1: Common sites of eschar.**

Eschar was found in the skin folds of the axilla, genitalia, inguinal areas, groin, and perianal areas, behind the ear, scalp, and umbilicus. Rash was seen in 24 (14.63 percent) of children only. Generalized anasarca (17.68 percent), GI bleed (16.64 percent), and oliguria (7.32 percent) were other important clinical features encountered (Table 1).

In scrub typhus positive cases, 78 (47.56 percent) children suffered shock, where 42 (25.60 percent) of children had a respiratory illness. Other major abnormalities were observed (Table 2) ARDS (103.6 percent), meningoenephalitis (7.32 percent), myocardial dysfunction (8 percent), DIC (2.44 percent), and MODS (1.22 percent). Ascites [61 (37.19 percent)] and pleural effusion [65 (39.63 percent)] were commonly observed.

In 122 (74.40 per cent) infants, thrombocytopenia (platelet <1,00,000/mm<sup>3</sup>) and anaemia (<11 gm per cent) were seen in 115 (70.12 per cent) children in the current report (Table 2) [78 (47.56 percent)], elevated liver enzymes (SGOT, SGPT), elevated renal parameters [27 (16.46 percent)], elevated S.

Other typical laboratory parameters seen in the sample community included bilirubin [13 (7.93 percent)], hyponatremia [28 (19 percent)]. Thickening of the gall bladder wall in the USG abdomen in our research population [91 (55.48 percent)].

**Table 2: Complications and investigations among children with scrub typhus (n=164).**

Variables	Number of children	%
<b>Complications</b>		
Shock	78	47.56
Respiratory distress	42	25.60
Pleural effusion	65	39.63
Ascites	61	37.19
ARDS	17	10.36
Meningoencephalitis	12	7.32
Myocardial dysfunction	8	4.88
DIC	4	2.44
MODS	2	1.22
<b>Investigations</b>		
Thrombocytopenia	122	74.40
Anemia	115	70.12
Positive findings in USG abdomen	91	55.48
Elevated transaminases (SGOT, SGPT)	78	47.56
Hyponatremia	31	18.90
Elevated renal parameters	27	16.46
Elevated serum bilirubin	13	7.93

ARDS=adverse drug reactions, DIC=disseminated intravascular coagulation, MODS=multi organ dysfunction syndrome, USG=ultrasonography test

In 84 (51.21 percent) children, doxycycline was used for treatment (Table 3).

**Table 3: Treatment modalities for scrub typhus (n=164).**

Treatment	Number of children	%
<b>Doxycycline alone</b>	84	51.21
<b>Azithromycin alone</b>	21	12.80
<b>Both doxycycline and azithromycin</b>	59	35.97
<b>Fluids alone for shock</b>	12	9.15
<b>Dopamine</b>	61	37.19
<b>Adrenaline</b>	3	1.82
<b>Non-adrenaline</b>	21	12.80
<b>Nasal oxygen</b>	12	7.31
<b>O<sub>2</sub> through Jackson Rees circuit</b>	39	23.78
<b>Non-invasive ventilation</b>	11	6.70

Azithromycin was prescribed to 21 children who did not tolerate doxycycline (12.80 percent). 59 (35.97 percent) of children who became severely ill were given these medications. For septic shock, 12 (9.15 percent) children needed fluids alone, while 64 (39.02 percent) children needed fluids and inotropes [dopamine 61 (37.19 percent), adrenaline 3 (1.82 percent), and non-adrenaline 21 (12.80 percent)]. Nasal O<sub>2</sub> was needed for respiratory failure in

12 (7.31 percent) infants, while oxygen was lifesaving in 39 (23.78 percent) and 11 (6.70 percent) respectively by Jackson Rees circuit, non-invasive ventilation. Over the research time, only one child died (0.6 percent) due to MODS.

## DISCUSSION

In this study, we noticed that the prevalence of scrub typhus was more from September to December, and the majority of cases were reported. Many pediatric and adult studies from various parts of India, like Kumar et al, also observed the maximum number of cases from September to February, which is considered cooler months.<sup>13</sup> However, Weitzel et al in their study conducted in South America, noticed the appearance of all cases of scrub typhus between January and February, suggesting that the summer may be the main period of activity of the vector.<sup>14</sup>

We observed equal distribution among males and females, whereas a prospective study from Pondicherry by Murali et al and Manish et al in their studies, noticed a slight male preponderance (male: female-1.10:1).<sup>13,15</sup>

We observed a high prevalence of cases in and around Nellore, which could potentially be due to case selection bias.

We also observed that high-grade fever lasted for more than three days in all infants. Other primary symptoms observed were chills and cough, cold after fever (56.10 percent), and vomiting (37.20 percent). Cough (73 percent) and vomiting (59 percent) were also seen by Palanivel et al<sup>23</sup> as prevailing symptoms after fever.<sup>16</sup>

As the most frequent symptoms at presentation, we noted lymphadenopathy (68.30 percent), eschar (63.41 percent), rash (14.63 percent), and anasarca (17.63 percent).

Eschar is a useful sign of variable occurrence and must be differentiated from anthrax and other rickettsial infections. It is the result of a painless chigger bite and is often located in areas that are hard to examine, such as the genital region or under the axilla. It evolves as a small papule, enlarges, undergoes central necrosis, and acquires a blackened crust. In our study, we observed eschars in the scalp, postauricular groove, axilla, or perineum, which was in concordance with other pediatric studies.

Few notable laboratory findings were thrombocytopenia (74.40 percent) with elevated SGOT and SGPT among 47.56 percent of the study population.

In concordance to our study, Palanivel et al also observed elevated liver enzymes in 64% of cases, and Krishnan et al also observed thrombocytopenia in more than 50% of children.<sup>15,16,21</sup>

The response to treatment and time to defervescence was within 24-48 hour in many cases, which was similar to

other pediatric studies, like Palanivel et al study.<sup>16</sup> We noted that shock (47.56 percent), ARDS (10.36 percent), serum bilirubin (7.93 percent), meningoenzephalitis (7.32 percent), MODS (1.22 percent), and DIC (2.44 percent).

A study by Palanivel et al also had similar findings stating that the causes of death shocked, ARDS, MODS, and DIC.<sup>16</sup> Late referral to a hospital with organ dysfunction was among the reasons for an unfavorable outcome.

Azithromycin was given to 12.80 percent of children who were not tolerating doxycycline. Both the drugs were given to 35.97 percent of children who were seriously ill.

## CONCLUSION

Rickettsial infections in different parts of India, including Nellore, are more prevalent. In the latest report, more than 40 percent of fever cases are positive for scrub typhus. The main clinical characteristics of these diseases include acute febrile fever, lymphadenopathy, eschar in secret parts of the body, hepatosplenomegaly, thrombocytopenia anemia, and capillary leakage. The major complications of scrub typhus are shock, respiratory illness, ARDS, renal, hepatic dysfunction, meningoenzephalitis, and DIC with MODS. Empirical doxycycline or azithromycin is very much useful if clinical suspicion of scrub typhus as delay in treatment leads to severe complications. Proper fluid boluses, inotropes, O<sub>2</sub> through Jackson Rees circuit, early non-invasive ventilation are the mainstay of therapy for complications. Having a high index of suspicion of early diagnosis of scrub typhus and early effective management of complications will reduce childhood morbidity and mortality.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Kishore E, Sreedhar SVS. Clinical profile and complications: scrub typhus in children at a tertiary hospital in south India, Nellore. *Int J Contemp Pediatr* 2021;8:545-9.