

Clinical Profile, Morbidity Pattern and Outcome of Children with Scrub Typhus

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Abstract

Introduction: The presentation of scrub typhus is variable and it can present as severe multi-organ dysfunction. Prompt recognition is the key to specific treatment and good outcome.

Aim: To find out the clinical profile and outcome of scrub typhus in children attending a tertiary care hospital.

Materials and Methods: This prospective cross-sectional diagnostic study was carried out in children presented with signs and symptoms of suspected scrub typhus. All the children were examined clinically and findings were recorded. Along with routine fever workup, blood samples were tested for immunoglobulin M enzyme-linked immunosorbent assay for scrub typhus.

Results: The most common symptom was fever >7 days along with predominant gastrointestinal symptoms; characteristic eschar was seen in 54% of the children in the study group. 92.3% of children showed positive IgM serology for scrub typhus. 48.5% of children responded well to doxycycline, the duration of hospital stay was <7 days. 39.2% of children also responded to doxycycline but required <7 days of hospital stay. The overall mortality rate was 6.2%.

Conclusion: Symptoms of scrub typhus are quite non-specific. Early recognition of the disease is a very important as any delay in treatment can lead to severe morbidity and high mortality.

Key words: Clinical outcome, Enzyme-linked immunosorbent assay, Immunoglobulin M, Scrub typhus

INTRODUCTION

Scrub typhus is an emerging infectious disease that is caused by *Orientia tsutsugamushi* from chigger bite. It is common in Asia-Pacific countries the term scrub is used because the type of vegetation (terrain between the woods and cleanings) facilitate to harbor the vectors.¹ There was significant morbidity from scrub typhus during world war 11 among both American and Japanese soldiers. Human beings are infected when they trespass into these mite islands and are bitten by the mite larvae (chiggers).² It is

usually acquired during agricultural/occupational exposure because rice fields are important sources of reservoirs for transmission.³ One billion people are at risk for scrub typhus and around one million people suffer annually.⁴ The mortality rate in untreated children ranges from 0% to 30%. The WHO identifies scrub typhus is a re-emerging disease in South-East Asia and South-Western Pacific region with a case fatality rate of 30% if left untreated.⁵ Scrub typhus has been reported from various parts of India and it is one of the important neglected zoonoses of public health importance. Scrub typhus may present as a fever of unknown origin. The clinical course and prognosis may vary depend on the type of endemic strain. This disease may cause loss of vision, hearing loss, multi-organ failure and death of the child if we fail to recognize the disease in the early stages itself.⁶ Hence, this study was aimed to study the clinical profile and outcome of children with scrub typhus in our setting and also to find out the morbidity predictors in children.

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MATERIALS AND METHODS

Prospective cross-sectional diagnostic study was conducted in the pediatric medical unit of Tertiary care hospital from March 2012 to August 2014. Ethical committee approval and informed consent from the children's parents were obtained. Study population: Children aged 6 months to 12 years were included in the study. 130 children presenting with fever for more than 5 days with any one of the following features such as abdominal pain, vomiting, third space losing, ascites, pedal edema, maculopapular rash, regional lymphadenopathy, thrombocytopenia, abnormal leukocyte count, hepatosplenomegaly, eschar were included in the study. Children have fever with clinical and laboratory evidence of foci of other infections were excluded from the study. The detailed clinical history from the child's parents had been taken and entered in the structured pro forma. The children were examined clinically for signs and symptoms of scrub typhus and findings were recorded. Complete hemogram, urine routine, renal function test, liver function test, fever work up for enteric fever, dengue, leptospirosis investigations were sent to the laboratory. If a child presented with abdominal distension, respiratory distress, necessary imaging like X-ray chest, ultrasonography (USG) abdomen and chest were taken. Initial supportive treatment had been started in the wards. Along with all fever workup, blood samples were investigated for immunoglobulin M enzyme-linked immunosorbent assay (IgM ELISA) for scrub typhus. All children were followed up in the ward. These children were examined thoroughly two times a day for the emergence of new symptoms or for the resolution of presenting symptoms, and complications, course of the disease in the hospital which were recorded. If any child develops new skin lesions, appropriate treatment was started immediately. The children, who showed signs of deterioration in the hospital stay were shifted to ICU for continuous monitoring, and for early intervention of hemodynamic compromise, elevated liver and hepatic parameters. The children who were afebrile for 3 days and who showed

Table 1: Age distribution of cases (n=130)

Age group	Frequency (%)
6 month - 2 year	52 (40)
2-4 year	52 (40)
4-8 year	17 (13.1)
8-12 year	9 (6.9)

Table 2: Gender distribution of cases (n=130)

Valid	Frequency (%)
Male	68 (52.3)
Female	62 (47.7)

The male:female ratio 1.09:1

improvement in clinical symptomatology with normal renal and liver parameters with adequate food intake were considered fit for discharge. The parents were counseled about personal hygiene, nutritional supplementation, routine vaccination, and preventive measures against mite bite with a special emphasis on environmental sanitation, and they were advised to bring their children for follow-up. During the visits children were examined for nutritional status, the appearance of any new signs and symptoms. Data were analyzed using SPSS 17 version software and *P* value was calculated using chi-square test.

RESULTS

A total number of children enrolled in the study were 166, 36 of them were excluded as per exclusion criteria (diagnosed as viral fever, UTI, Enteric fever, leptospirosis, and malaria). The results of 130 children with positive IgM ELISA for scrub typhus were analyzed.

About 82.3% of children presented with fever >7 days, other common symptoms were vomiting (86.2%), hepatosplenomegaly (80.6%), and abdominal pain and eschar (55.5% Tables 1 and 2).

Anemia (hemoglobin <9.0 g%) was present in 55.8%, thrombocytopenia (platelet count <1,00,000/mm³) in 60.6%, and elevated liver enzymes serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase in 30.6% children.

Table 3: Analysis of morbidity indicators versus hospital stay (n=130)

Symptoms	Hospital stay		P value
	<7 days	>7 days	
Eschar	53	19	<0.0001
Facial puffiness	19	45	<0.0001
Hepatosplenomegaly	43	62	<0.0001
Thrombocytopenia <1,00,000	24	55	<0.0001
Elevated liver enzymes	9	31	<0.0001
Toxic appearance	18	48	<0.0001
X ray-pleural fluid, pneumonia	6	29	<0.0001
USG - FF	7	31	<0.0001

USG: Ultrasonography

Table 4: Cross tabulation between duration of fever and various clinical features (n=130)

Clinical features	Fever		P value
	<7 days	>7 days	
Abdominal distension	7	46	0.042
Bleeding manifestation	1	23	0.051
Toxic appearance	5	61	0.002
Thrombocytopenia <1,00,000	9	70	0.014

DISCUSSION

Scrub typhus is an emerging infectious disease; it presents as an acute febrile illness with non-specific signs and symptoms. This study was primarily done to find out the varying clinical presentations, morbidity pattern, and complications associated with scrub typhus. The various observations were analyzed. The predominant age group in the study population was 6 months to 4 years old accounting for 80% followed by 13.1% of children between the age group of 4-8 years and slight male predominance male to female ratio of 1.09:1. Similar results were observed in a study carried out by Kumar Bhat⁷ *et al.* in which the male-to-female ratio was 1.44:1, which is probably due to a higher prevalence of exposure to chiggers among boys, who like to play outdoors. The common symptoms seen in our study were fever >7 days (82.3%), vomiting (86%), and abdominal pain (Figure 1, 55.4%). The predominant gastrointestinal symptoms differentiate scrub typhus from other febrile illness like malaria, dengue, leptospirosis as observed by Aung-Thu⁸ *et al.*, Liu⁹ *et al.* and Khandelwal *et al.*¹⁰ in their studies, accounting to 65-80% gastrointestinal symptoms. Children presented with the characteristic eschar in their axilla, groin, neck, or genitalia were 72 (55.4%) and similar findings were observed by Varghese *et al.* (56%).¹¹ Eschar was absent in 44.6% of children in our

study. Scrub typhus should be suspected in any child having fever for <7 days and with predominant gastro intestinal symptoms. The distribution of eschar is similar to study of Kundavaram *et al.*¹² De Silva *et al.*,¹³ reported eschar in 35% of patients only. The lower prevalence of eschar is a known phenomenon in patients with scrub typhus in Asia as they are dark skinned. The eschars were primarily detected by medical officer on routine examination and not noted or commented on by the patient or care giver, this highlights the need for careful examination for the presence of eschars by the health-care professional. Other common clinical findings encountered in the study group were hepatosplenomegaly (80.6%) and pallor (64.4%). Similar to the findings of Palanivel *et al.*¹⁴ Icterus, pedal edema and lymphadenopathy were also found in a few children included in our study. In our study, only 29.4% of children had ascites, pleural effusion and pneumonitis in 26.9% of children in contrast to the earlier study by Palanivel *et al.*¹⁴ where 47% of children had ascites and 67% of children had pneumonitis (Table 3). Children presented with complications of bleeding manifestation, altered level of consciousness, (lethargy and loss of consciousness), decreased urine output (Acute kidney injury), seizures (manifestation of febrile seizure meningoencephalitis) and visual disturbances were 18.5%, 18.5%, 10.8%, 10% and 6.9%, respectively. The percentage of complications was very much reduced in our study when compared to the previous study (Palanivel *et al.*, Kumar *et al.*^{14,15} In our study, children presented with leukocytosis (93.6%), hemoglobin level <9 g/dl (55.8%), thrombocytopenia (60.8%), and elevated liver enzymes (30.8%). The previous study by Pazhanivel *et al.*¹³ reported 49%, 55%, 77%, and 64%, respectively, in the study group. Children showed x-ray features of pleural effusion were 35 (26.9%). Around 38 (29.2%) children presented with free fluid abdomen which was detected by USG investigation. In the presence study, 92.3% of the children presented with positive IgM ELISA for scrub typhus (Figure 2). In the study group,

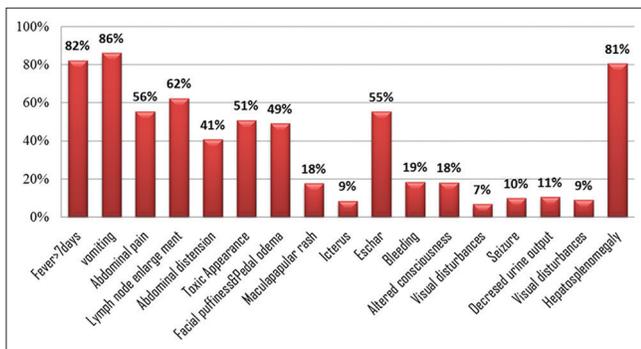


Figure 1: Clinical profile of children with scrub typhus

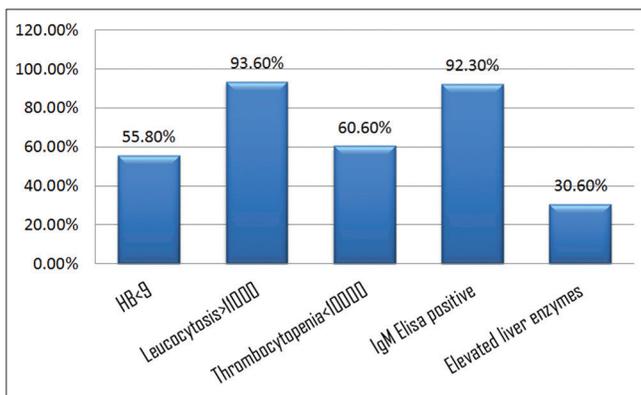


Figure 2: Results of lab parameters

Table 5: Clinical response to different drugs

Drugs	Hospital stay		P value
	<7 days	>7 days	
Doxycycline	63	51	<0.0001
Azithromycin	2	29	<0.0001

Table 6: Analysis of clinical outcome/mortality in children with scrub typhus (n=130)

Hospital stay	Outcome		P value
	Death	Improved	
<7 days	1	63	0.032
>7 days	7	59	

64 (49.2 %) required in-patient care for <7 days, around 66 (50.8%) required in-patient care for >7 days. In the study group, 8 (6.2%) were expired (due to ARDS, acute kidney injury, liver failure, meningoencephalitis and DIC) and 93.8% were improved. The overall mortality was 6.2% in our study related studies by Kumar Bhat *et al.*⁷ also reported 7.5%. However, Palanivel *et al.*¹⁴ showed 11.94% (Table 6). In the study group, children with >7 days of fever, who had abdominal distension, were around 86%, thrombocytopenia (88.5%), bleeding manifestation (95.4%), toxic appearance (92.5%), whereas among children with <7 days of fever had 14%, 11.5%, 4.5%, 7.5%, respectively (with significant $P < 0.0001$ (Table 4). 55.4% of children presented with eschar and they stayed in the hospital <7 days. 44.6% of children in our study did not have any eschar but they stayed in the hospital for more than 7 days ($P = 0.01$) probably due to the delay in the diagnosis. In our study, children presented in the late stages of disease with complication like facial puffiness, pedal edema, toxic appearance, thrombocytopenia, plural effusion, ascites, elevated liver enzymes, decreased urine output stayed in the hospital <7 days ($P = 0.05$). The overall mortality was 8 (6.2%) in our study, but Palanivel *et al.*¹⁴ and Chrispal *et al.*¹⁶ reported 11.94% and 12.2%, respectively. Among the 8 children who died, only one death had occurred in the group of children required <7 days of hospitalization, whereas 7 children who required >7 days of hospital stay ($P = 0.03$). 63 children responded well to doxycycline, the duration of hospital stay was <7 days correlated well with the studies reported by Sirisanthana *et al.* and, Silpajajakul *et al.*^{17,18} 51 children also responded to doxycycline but required >7 days of hospital stay ($P < 0.0001$). 2 children who responded well to azithromycin discharged in <7 days, but 29 children required >7 days ($P < 0.0001$) (Table 5).

CONCLUSION

Scrub typhus is an emerging infectious disease presenting as an acute febrile illness with non-specific signs and symptoms. It is difficult to suspect and diagnose early due to a wide spectrum of symptomatology. The patients should be thoroughly examined for the presence of eschar, especially over the covered areas such as the groin, genitalia and axilla as it is the most useful diagnostic clue in patients with acute febrile illness in areas endemic for scrub typhus. When a child presents with acute febrile illness, maculopapular rash, lymphadenopathy, hepatosplenomegaly, thrombocytopenia and features suggestive of third space losing, diagnosis

of scrub typhus must be considered. The child should be started on doxycycline as an empirical therapy which is life-saving. Azithromycin should be started in children who did not respond to doxycycline. In children scrub typhus can present with variable, non-specific, signs and symptoms with a potential to deteriorate into severe multi-organ dysfunction. Early recognition and an appropriate intervention are the key factors for a favorable outcome.

REFERENCES

1. Pavithran S, Matha E, Moses PD. Case report of Scrub Typhus. Available from: <http://www.indianpediatrics.net/2002>. [Last cited on 2016 Apr 28].
2. Parthasarathy A. Textbook of Pediatric Infectious Diseases. Philadelphia, PA: Jaypee Digital; 2013.
3. Ananthanarayan R. Paniker's Textbook of Microbiology. Hyderabad, India: The Universities Private Limited; 2009.
4. Park K. Park's Textbook of Preventive and Social Medicine. Jabalpur, MP: Bhanot; 2012.
5. Kliegman R, Nelson W. Nelson Textbook of Pediatrics. Philadelphia, PA: Elsevier/Saunders; 2011.
6. Longo D. Harrison's Principles of Internal Medicine. New York: McGraw-Hill; 2012.
7. 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;24:387-92.
8. Aung-Thu, Supanaranond W, Phumiratanapapin W, Phonrat B, Chinprasatsak S, Ratanajaratroj N. Gastrointestinal manifestations of septic patients with scrub typhus in Maharat Nakhon Ratchasima Hospital. *Southeast Asian J Trop Med Public Health* 2004;35:845-51.
9. Liu YX, Jia N, Suo JJ, Xing YB, Liu G, Xiao HJ, *et al.* Characteristics of pediatric scrub typhus in a new endemic region of northern China. *Pediatr Infect Dis J* 2009;28:1111-4.
10. Khandelwal S, Meena JK, Sharma BS. Scrub typhus in children: Clinical profile and complications. *Pediatric Oncall Journal*. Available from: <http://www.Pediatriconcall.com>. 2015. [Last accessed on 2016 Apr 28].
11. Varghese GM, Janardhanan J, Trowbridge P, Peter JV, Prakash JA, Sathyendra S, *et al.* Scrub typhus in South India: Clinical and laboratory manifestations, genetic variability, and outcome. *Int J Infect Dis* 2013;17:e981-7.
12. Kundavaram AP, Jonathan AJ, Nathaniel SD, Varghese GM. Eschar in scrub typhus: A valuable clue to the diagnosis. *J Postgrad Med* 2013;59:177-8.
13. De Silva N, Wijesundara S, Liyanapathirana V, Thevanesam V, Stenos J. Scrub typhus among pediatric patients in Dambadeniya: A base hospital in Sri Lanka. *Am J Trop Med Hyg* 2012;87:342-4.
14. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. *Indian J Pediatr* 2012;79:1459-62.
15. Kumar M, Krishnamurthy S, Delhikumar CG, Narayanan P, Biswal N, Srinivasan S. Scrub typhus in children at a tertiary hospital in southern India: Clinical profile and complications. *J Infect Public Health* 2012;5:82-8.
16. Chrispal A, Boorugu H, Gopinath KG, Prakash JA, Chandy S, Abraham OC, *et al.* Scrub typhus: An unrecognized threat in South India - Clinical profile and predictors of mortality. *Trop Doct* 2010;40:129-33.
17. Sirisanthana V, Puthanakit T, Sirisanthana T. Epidemiologic, clinical and laboratory features of scrub typhus in thirty Thai children. *Pediatr Infect Dis J* 2003;22:341-5.
18. Silpajajakul K, Varachit B, Silpajajakul K. Paediatric scrub typhus in Thailand: A study of 73 confirmed cases. *Trans R Soc Trop Med Hyg* 2004;98:354-9.

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