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Original Research Article

A study on clinical profile, complications and outcome of scrub typhus in south Indian children

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ABSTRACT

Background: Rickettsial diseases including Scrub Typhus are emerging as an important cause of acute undifferentiated febrile illness throughout the Asia-Pacific region. The objectives of the study are to study the clinical profile, complications and outcome of Scrub Typhus cases admitted in rural medical college.
Methods: This prospective descriptive study was done at Government Dharmapuri Medical College Hospital, Tamilnadu, between Jul'2015 and Jan'2016. The children who were positive for Scrub Typhus by IgM Elisa were analyzed.
Results: During the study period, 151 children (40% of fever cases) were positive for Scrub Typhus. All the children were presented with fever. High-grade fever, chills, vomiting, cough, head ache, were seen in 83%, 41%, 57%, 56% and 32% respectively. 54% of children had lethargy and 10% children brought with convulsions to hospital. Eschar was seen in 68% of children. Lymphadenopathy (70%) and hepatosplenomegaly (more than 56%) were common findings. Shock, respiratory distress, pleural effusion and ascites were seen in 46%, 36%, 40% and 37% respectively. Anemia (74%) and thrombocytopenia (81%) were common lab findings. Shock (46%), ARDS (12%), Meningoencephalitis (10%) and MODS (1.3%) were complications reported. Doxycycline (53%), Azithromycin (11%) and both drugs (36%) were used. Along with fluids, Dopamine (38%), nor-adrenaline (12%), Oxygen through Jackson-Rees Circuit (28%), Non-invasive ventilation (9%) was needed to treat the complications.
Conclusions: When a child presents with acute febrile illness, hepatospleenomegaly, lymphadenopathy, anemia with thrombocytopenia and features suggestive of capilary leak diagnosis of Scrub Typhus must be considered. Doxycycline or Azithromycin, proper fluid boluses, Inotropes and O2 through Jackson-Rees Circuit are life saving for scrub typhus and its complications.

Keywords: ARDS, Children, Doxycycline, Rickettsial infections, Scrub typhus, Shock

INTRODUCTION

Scrub Typhus is becoming an important cause of acute undifferentiated febrile illness throughout the Asia Pacific region including India.[1] Infection is caused by *Orientia Tsutsugamushi* an obligate intracellular gram negative microbe. Scrub Typhus cases are being reported widely all over the India including Tamilnadu.[2,3] Diagnosis of Scrub Typhus is often not thought or missed because of close resemblance to other common diseases, non-specific signs and symptoms, absence of widely available sensitive and specific diagnostic tests, as well as low index of suspicion. Delay in diagnosis and initiation of appropriate treatment can result in severe complications and death in children.[3] Knowledge in diagnosis of the Scrub Typhus early when presented without complications, expecting the complications in late arrivals and management strategies for the disease and its complications is a requisite for every pediatrician in the current scenario.

This study was undertaken with the aim to evaluate the clinical profile, complications and outcome of serologically confirmed Scrub Typhus cases admitted in a rural medical college in South India.

METHODS

Study design

This is a prospective descriptive study.

Study place

Pediatric Department, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamilnadu, India.

Study period

Study period was from July 2015 to January 2016.

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.[3,4] It is 91% sensitive and 100% specific. Investigation was done at Institute of Vector Control and Zoonoses, Hosur.

The children admitted with fever in the paediatric 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 were obtained.

RESULTS

During the study period, the 381 fever cases were screened for Scrub Typhus. 151 out of 381 (40%) fever cases were Scrub Typhus positive with male: female ratio of 1.13: 1. Majority of cases 105 (70%) were reported in October, November and December months.

Lowest age reported was 8 months. Majority of children were in the age group of 1 to 6 years [89 (59%)]. 13 (9%) children were less than 1 year and 49 (32%) were above 6 years of age. 117 (77%) children were from rural area and 34 (23%) of children were from urban area (Table 1).

Table 1: Clinical profile of scrub typhus (n=151).

Clinical profile	No.	(%)
Age distribution		
< 1 year	13	9%
1 – 6 years	89	59%
6 – 12 years	49	32%
Sex distribution		
Male	80	53%
Female	71	47%
Locality distribution		
Rural	117	77%
Urban	34	23%
Symptoms		
High grade fever	125	83%
Chills	62	41%
Vomiting	86	57%
Cough and cold	84	56%
Lethargy	82	54%
Head ache	48	32%
Myalgia	40	26%
GI Bleed	33	22%
Abdominal pain	30	20%
Diarrhea	17	11%
Altered sensorium	17	11%
Seizures with posturing	15	10%
Oliguria	15	10%
Incessant cry	6	4%
Signs		
Lymphadenopathy	106	70%
Eschar	102	68%
Hepatomegaly	94	62%
Splenomegaly	85	56%
Anasarca	27	18%
Rash	25	17%

Figure 1: Typical eschar of scrub typhus.

All the 151 children had fever in a range of 3 days to 25 days with a median of 9 days. In many children, fever was high grade [125 (83%)] and associated with chills [62 (41%)]. Cough, cold [84 (56%)] and vomiting [86 (57%)] were common symptoms. Lethargy, head ache, myalgia, abdominal pain, diarrhea, convulsions and

incessant cry were reported in 82 (54%), 48 (32%), 40 (26%), 30 (20%), 17 (11%), 15 (10%) and 6 (4%) children respectively.

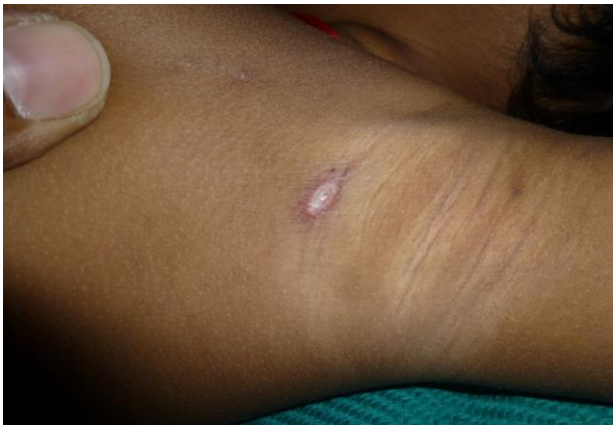

Figure 2: Eschar at axilla in scrub typhus.

Lymphadenopathy (70%), Eschar (68%), hepatomegaly (62%) and Splenomegaly (56%) were the major clinical findings in Scrub Typhus positive children (Figure 1).

Eschar was found in the skin folds of axilla, genitalia, inguinal areas, groin, perianal areas, behind the ear, scalp and umbilicus (Figure 2). Rash was seen in 25 (17%) of children only. Generalized anasarca (18%), GI bleed (22%) and oliguria (10%) were other important clinical features encountered (Table 1).

70 (46%) children presented with shock in Scrub Typhus positive cases where as 55 (36%) of children had respiratory distress. (Table 2) ARDS (12%), meningoencephalitis (10%), myocardial dysfunction (8%), DIC (3%) and MODS (1.3%) were other important complications encountered.

Table 2: Complications and investigations among children with scrub typhus (n=151).

Complications	No.	%
Shock	70	46%
Respiratory Distress	55	36%
Pleural effusion	60	40%
Ascites	56	37%
ARDS	18	12%
Meningoencephalitis	15	10%
Myocardial dysfunction	12	8%
DIVC	5	3%
MODS	2	1.3%
Investigations		
Thrombocytopenia	122	81%
Anemia	112	74%
Positive findings in USG abdomen	86	57%
Elevated transaminases (SGOT, SGPT)	80	53%
Hyponatremia	28	19%
Elevated renal parameters	23	15%
Elevated S. Bilirubin	13	9%

Table 3: Treatment modalities for scrub typhus (n=151).

Treatment	No.	%
Doxycycline alone	80	53%
Azithromycin alone	17	11%
Both Doxycycline and Azithromycin	54	36%
Fluids alone for shock	10	7%
Dopamine	57	38%
Non-adrenaline	18	12%
Adrenaline	2	1.3%
Nasal oxygen	15	10%
O_2 through Jackson Rees Circuit	42	28%
Non-invasive Ventilation	13	9%

Thrombocytopenia (platelet <1,00,000/mm3) was seen in 122 (81%) children and anemia (< 11 gm%) was seen in 112 (74%) children in the present study (Table 2). Elevated liver enzymes (SGOT, SGPT) [80 (53%)], elevated renal parameters [23 (15%)], elevated S. bilirubin [13 (9%)], hyponatremia 28 (19%) were other common lab parameters seen in the study group. In our study group, gall bladder wall thickening in USG abdomen [86 (57%)], pleural effusion [60 (40%)], ascites [56 (37%)] and perihilar and hepatic lymphadenopathy [32 (21%)] were commonly seen. Other co-infections reported were typhoid, dengue, malaria and sepsis in 10%, 7%, 2% and 2% respectively.

Doxycycline was used for treatment in 80 (53%) children (Table 3). Azithromycin was given to 17 (11%) children who were not tolerating doxycycline. Both the drugs were given to 54 (36%) of children who were seriously ill.

For septic shock, fluids alone needed in 10 (7%) children, whereas fluids and inotropes were needed in 59 (39%) [Dopamine 57 (38%), non-adrenaline 18 (12%) and adrenaline 2 (1.3%)] children. For respiratory distress Nasal O2 needed in 15 (10%) children, whereas oxygen through Jackson rees circuit, non-invasive ventilation was lifesaving in 42 (28%) and 13 (9%) respectively. Only one child died (0.7%) due to MODS during study period.

DISCUSSION

Scrub typhus is an under diagnosed, acute febrile illness, can result in severe complications and death in children if not treated early. *O. Tsusugamushi* is transmitted via the bite of an infected chigger-the larval stage of trombiculid mites (Leptotrombidium Deliense in India). Wild rats, field mice and birds serve as the natural reservoir for the chiggers. Transovarian transmission in the mites also occurred. Disseminated perivasculitis of small blood vessel (haemorrahagic) is the initial event leads to vascular leakage and finally end organ injury (mostly brain and lungs).[5]

Infection commonly presents as an acute febrile illness 7 to 10 days after the painless and unnoticed bite of an

infected chigger (1-3 weeks). The bacteria multiply at the inoculation site with the formation of a papule that ulcerate and become necrotic, evolving into an eschar, with regional lymphadenopathy that may progress to generalized lymphadenopathy within few days.

In our study about 40% of the fever cases were scrub typhus positive. Rathi et al reported a large series of Rickettsial infections from Central India.[4]

In our study, clusters of cases reported during the cooler months of the year with a peak incidence in October to December as reported by Vivekanandan et a and Palanivel et al. But in Rathi et al study, majority of cases reported in June to October.[3,4,6]

Slightly male preponderance was seen in our study, whereas male to female ratio of 1:1.3 was reported in Palanivel et al study.[3]

The lowest age reported in the present study was 8 months. But in Palanivel et al and Rathi et al study it was 60 days.[3,4]

The clinical manifestation of Scrub Typhus in children is mostly non-specific and likely to be easily misdiagnosed. Many children presented with high grade fever with chills in our study as reported by Rathi and Rathi and Digra et al.[7,8] Fever usually accompanies capillary leak which is an important clinical finding to differentiate it from dengue fever. The presence of an eschar is a valuable clinical clue in the diagnosis of scrub typhus (though its frequency varies from 7-97%).[9]

Eschar is a black necrotic lesion resembling a cigarette burn usually found in areas where skin is moist or wrinkled and where clothing is tight like axilla, genitalia and inguinal area, neck, scalp, etc. It is usually missed if not looked into carefully because they may lack the black scab and appear as shallow yellow based ulcers without surrounding hyperemia.[10]

Figure 3: Eschar at inguinal area in scrub typhus.

Eschar was reported in 4% to 46% from various studies in India.[3,6,11,12] Eschar was seen in 68% of cases in our study. It is mainly because of asking the mother that any ulcer like lesion present in the children or not during routine history taking. As eschar is painless lesion, mother or child may not give importance. If we enquire, she may show the lesion if present, also, it is very important to look out for the eschar in specified hidden areas (Figure 3).

In the present study, cough, vomiting, lethargy, GI bleed, altered sensorium were seen in 56%, 57%, 54%, 22%, 11% cases respectively. Palanivel et al from Chennai reported altered sensorium in 58% and GI bleed in 40% of cases.[3] So, scrub typhus affects all organs and there may be pleomorphic manifestations. Lymphadenopathy was reported in 70% cases in our study whereas 59% in Palanivel et al and 61% in Digra et al study.[3,8] Hepatosplenomegaly may give clue to diagnose the scrub typhus as it is one of the common findings in many studies including our study.[3,4,6,7]

Scrub typhus patients who are not treated may develop severe complications and may even die. Prognosis is very bad if they come very late as complications usually occur in the 2nd week of illness.[10] Shock (46%), Respiratory distress (36%) were the most common complications followed by ARDS (12%), meningoencephalitis (10%), myocardial dysfunction (8%), DIVC (3%) with MODS (1.3%), etc. in the present study.

Shock was reported as one of the commonest complications (4 to 44%) in various studies.[3,6,13] Wide pulse pressure shock is the common finding in scrub typhus contrast to dengue, where narrow pulse pressure shock is common. So, measuring the diastolic BP is must in critically ill children. Meningoencephalitis was observed in 6% cases in Palanivel et al[3] study and 5% in Rathi et al.[4] ARDS is another important complication (4 to 22%) reported in various studies.[3,4,6,13,14]

Thrombocytopenia is the major laboratory finding observed in the present study (81%). Similar findings were reported in other studies also.[3,6,15] When the child present with fever and thrombocytopenia, important differential diagnosis is scrub typhus along with dengue. Anemia with thrombocytopenia without elevation of hematocrit helps us to differentiate from dengue. Elevated transaminases were observed in 53% of cases in our study as reported in other studies also.[6,13]

Positive findings favours scrub typhus in USG abdomen was seen in 86 (57%) children in the present study. Gall bladder wall thickening and edema was seen in many conditions like dengue, scrub typhus and hepatitis, etc., But, perihilar and hepatic lymphadenopathy, Splenomegaly and minimal pleural effusion and ascities favours scrub typhus. Whereas, massive 3rd spacing and hepatomegaly common in dengue.

Doxycycline (53%) and Azithromycin (11%) were antibiotics used for the treatment of scrub typhus cases. Fever responds dramatically to these drugs may be taken

as diagnostic test. When the children were very sick, we used both the drugs (36%). Palanivel et al used doxycycline in 69% children and azithromycin in 31% children.[3]

Fluids, early appropriate inotropes are necessary to correct shock. In our study, dopamine was used in 38% cases, non-adrenaline in 12% cases and adrenaline in 1.3% cases along with fluids to correct shock. Scrub typhus is a disease causing respiratory distress due to pneumonia, pleural effusion and ARDS. So, early oxygen through Jackson rees circuit (28%), which provides PEEP and early non-invasive ventilation (9%) were needed to treat the respiratory distress in the present study. Mortality rate in our study was very low (0.7%), whereas it was 9 to 15% reported in other studies.[2,3,4,13]

CONCLUSION

Rickettsial infections are more prevalent in various parts of India including Tamilnadu. 40% fever cases are positive for scrub typhus positive in the present study. Acute febrile illness, lymphadenopathy, eschar in hidden areas of body, hepatosplenomegaly, anemia with thrombocytopenia and capillary leak are key clinical features of these infections. Shock, respiratory distress, ARDS, renal, hepatic failure, meningoencephalitis, DIC with MODS are the main complications of the scrub typhus. 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, O2 through Jackson rees circuit, early non-invasive ventilation are main stay of therapy for complications.

Having a high index of suspicion of early diagnosis of scrub typhus and early effective management of complications will reduce the childhood morbidity and mortality.

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