

# CLINICAL PROFILE OF SCRUB TYPHUS AMONG PAEDIATRIC AGE GROUP IN A TERTIARY CARE CENTER

## Abstract

### INTRODUCTION:

Scrub typhus, a dreaded disease in the pre-antibiotic era, was a serious military disease that killed thousands of people in the Far East during WWII. It is a zoonosis that is common throughout Asia and the Pacific Islands. Scrub typhus is a febrile illness characterised by a wide range of symptoms and indications. This disease has a wide spectrum of clinical symptoms, from subclinical through organ failure to death. The objective of this study was to assess the clinical profile of scrub typhus infection among children in a tertiary care hospital in south India.

### METHODOLOGY:

This is a retrospective study of the clinical profile of 50 paediatric children, who were admitted in the Paediatric ward of a tertiary care hospital, during the study period of JAN 2020 to DEC 2020.

### RESULTS:

All children presented with fever. Other common symptoms were vomiting (56%), facial swelling (52%), cough (35%), abdominal pain (33%), breathlessness (29%) and decreased urine output (29%). High grade fever ( $>101^{\circ}\text{F}$ ) was recorded in 91% of children. Other common signs were hepatomegaly, splenomegaly, edema, tender lymphadenopathy and hypotension, observed in 82%, 59%, 39%, 38% and 36% of cases, respectively. An eschar and a maculopapular rash each were observed in 20% of patients. Within 48 hours of starting an appropriate antibiotic, 90% of the children became afebrile. Overall, there was a 7.5 percent mortality rate. Refractory shock, meningoencephalitis, acute respiratory distress syndrome, bronchopneumonia, acute renal damage, and myocarditis were among the causes of mortality.

### CONCLUSION:

In any febrile child with a maculopapular rash, hepatosplenomegaly, tender lymphadenopathy, thrombocytopenia, or symptoms indicative of capillary leak, paediatricians should have a high index of suspicion for scrub typhus. Pending serological confirmation, empirical therapy with doxycycline or azithromycin should be initiated immediately, since any delay in treatment could lead to life-threatening consequences.

**KEY WORDS:**Scrub Typhus, Fever, Eschar, Rash.

## **INTRODUCTION:**

Scrub typhus is a zoonotic illness transmitted by the bite of a larval trombiculid mite, commonly referred to as a chigger. Scrub typhus is still a common aetiology for an acute undifferentiated febrile disease in children especially during monsoon, which is defined as a fever without any evidence of localized infections that lasts for more than 14 days.<sup>(1,2)</sup> The causative agent of this zoonotic disease, *Orientia tsutsugamushi*, is an obligatory intracellular bacterium. It has a triangle-shaped distribution that stretches from northern Japan and far-eastern Russia in the north to northern Australia in the south, Pakistan and Afghanistan in the west, and the islands of the western Pacific and Indian Oceans in the middle.<sup>(3,4)</sup> Scrub typhus is widespread in India, with cases reported from all regions, including Tamil Nadu.<sup>(5,6)</sup> It affects people of all ages, and if left untreated, it can lead to significant complications such as pneumonitis, ARDS, Meningoencephalitis, septic shock, multi-organ failure, and death. Until recently, the sickness was difficult to identify, mainly due to a low index of suspicion and the frequency of severe diseases like dengue and malaria during the monsoon season. In India, nonspecific clinical signs and symptoms, combined with limiting access to more sensitive and specific tests to diagnose scrub typhus, result in sparse reporting and higher morbidity and death.<sup>(5)</sup> Scrub typhus has been reported widespread in Maharashtra, Meghalaya, Jammu and Kashmir, Karnataka, Himachal Pradesh, Kerala, Uttaranchal, Rajasthan, West Bengal, Tamil Nadu, and Pondicherry over the last decade.<sup>(6-11)</sup>

We conducted a retrospective observational study at a tertiary hospital in south India, to study the clinical features of pediatric scrub typhus. The objective of the study was to assess the clinical profile of scrub typhus infection among children in a tertiary care hospital in south India.

## **SUBJECTS AND METHODS:**

A retrospective study was conducted among the pediatric age group children [up to 18 years of age] in the Department of Pediatrics, Saveetha Medical College and Hospital, Saveetha University, a tertiary care hospital at Thandalam, Chennai, Tamil Nadu, India over a period of 1 year from January 2020 to December 2020.

**INCLUSION CRITERIA:**Children under the age of 18 who had fever without a focus

**EXCLUSION CRITERIA:** Children with previous systemic illness

Most of these cases were admitted between September and January (monsoon season).

All patients received a complete blood count with differential counts, a peripheral smear for malarial parasite, urine analysis, and blood culture, all of which were repeated if clinically required, as per unit protocol. When clinically indicated, serum electrolytes, liver function tests, renal function tests, Widal tests, chest x-rays, and echocardiograms were performed. Scrub typhus was confirmed by IgM ELISA using INBIOS kit for scrub typhus which is 91% sensitive and 100% specific. Serology was done in all children who had fever for > five days.

## **RESULTS:**

During the study period, scrub typhus was diagnosed in 50 children. There were 23 boys (46%) and 27 girls (54%) among the 50 children. The children's ages ranged from five months to eighteen years, with an average age of eight years at the time of presentation. The number of cases per age group (0-5 years, 6-10 years, 11-18 years) were almost equal. The vast majority of the patients were from rural areas (88 %). (TABLE 1)

**TABLE 1**

### **Demographic profile of Scrub Typhus:**

<b>Demographic data</b>		<b>N</b>	<b>%</b>
<b>Age</b>	<b>0-5 years</b>	<b>16</b>	<b>32</b>
	<b>6-10 years</b>	<b>17</b>	<b>34</b>
	<b>11-18 years</b>	<b>17</b>	<b>34</b>
<b>Sex</b>	<b>Male</b>	<b>23</b>	<b>46</b>
	<b>Female</b>	<b>27</b>	<b>54</b>
<b>Area</b>	<b>Rural</b>	<b>44</b>	<b>88</b>
	<b>Urban</b>	<b>6</b>	<b>12</b>

During the monsoon season (between September and January), the highest number of cases (39;78%) were reported.

Fever was a common occurrence in all scrub cases. Only about a quarter of the youngsters (13;26 percent) had a fever that lasted less than a week when they were admitted to the hospital. The majority of pediatric scrub patients had a fever for more than a week (60%) and a minor group (14%) had a fever for more than two weeks. Other clinical features reported were headache and myalgia (11% each), cough and runny nose (48%). The gastrointestinal system was significantly affected in patients with scrub typhus with symptoms such as vomiting, diarrhea and abdominal pain 26(52%), 6(12%) and 16 (32%) respectively. Eschar, a pathognomonic characteristic of scrub typhus, was observed in 32 of the cases (64%).

Eschar was most commonly found in the axilla and groin. Hepatosplenomegaly was another common symptom of scrub typhus. Hepatomegaly was observed in (n=10; 20% of the children) while splenomegaly was observed in (N=22; 44% of the children). Only (N=6; 12%) of the cases had isolated splenomegaly. Altered sensorium was documented in 7(14%), seizures were observed in 5(10%), maculopapular rashes were noticed among 9(18%) of patients.

Another common sign of scrub typhus was lymphadenopathy which was observed in (n=24;48 % of the children). In addition, one-quarter of the admitted children had enlarged regional lymph nodes.

In scrub typhus patients, laboratory examination revealed the involvement of all three cell lines. Anaemia, abnormal total leukocyte counts, and thrombocytopenia were found in 33, 17 and 29 of the patients, respectively.

The majority of the patients 32(64%) had mild to moderate anaemia. Only one case of severe anaemia was observed.

The majority of the patients had normal total leukocyte counts. Leukocytosis and leukopenia were found in 13 (26%) and 4 (8%), respectively.

Although thrombocytopenia was a common laboratory finding in paediatric scrub cases, it was only mild to moderate in nearly half of them. Severe thrombocytopenia was only found in two cases. Only 4/14 individuals had elevated SGOT and SGPT, 1/8 had elevated creatinine, and 1/20 had hyponatremia.

Scrub typhus was diagnosed based on a positive serum IgM test. IgM was found positive in all of the patients. Eschar was found in 32 (64 percent) of the 50 individuals studied

## TABLE 2

### Clinical profile of Scrub Typhus:

CLINICAL MANIFESTATIONS	N	%
Fever	50	100
<7 days	13	26
7-14 days	30	60
>14 days	7	14
High grade Fever >101°F	49	98
Vomiting, Nausea	26	52
Cough	24	48
Headache	11	22
Myalgia	11	22
Abdominal pain	16	32
Jaundice	1	2
Diarrhea	6	12
Eschar	32	64
Maculopapular rash	9	18
Breathlessness	13	26
Altered sensorium	7	14
Seizures	5	10
Hepatomegaly	10	20
Splenomegaly	6	12
Hepatosplenomegaly	22	44
Lymphadenopathy	24	48
Bleeding	5	10
Edema	20	40
Oliguria	7	14

**TABLE 3:**

**Laboratory profile of Scrub Typhus :**

Variable		N	%
Anaemia (hg in gm/dl)	Mild(10.1-11)	20	40
	Moderate(7-10)	12	24
	Severe(<7)	1	2
WBC count(x 10 <sup>3</sup> μL)	> 11,000	13	26
	4000-11000	33	66
	< 4000	4	8
Thrombocytopenia (x 10 <sup>3</sup> μL)	1,00000-1,50,000	12	24
	1,00000-50,000	15	30
	< 50000	2	4
↑ ALT/AST	>40 (IU/L)	4/14	28.5
↑ Creatinine	(1 mg/dl)	1/8	12.5
↓ Na(<135 Meq/L)		1/20	5
Abnormal Chest X-ray		2/7	28.5
Scrub IgM		50/50	100

## DISCUSSION:

Tsutsugamushi fever, commonly known as scrub typhus, is one of the most common causes of acute undifferentiated fever in people of all ages, especially children. Several outbreaks have recently been recorded from across India, particularly during the rainy season (June to December) in south India and the winter season (September to January) in north India.<sup>(12,17-21)</sup> Majority of the cases presented with prolonged fever and non-specific signs and symptoms of acute undifferentiated fever.

However, Acute encephalitis syndrome, multiorgan dysfunction syndrome (MODS) pneumonia, acute respiratory distress syndrome (ARDS), hemophagocytic lymphohistiocytosis, and aortic valve endocarditis were all common serious complications. Although eschar is a pathognomonic sign, it was only found in a limited percentage of cases, making clinical diagnosis difficult.<sup>(15, 22-27)</sup> Delay in diagnosis was the primary risk factor for increased morbidity and mortality.<sup>(28)</sup>

In the current study, 72 percent of children attend school and thus are exposed to sick chiggers in the shrubs. However, an unexpected result is the incidence of scrub typhus in under one-year-old infants who spend most of their time indoors, which is most likely connected to the change in chigger habitat during the monsoon season.<sup>(21)</sup>

In contrast to the previous studies, the incidence of scrub typhus is slightly more in females 27(54%) than males 23(46%).

The incidence of scrub typhus in the state of Tamil Nadu increases during the monsoon season, according to this study (September to January). However, Bhat K et al. identified a rise in the number of scrub typhus cases during the post-monsoon season (between September and November), which coincides with a wet season ideal for the growth of vegetation and the trombiculid mite, comparable to earlier studies done in northern and northeast India. During the monsoon season, chiggers may migrate to a safer environment (within a home), which could explain the greater frequency of scrub typhus in newborns in the current study.<sup>(14,17,19)</sup>

The most common clinical finding in this study was mild to moderate fever. This fever symptom is compatible with the majority of previous studies and literature.<sup>(17,29)</sup> Seventy-four percent of the participants in the current study had a fever that lasted more than a week.

The counter availability of antibiotics in the locality contributes to the low frequency of prolonged fever for more than two weeks. In contrast to prior studies, maculopapular rashes were found in 18% of cases<sup>(20)</sup>. The low reporting of rashes in this study is likely due to the study population's dark complexion, which makes rashes more difficult to detect.

Vomiting (n=26;52 %), diarrhoea (n=6;12%), and abdominal pain (n=16;32 %) were all noted, which is consistent with earlier research. According to Narayanasamy et al, the gastrointestinal tract was the most commonly affected system (51%) and the most common symptoms were vomiting (68%) and abdominal pain (42%).<sup>(16)</sup>

Eschar was found in 64% of the current population, mostly in the axilla and groyne. According to previous studies, eschar content ranged from 30 to 67 percent. Eschars were also found on the hairline, umbilicus, gluteal groove, nape of the neck, and behind, among other places. In those instances where there was a high clinical suspicion of scrub typhus, the greater prevalence of eschar in the current study provides direct evidence of good clinical examination and concentrated search for eschar in hidden areas.

In contrast to prior studies that reported predominantly hepatomegaly<sup>(13)</sup>, this study identified hepatosplenomegaly (n=22; 44%) as a significant finding, with hepatomegaly alone being observed in only (n=10; 20%) instances. Co-infections were found in every case of isolated splenomegaly.

The complications included oedema, respiratory distress, shock, and oliguria in children with coinfections (n=3, 1-malaria, 2-dengue). Furthermore, no deaths were documented in this trial. This excellent treatment of scrub cases without death may be due to the clinician's recognition of scrub typhus cases as a common cause of protracted fever during the monsoon season.

A considerable majority of children (64%) had mild to moderate anaemia, according to laboratory results. This significant anaemia burden must be viewed in the context of underlying nutritional anaemia, which was reported in the NFHS-IV to be 50.4 % among children aged 6 to 59 months in Tamilnadu.

The lack of significance of anaemia as a substantial risk factor in the current study, in contrast to Thomas et al's result's after evaluating 262 children, should be considered in the context of the limited number of patients enrolled.<sup>(13)</sup>

The current study's blood picture differs from the conventional findings in nutritional anaemia, where thrombocytosis is expected. Thrombocytopenia was reported by 58% of the participants in this study. The current study showed a much greater rate of mild thrombocytopenia than prior studies. Co-infection was found in two cases of severe thrombocytopenia.<sup>(30,31)</sup>

Despite the fact that liver enzymes were increased in a few individuals, none of them showed clinical or biochemical signs of jaundice. Only individuals with oliguria or oedema had their renal function tested. In individuals with tachycardia and oedema, the echo was normal. Myocarditis was not found to be present.

ELISA IgM positive was used to diagnose scrub typhus. Scrub typhus is diagnosed in the majority of cases based on clinical suspicion, the presence of eschar, anaemia, thrombocytopenia, and serum IgM positivity. Children less than eight years were given Azithromycin (10 mg/kg/day x 5 days) and those older than eight years were given Doxycycline (5 mg/kg/day x 5 days) according to unit protocol, resulting in complete clinical cure with no recurrence during follow-up.

## **CONCLUSION:**

Scrub typhus is a common cause of acute undifferentiated fever in children and should always be considered as a differential diagnosis, even in babies. The presence of eschar, lymphadenopathy, and capillary leak in febrile children is the hallmark of this disease.

Almost all cases of scrub typhus may be detected with a high index of clinical suspicion, clinical expertise, and serum IgM positivity. Scrub typhus should be recognised as a differential in any undifferentiated febrile illness obtained in the community, regardless of the appearance of an eschar, and requires empirical therapy as well as scrub typhus tests.

## REFERENCE:

1. Silpapojakul, K. Scrub typhus in the Western Pacific Region. *Ann Acad Med Singapore*. 1997;26(6):794–800. [[PubMed](#)] [[Google Scholar](#)]
2. Panpanich R, Garner P. Antibiotics for treating scrub typhus. *Cochrane database Syst Rev*. 2002;(2):CD002150. [[PubMed](#)] [[Google Scholar](#)]
3. Lee CS, Min IS, Hwang JH, et al. Clinical significance of hypoalbuminemia in outcome of patients with scrub typhus. *BMC Infect Dis*. 2010;10:216. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
4. Vivekanandan M, Mani A, Priya YS, et al. Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India*. 2010;58:24–8. [[PubMed](#)] [[Google Scholar](#)]
5. Mahajan SK, Rolain JM, Sankhyan N, et al. Pediatric scrub typhus in Indian Himalayas. *Indian J Pediatr*. 2008;75(9):947–9. [[PubMed](#)] [[Google Scholar](#)]
6. Rathi NB, Rathi AN, Goodman MH, et al. Rickettsial diseases in Central India: proposed clinical scoring system for early detection of spotted fever. *Indian Pediatr*. 2011;48(11):867–72. [[PubMed](#)] [[Google Scholar](#)]
7. Somashekar HR, Moses PD, Pavithran S, et al. Magnitude and features of scrub typhus and spotted fever in children in India. *J Trop Pediatr*. 2006;52(3):228–9. [[PubMed](#)] [[Google Scholar](#)]
8. Murali N, Pillai S, Cherian T, et al. Rickettsial infection in south India - how to spot the spotted fever. *Indian Pediatr*. 2001;38(12):1393–6. [[PubMed](#)] [[Google Scholar](#)]
9. Digra SK, Saini GS, Singh V, et al. Scrub typhus in children: Jammu experience. *JK Science*. 2010;12:95–7. [[Google Scholar](#)]
10. Pavithran S, Mathai E, Moses PD. Scrub typhus. *Indian Pediatr*. 2004;41(12):1254–7. [[PubMed](#)] [[Google Scholar](#)]
11. Joshi R, Punde A, Ohri A. Rickettsial infections seen in rural India. *Bombay Hosp J*. 2009;51:385–7. [[Google Scholar](#)]
12. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. *Indian J Pediatr*. 2012;79(11):1459–62.
13. Thomas R, Puranik P, Kalal B, Britto C, Kamalesh S, Rego S, et al. Five-year analysis of Rickettsial fevers in children in South India: Clinical manifestations and complications. *J Infect Dev Ctries*. 2016;10(6):657–61.
14. Kumar Bhat N, Dhar M, Mittal G, Shirazi N, Rawat A, Prakash Kalra B, et al. Scrub typhus in children at a tertiary hospital in north India: clinical profile and complications. *Iran J Pediatr*. 2014;24(4):387–92
15. Giri PP, Roy J, Saha A. Scrub Typhus - a major cause of pediatric intensive care admission and multiple organ dysfunction syndrome: A single-center experience from India. *Indian J Crit Care Med PeerRev off Publ Indian SocCrit Care Med*. 2018;22(2):107–10.
16. Narayanasamy DK, Arunagirinathan AK, Kumar RK, Raghavendran VD. Clinico - Laboratory profile of scrub typhus - an emerging rickettsiosis in India. *Indian J Pediatr*. 2016;29

17. Dass R, Deka NM, Duwarah SG, Barman H, Hoque R, Mili D, et al. Characteristics of Pediatric scrub typhus during an outbreak in the North Eastern region of India: peculiarities in clinical presentation, laboratory findings and complications. *Indian J Pediatr.* 2011;78(11):1365-70.
18. Premraj SS, Mayilananthi K, Krishnan D, Padmanabhan K, Rajasekaran D. Clinical profile and risk factors associated with severe scrub typhus infection among non-ICU patients in Semi-urban south India. *J Vector Borne Dis.* 2018;55(1):47-51.
19. Sharma PSR, Kakkar, R Kaore SN, Yadav VK. Geographical distribution, effect of season and life cycle of scrub typhus. *JK Sci.* 2010;12(2):63-4.
20. Rapsang AG, Bhattacharyya P. Scrub typhus. *Indian J Anaesth.* 2013;57(2):127-34.
21. Rahi M, Gupte MD, Bhargava A, Varghese GM, Arora R. DHR-ICMR Guidelines for Diagnosis and management of Rickettsial diseases in India. *Indian J Med Res.* 2015; 141(4):417-22.
22. Jain P, Prakash S, Tripathi PK, Chauhan A, Gupta S, Sharma U, et al. Emergence of Orientia tsutsugamushi as an important cause of acute encephalitis syndrome in India. *PLoS Negl Trop Dis.* 2018; 12(3):e0006346.
23. Malik R, Sharma S, Gupta R, Sehgal R. Scrub typhus: a rare cause of encephalitis in Pediatric age group. *Pediatr Infect Dis.* 2015;7(3):71-3.
24. Ramyasree A, Kalawat U, Rani ND, Chaudhury A. Seroprevalence of Scrub typhus at a Tertiary care hospital in Andhra Pradesh. *Indian J Med Microbiol.* 2015;33(1):68-72.
25. Zhou Y-H, Xia F-Q, Van Poucke S, Zheng M-H. Successful treatment of scrub typhus-associated hemophagocytic lymphohistiocytosis with chloramphenicol: a report of 3 pediatric cases and literature review. *Medicine (Baltimore).* 2016; 95(8):e2928.
26. Yu S, Yu X, Zhou B, Liu D, Wang M, Zhang H, et al. Tsutsugamushi disease presenting with aortic valve endocarditis: a case report and literature review. *Am J Cardiovasc Dis.* 2016; 6(4):185-90.
27. Rose W, Rajan RJ, Punnen A, Ghosh U. Distribution of Eschar in Pediatric Scrub Typhus. *J Trop Pediatr.* 2016;27;fmw027.
28. Chrispal A, Boorugu H, Gopinath KG, Prakash JAJ, Chandy S, Abraham OC, et al. Scrub typhus: an unrecognised threat in South India - clinical profile and predictors of mortality. *Trop Doct.* 2010;40(3):129-33.
29. Basu S, Saha A, Sarkar S, Sinha MK, Das MK, Datta R, et al. Clinical Profile and Therapeutic Response of Scrub Typhus in Children: A Recent Trend from Eastern India. *J Trop Pediatr.* 2018;23
30. Kalal BS, Puranik P, Nagaraj S, Rego S, Shet A. Scrub typhus and spotted fever among Hospitalised children in South India: Clinical profile and serological epidemiology. *Indian J Med Microbiol.* 2016;34(3):293-8.

31. Jeong YJ, Kim S, Wook YD, Lee JW, Kim K-I, Lee SH. Scrub typhus: clinical, pathologic, And imaging findings. Radiogr Rev PublRadiol Soc N Am Inc. 2007;27(1):161-72.

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