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Original Research Article

Clinical and laboratory profile of pediatric scrub typhus in a tertiary care teaching hospital in Southern India

Selvakumar Lakshmanan*, Benjamin Sagayaraj M., Balamma Sujatha, Lal Devayani Vasudevan

Department of Paediatrics, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Selvakumar Lakshmanan,
E-mail: skselvak1@gmail.com

ABSTRACT

Background: Scrub typhus is a common aetiology for an acute undifferentiated fever among children. Early recognition and prompt management help to reduce morbidity and mortality.
Methods: All children who visited our pediatric out-patient department between January 2016 and February 2018, admitted with clinical suspicion of scrub typhus and having positive serum IgM by ELISA were included in the study.
Results: A total of 83 cases were enrolled during the study period. Of these 55 were boys and 28 girls. The average age of presentation was seven years, and the youngest was just five months old. Majority of these patients were from rural areas (86%). Roughly, two-thirds (77%) of the study group practiced open defecation. A maximum number of cases (65;78.3%) were reported during monsoon season (between September and January).
Prolonged fever (100%), gastrointestinal symptoms (76%) such as vomiting, diarrhoea and abdominal pain, lymphadenopathy (96%) and hepatosplenomegaly (61%) were common signs and symptoms of pediatric scrub typhus. Only six patients had severe illnesses. The diagnosis was based on the positive serum IgM for scrub typhus. All the patients were IgM positive. Out of these 83 patients, eschar was seen in 50 (60%) patients. Weil Felix test was positive in 15 cases out of 33 tested cases. Six children had co-infection with 2 cases of malaria and four dengue fever cases.
Conclusions: Scrub typhus is one of the common causes for acute undifferentiated fever among children. A high index of clinical suspicion and a lookout for an eschar shall facilitate an early diagnosis of scrub typhus.

Keywords: Acute undifferentiated fever, Eschar, Orientia tsutsugamushi, Rickettsial infections, Scrub typhus, Weil-Felix test

INTRODUCTION

Scrub typhus, a zoonotic disease, is transmitted to humans by the bite of a larval trombiculid mite, popularly known as a chigger. Nowadays, particularly during the monsoon, Scrub typhus remains as a common aetiology for an acute undifferentiated febrile illness in children which is defined as fever without any evidence of localised infections and lasting for ≤ 14 days.[1,2] Orientia tsutsugamushi, the causative agent of this zoonotic disease is an obligatory intracellular bacteria and is distributed from northern Japan and far-eastern Russia in the north to northern Australia in the south and Pakistan and Afghanistan to the west, as well as in the islands of the western Pacific and Indian Oceans in a triangle pattern.[3,4] In India, Scrub typhus is widely spread and reported from all the regions including Tamil Nadu.[5,6] It affects people of all ages, and if untreated, serious

complications such as pneumonitis, acute respiratory distress syndrome, Meningoencephalitis, septic shock, multi-organ failure and death may ensue. Till recently, the disease remained challenging to diagnose primarily due to low index of suspicion and occurrence of dreadful diseases such as dengue and malaria during the monsoon. Additionally, nonspecific clinical signs and symptoms with limited accessibility for more sensitive and specific test to diagnose scrub lead to sparse reporting and increased morbidity and mortality in India. [5] However, during the last decade, scrub typhus is being reported widely from Maharashtra, Meghalaya, Jammu and Kashmir, Karnataka, Himachal Pradesh, Kerala, Uttaranchal, Rajasthan, West Bengal, Tamil Nadu and Pondicherry.[6-11]

The previous studies were mostly retrospectively analysed data during the outbreak seasons. Hence, we decided to do a prospective survey to investigate the seasonal variations and common clinical and laboratory parameters of scrub typhus of children admitted to our tertiary care medical college hospital.

METHODS

Children less than 12 years, who were hospitalized from January 2016 to February 2018 in a tertiary care teaching medical college hospital with acute undifferentiated fever in whom clinical and laboratory features consistent with scrub typhus recruited in the present study. The total number of such children with serological confirmation was 83. Majority of these cases were admitted between September and January (monsoon season).

As per unit protocol, complete blood count with differential counts, peripheral smear for malarial parasite, urine analysis and blood culture were sent for all patients and repeated if clinically warranted. Serum electrolytes, Liver function test, renal function test, Widal test, chest x-ray and Echocardiogram were done when clinically indicated.

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 more than five days. Weil Felix test was done along with serum IgM to those children (34) who had clinical and laboratory features consistent with scrub, but without eschar. Statistical analysis was done with SPSS-21 and mean, and standard deviation and proportions were analyzed.

RESULTS

A total of 83 children were diagnosed to have scrub typhus during the study period. Among these 83 children, 55(66%) were boys, and 28(34%) were girls. The age of these children ranged from 5 months to 12 years of age with an average age of presentation of seven years. Children aged between 7 to 12 years accounted for nearly 60 % of the total cases. Majority of these patients were from nearby districts of Tamil Nadu and lived in rural areas (86%). Roughly, two-thirds (77%) of the study group practised open defecation (Table 1).

Table 1: Demographic details of the study population.

Demographic data		Total cases (n=83)	%
Age	< 6 months	2	2
	7-12 months	5	6
	1-6 years	28	34
	7-12 years	48	58
Sex	Male	55	66
	Female	28	34
Area	Rural	72	87
	Urban	11	13
Open defecation	Yes	64	77
	No	19	23

A maximum number of cases (65;78.3%) were reported during monsoon season (between September and January) Figure 1.

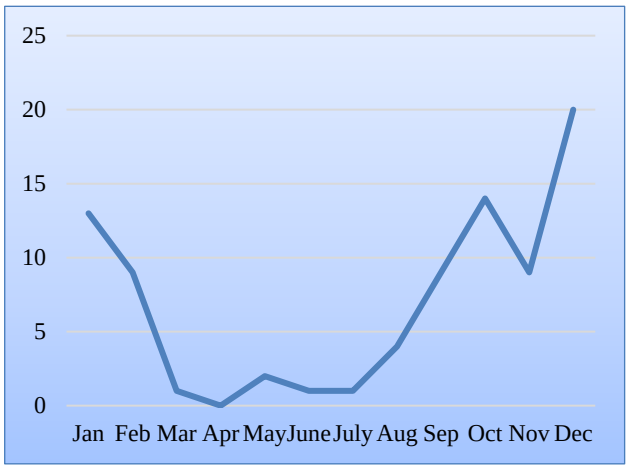

Figure 1: Month-wise distribution of scrub typhus cases during the study period (January 2016 to February 2018).

Fever was a consistent finding in all scrub cases with 95% having either mild or moderate fever. Only just over one-third (26;31%) of children reported fever for less than a week at hospitalization.

Majority of pediatric scrub cases had fever for more than a week (56%), and a small group (13%) had fever lasting for more than two weeks. Over one-quarter of these febrile patients had chills or rigour. Maculopapular rashes were noticed among 14(17%) of patients.

Other clinical features reported were headache and myalgia (12% each), cough and runny nose (25%). The gastrointestinal system was significantly affected in patients with scrub typhus which was evident in 76% of

patients who had symptoms such as vomiting, diarrhoea and abdominal pain 43(52%),4(5%) and 19% (16) respectively. Symptoms suggestive of severe illness were observed in a small number of cases. Tachypnea was noticed in 6 cases, and 4 of them had retractions also. Tachycardia was documented in 12(14%) cases. Nevertheless, only one patient had shock and oliguria. Presentation of oedema varied with facial puffiness in 4, and ascites and/or pleural effusion noted in 2 out of 6 (7%) cases of oedema.

Table 2: Clinical signs and symptoms of Scrub typhus in the pediatric population.

Signs and symptoms							
Clinical features		**n**	**%**	**Clinical features**		**n**	**%**
Fever	> 100.4°F	83	100	Tachypnea		6	7
Fever > 100.4°F	< 104°F	79	95	Breathlessness* (Retractions)		4	5
	> 104°F	4	5	Tachycardia		12	14
Duration	< 7 days	26	31	Shock		1	1
	7-14 days	46	56	Facial Puffiness		4	5
	> 14 days	11	13	Edema* (Pleural effusion/Ascites)		2	2
Chills and Rigor		22	27	Oliguria		1	1
Cough and cold		21	25	Eschar		50	60
Headache		10	12	Lymphadenopathy	Absent	3	4
Myalgia		11	13		Regional	21	25
Rashes		14	17		Generalized	59	71
Gastrointestinal	Vomiting	43	52	Organomegaly	Hepatomegaly	27	32
	Diarrhoea	4	5		Splenomegaly	5	7
	Abdominal pain	16	19		Hepatosplenomegaly	51	61

On clinical assessment, 96% of children had lymphadenitis with the majority of them (n=59; 71%) presenting with generalized lymph node involvement. Additionally, enlarged regional lymph nodes were noticed among a quarter of the admitted children. Eschar, which is considered as a pathognomonic feature of scrub typhus was seen in 50 cases (60%).

Common sites of eschar were axilla and groin. Another common finding in scrub typhus was hepatosplenomegaly. Hepatomegaly was noticed in (n=27; 32%) children and hepatosplenomegaly in (N=51; 61%) children. Isolated splenomegaly was found only in (N=5; 7%) cases (Table 2).

Laboratory analysis showed the involvement of all three cell lines in scrub typhus cases. Anaemia, Abnormal total leukocyte counts, and thrombocytopenia were noted in 58, 26 and 45 patients respectively.

Nearly all the patients 56(68%) had mild to moderate anaemia. Severe anaemia was seen only in 2 cases.

Table 3: Laboratory parameters among pediatric Scrub typhus cases.

Laboratory parameters in children with scrub typhus							
Variable		**n**	**%**	**Variable**		**n**	**%**
Anaemia (Hg in gm/dl)	Mild (10.1-11)	34	41	↑ ALT/AST	>40 (IU/L)	5/24	21
	Moderate (7-10)	22	27	↑ Creatinine	(1 mg/dl)	1/7	14
	Severe (< 7)	2	2	↓ Na (<135 Meq/L)		1/32	3
WBC count (x 10^3 µL)	> 11,000	18	22	Abnormal Chest X-ray		4/10	40
	4000-11000	57	69	Weil Felix test	1: 80	5	
	< 4000	8	10		1:160	2	
Thrombocytopenia (x 10^3 µL)	1,00000-1,50,000	18	22		1:320	8	
	1,00000-50,000	21	25		Total	15/33	44
	< 50000	6	7	Scrub IgM		83/83	100

Total leukocyte counts were normal in the majority of patients. Leukocytosis and leukopenia were observed in 18(22%) and 8(10%) children respectively. Although thrombocytopenia was a prominent laboratory parameter among pediatric scrub cases which was noted in 48(54%) cases, nearly 50% of them had only mild to moderate thrombocytopenia. Only 6 cases had severe thrombocytopenia. Only a small number of patients showed raised SGOT and SGPT (5/24), elevated creatinine (1/7) and hyponatremia (1/32).

The diagnosis was based on positive serum IgM for scrub typhus. All the patients were IgM positive. Out of these 83 patients, eschar was seen in 50(60%) patients. Weil Felix test was positive in a total of 15 cases among 33 tested cases. The positive titre of 1: 80, 1:160 and 1:320 was seen in 5, 2 and 8 children respectively (Table 3).

DISCUSSION

Scrub typhus, also known as Tsutsugamushi fever, is one of the common causes for acute undifferentiated fever among all age groups, particularly in children. Recently, several outbreaks reported from all parts of India, notably, during the rainy season (June to December) in south India and winter (September to January) in north India.[1,12,11,13-15] Majority of the cases presented with prolonged fever and non-specific signs and symptoms of acute undifferentiated fever.

However, serious complications such as acute encephalitis syndrome, multiorgan dysfunction syndrome (MODS) pneumonia, acute respiratory distress syndrome (ARDS), hemophagocytic lymphhistiocytosis and aortic valve endocarditis were not uncommon. Although eschar being the pathognomonic features, was identified only in a small number of cases which challenges clinical diagnosis.[16,17,9,18,19,20,21] Primary risk factor for increased morbidity and mortality was delayed diagnosis.[22]

In the present study, 58% of children are school going and hence exposed to the presence of infected chigger in the shrubs. However, an unexpected finding is the occurrence of scrub typhus in less than one-year-old infants who are predominantly indoor which probably related to the change in the habitat of chiggers during monsoon season.[15]

The increased incidence of scrub typhus among males in the present study like in previous studies may be the result of the social behavior which allows male children venture out during play time.

The absolute increase among the rural population is understandable, considering the habitat of the chiggers. Seventy-seven per cent of the study population reported open defecation which is closely linked to the possibility of exposure to trombiculid mite.[5,13,23] Since this study was conducted before the introduction of government measures to reduce open defecation by providing toilets at home, a survey done later may give a different data following the use of indoor toilets.

This study depicts an increase in the incidence of scrub typhus during monsoon season in the state of Tamil Nadu (September to January). However, Bhat K et al., similar to other studies done in northern and northeast India, reported a peak in the number scrub typhus cases during the post-monsoon season (between September and November) which coincide with wet season suitable for the growth of vegetation and trombiculid mite. The possibility of chigger migrating to a safer place (inside a home) during monsoon season may probably explain the higher incidence of scrub typhus in infants in the present study.[8,11,13]

Mild to moderate fever was the most consistent clinical finding in the present study. This fever symptom is in concurrence with most of the previous reviews and available literature.[11,24] Sixty-nine per cent of the current study population presented with fever lasting for more than a week.

The low incidence of prolonged fever for more than two weeks is related to over the counter availability of antibiotic in the locality.[6,25] Maculopapular rashes were noted in 17% of the cases, which is a stark contrast with the previous studies.[14] Low reporting of rashes in this study may probably be related to the dark complexion of the study population which makes rashes less discernable.

The gastrointestinal system such as vomiting (n=43;52%), diarrhea (n=4; 5%) and abdominal pain (n=19%;16) reported which in congruence with previous studies. Narayanasamy et al documented Gastrointestinal tract was the most commonly affected system(51 %) and vomiting (68 %) and pain abdomen (42 %) were the most common symptoms.[10]

Sixty per cent of the present population had eschar, mainly in the axilla and groin. Previous studies had shown eschar ranged between 30% and 67% (Figure 2).[23,26] Additionally, eschars were observed in different locations like hairline, umbilicus, gluteal groove, nape of the neck and backside. The higher incidence of eschar in the present study gives direct evidence of proper clinical examination and focused search for eschar in hidden areas in those cases where there was a high clinical suspicion of scrub typhus.

Lymphadenopathy was a common finding in children with scrub typhus. Regional lymphadenitis at the site of eschar was the characteristic findings in previous studies.[14] Although, eschars were noted in 60% of cases in the present study, only (24; 29%) children presented with localized lymphadenitis. The majority (59/83) of the cases with or without eschar presented with generalized lymphadenopathy and many of them had bilateral epitrochlear lymphadenopathy. None of the previous studies has reported this clinical finding.

In the clinical setting of high suspicion of scrub typhus and the absence of eschar examination of the epitrochlear lymph node may give, a possible clue. Hence, the significance of this finding has to be pondered through a more extensive study and appropriate investigation.

Compared to previous studies which reported predominant hepatomegaly[6], this research documented hepatosplenomegaly (n=51; 61%) as a significant finding and hepatomegaly alone was noticed only in (n=27; 32%) cases. All the cases of isolated splenomegaly were related to co-infections.

The co-infections related were two cases of positive smear malaria and four cases of dengue. The high incidence of hepatosplenomegaly and generalized lymphadenopathy is a pointer towards reticuloendothelial system involvement in scrub typhus. Localized lymphadenitis may not have such significant involvement of the reticuloendothelial system. The significance of this finding needs further exploration.

Figure 2: Common sites of eschar; A: shows an ulcer at the bitten site by trombiculid mite; B: shows a healing ulcer with the central necrotic area which forms as an eschar.

The complications were noted among children who had coinfections (n=6, 2-malaria, 4-dengue) accounting for oedema, respiratory distress, shock and oliguria. Moreover, no mortality was reported in the present study. This successful treatment of scrub cases without mortality may attribute to the clinician's awareness of scrub typhus cases during monsoon season as a common cause for prolonged fever.

Analysis of laboratory parameters show a significant proportion of children (69%) had mild to moderate anaemia. This high anaemia burden has to be seen in the backdrop of underlying nutritional anaemia at 50.4% among 6 to 59 months old children in Tamilnadu as reported in NFHS-IV.

Even if the impact of the dietary component is compounded, there is still an unacceptably high incidence of anaemia in the study population. The absence of any specific pathology in peripheral smear with two positive malarial smears in nonmigratory population points to the need for immediate public health intervention.

The insignificance of anaemia as a significant risk factor in the present study in contrary to Thomas et al. conclusion after studying 262 children should be seen in the backdrop of a small number of patients recruited.[6]

The blood picture of the present study is in variance with the typical findings noted in nutritional anaemia where thrombocytosis is expected. Forty-seven per cent of present study population reported thrombocytopenia. Compared to previous studies the present study shows a significantly higher rate of moderate thrombocytopenia. [27,28] Six cases of severe thrombocytopenia had simultaneous co-infection.

Even though liver enzymes were elevated in a small number of cases, none of them had clinical or biochemical evidence of jaundice. Renal function was done only for those who had oliguria or oedema. Echo was normal in those with tachycardia and oedema. There was no evidence of myocarditis.

Scrub typhus was diagnosed based on ELISA IgM positivity. Weil-Felix was done in those children who seldom had eschar. Of the 33 cases which did not have eschar, Weil Felix was positive only in (15; 44%) cases. This low positive rate indicates the utility of Weil Felix as a tool for diagnosing scrub typhus. Clinical suspicion along with the presence of eschar, with anaemia, thrombocytopenia and serum IgM positivity clinch the diagnosis of scrub typhus in the majority of cases. As per unit protocol, children with less than eight years were treated with Azithromycin (10mg/kg/day x 5 days) and those more than eight years were administered Doxycycline (5 mg/kg/day x 5 days), resulting in complete clinical cure without any recurrence during follow up.

CONCLUSION

Scrub typhus is a common cause for acute undifferentiated fever in children which should be considered as a differential diagnosis even in infants.

A high index of clinical suspicion with clinical expertise along with serum IgM positivity picks up almost all cases of scrub typhus. Hence, Weil-Felix may not consider mandatory in poor resource settings. Hepatosplenomegaly with generalised lymphadenopathy especially with epitrochlear lymph node occurring in cases during favoured climatic conditions should trigger the clinician to suspect scrub typhus.

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