

# A Study on Clinical Profile & Outcome of Scrub Typhus in a Rural Medical College in West Bengal

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**Abstract:** Introduction. In the recent years the number of scrub typhus cases have been consistently on the rise in South Bengal districts. Scrub typhus can present with an array of symptoms and there are multifarious complications associated with the disease if not diagnosed in time and treated appropriately. With this background, we conducted this study to evaluate the clinical profile and outcome of Scrub typhus in a rural medical college in West Bengal. Aims & Objectives: The aims & objectives of this retrospective study were to know the clinical profile and treatment outcome of Scrub typhus. Material & Methods: We retrospectively analyzed the clinical profile and treatment outcome of scrub typhus based on cases diagnosed as Scrub Typhus in Pediatric ward in our unit from 1.5.2021 to 31.7. 2021, confirmed by IgM ELISA. Result: We treated a total of 52 patients who were diagnosed with scrub typhus. We had infants as young as 53days old suffering from this disease. We observed a variety of symptoms and signs of which fever, pallor, hepatosplenomegaly were most common. The major complications include meningoencephalitis, anemia, hepatitis, myocarditis and pneumonia. All patients responded well to antimicrobial therapy (azithromycin/doxycycline) and there were no mortality. Conclusion: Scrub typhus is treatable with specific antimicrobials, an early and accurate diagnosis is essential for reducing risks of severe complications and death.

**Keywords:** Pediatric, scrub typhus, clinical profile

## 1. Introduction

Scrub typhus is an acute febrile illness caused by rickettsia *Orientia tsutsugamushi*. The disease is transmitted to humans through the bite of an infected chigger, the larval stage of trombiculid mite<sup>[1]</sup>

Till 2017 Scrub typhus incidence in West Bengal was low and predominant mostly in the North Bengal districts. However in last 3years the scenario has changed considerably with districts of South Bengal like Bankura, Burdwan, Midnapur also bearing brunt of the disease to a larger extent.<sup>[2]</sup>

## 2. Objective

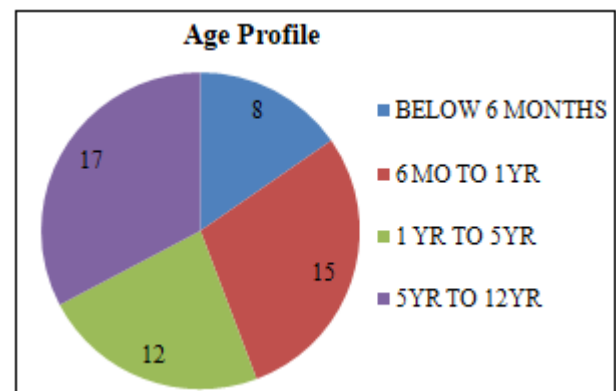
Majority of studies done on scrub typhus have been done on adult population<sup>[4,5]</sup> and there is dearth of studies on pediatric population.<sup>[6-13]</sup> In this study we tried to investigate the incidence, clinical profile and treatment outcome in children with Scrub Typhus infection in a rural teaching hospital of West Bengal.

## 3. Methods

Retrospective study based on cases diagnosed as Scrub Typhus in Pediatric ward in our unit from 1st MAY 2021 to JULY 31<sup>st</sup> 2021. Scrub typhus was confirmed by IgM ELISA. Rest of fever profile panel including MPDA, Dengue IgM, Widal, Urine analysis, COVID RTPCR analysis was normal in our study population. The selected patients were thoroughly examined for signs and symptoms, necessary investigations were done and their course of hospital stay was closely monitored.

## 4. Results

A total of 52 cases were found to be positive for scrub typhus, of which 30 were male and 22 female, ratio of 1.36:1 The age of patients ranged from 1month 23days to 12 years where mean age was 3.26 years.



The clinical features at the time of presentation have been summarised in [Table 1](#). All 52 patients presented with fever. The duration of fever on presentation ranged from 2 to 12 (mean 6.7 days). Other common symptoms were myalgia (69.2%), vomiting (55.7%), swelling especially facial puffiness (53.8%), cough (42.3%) and seizures (19.2%).

Anemia (hemoglobin <11.0 g %) was present in 36 (62%). Mean hemoglobin was found to be 8.15 on day of admission, while it was 9.78 during convalescent stages of the disease, thrombocytopenia (platelet count <1,00,000/mm<sup>3</sup>) in 44 (53%) and elevated liver enzymes (SGOT, SGPT) in 40 (51%) children. Leucocytosis (TLC>12000) was found in 45 patients (86.5% which was

predominantly lymphocytic. The median TLC was found to be 13370, highest being 33,400. Urea and

acute kidney injury (AKI), hepatitis, acute respiratory distress syndrome (ARDS).

Table 1

Symptoms	Number of Patients (%)
1.Fever	35/52=67.3
2. Swelling	28/52=53.8
3.Headache	20/52=38.4
4. Myalgia	36/52=69.2
5.Vomiting	29/52=55.7
6. Seizures	10/52=19.2
7. Headache	12/52=23.07
8. Cough	22/52=42.3
9. Bleeding Manifestations	3/52=5.76
10. Decreased Urine Output	2/52=3.84

High grade fever (>101°F) was recorded in 50 (96%) children. Other common signs include hepatomegaly, edema, pallor, tender lymphadenopathy which were observed in 82%, 61.5%, 34% respectively. An eschar and a maculopapular rash each were observed in 23% of patients. Chest and groin were the most common sites of eschar as listed in Table 2.

Table 2

SIGNS	No of Patients (%)
1. PALLOR	25/52=48.07
2. ICTERUS	5/52=9.61
3.TACHYPNEA	13/52=25
4. ESCHAR	12/52=23.07
5.MACULOPAPULAR RASH	5/52=9.61
6.LYMPHADENOPATHY	18/52=34.6
7. HEPATOMEGALY	43/52=82.7
8. SPLENOMEGALY	18/52=34.6
9. EDEMA	32/52=61.5
10. ASCITES	15/52=28.8
11. RAISED JVP	2/52=3.8
12. MENINGEAL SIGNS	10/52=19.2
13. ALTERED SENSORIUM	6/52=11.53
14. PETECHIA/PURPURA	2/52=3.8

creatinine was raised in 2 (3.8%) patients .Severe anemia (hemoglobin <6.0 g%) was present in 5 (6.1%) children and severe thrombocytopenia (platelet count <20,000/mm<sup>3</sup>) in 2 (3.8%) listed in Table 3.

Table 3

Laboratory Findings	Number of Patients (%)
1. Anemia	44/52=84.6
2. Leucocytosis	41/52=78.8
3. Thrombocytopenia	37/52=71.1
4. Elevated Transaminases	29/52=55.7
5. CSF Pleocytosis	12/52=23.07
6. Elevated Urea, Creatine	2/52=3.8

Complications seen with the disease are summarized in TABLE 4. Meningoencephalitis was the most common complication seen in 10 (19.3%) children. Lumbar puncture in all these children showed mononuclear pleocytosis, protein was mildly elevated (mean 46.3), sugar was found to be in normal range. Severe anemia (hemoglobin <6.0 g%) was present in 5 (6.1%) children and severe thrombocytopenia (platelet count <20,000/mm<sup>3</sup>) in 2 (3.8%) Other complications encountered in the present study were hepatitis, myocarditis, pneumonia, pleural effusion, shock,

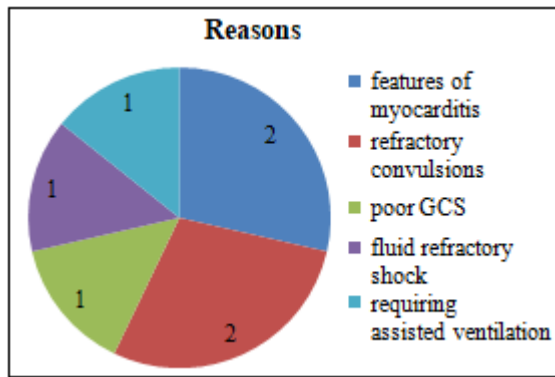
Table 4

Complications	Number of Patients (%)
1.Meningoencephalitis	10/52=19.2
2.Severe Anemia	5/52=9.6
3. Hepatitis	10/52=19.6
4.Myocarditis	7/52=13.4
5. Pneumonia	5/52=9.6
5.Pleural Effusion	4/52=7.7
6.Shock	5/52=9.6
7. Respiratory Failure	3/52=5.7
8. AKI	2/52=3.8
9. Thrombocytopenia<200000	2/52=3.8

- 1) Meningitis: fever with altered mental status, with or without nausea/vomiting, having signs of meningeal irritation and an abnormal cerebrospinal fluid (CSF) analysis. Encephalitis: inflammation of brain parenchyma associated with neurologic dysfunction.
- 2) Acute kidney injury (AKI): as per the latest Acute Kidney Injury Network (AKIN) classification guidelines<sup>[25]</sup>
- 3) Acute hepatitis: elevation of serum transaminases [aspartate aminotransferase (AST)/alanine aminotransferase (ALT)] more than four times the upper limit of normal. No patients developed features of hepatic encephalopathy Hepatic encephalopathy: (acute hepatitis with an altered level of consciousness with overt signs of liver failure)
- 4) Acute respiratory distress syndrome (ARDS): acute-onset non-cardiogenic pulmonary edema which manifests with bilateral alveolar or interstitial infiltrates on a chest radiograph, with a PaO<sub>2</sub>/FiO<sub>2</sub>≤200 mmHg on arterial blood gas analysis
- 5) Pneumonia: acute-onset fever and chills with cough/shortness of breath, with or without crackles/rhonchi, with radiographic evidence of consolidation or interstitial infiltrates
- 6) Myocarditis: chest complaints such as pain, breathlessness, or palpitations with clinical findings such as appearance of murmurs, gallop rhythm, basal crepts, tender hepatomegaly and electrocardiographic evidence of either diffuse ST elevation or T wave inversion, with elevated markers of myocardial damage: creatine kinase-MB/troponin.

Out of 52 children who were found positive for scrub typhus, 8 required PICU management, rest were managed in Pediatrics ward.

The reason for PICU admission are as follows



All the children who did not have neurologic manifestations (total 40 children) were started with oral azithromycin (10mg/kg/day). 29 of them became afebrile within 2 days of starting of azithromycin. 4 patients became afebrile within 3-5days. 7 patients required starting of oral doxycycline as add-on drug following unsatisfactory response to azithromycin. All of them responded well to doxycycline (5mg/kg/day) and fever resolved with 48hours after commencing tablet doxycycline. Studies done in Thailand have shown equal efficacy of azithromycin and doxycycline in treatment of scrubs typhus, however defervescence time with doxycycline is shorter<sup>[21,24]</sup> which is also in accordance to our study.

Patients with neurologic symptoms were started with iv ceftriaxone and iv/oral doxycycline All of them responded well with improvement of neurologic functions within 48hours of starting of treatment. We did not use iv chloramphenicol in our institute.

Supportive treatment such as digoxin, furosemide and anticonvulsants were used in patients who developed CCF and neurologic manifestations respectively.

All the patients were cured and there was no case fatality. Average duration of hospital stay was **5.8 days** with the maximum of 14days

## 5. Discussion

In this prospective study, we have described the clinical profile of pediatric scrub typhus at a rural medical college in South Bengal. There were more male patients than female patients, and the male-to-female ratio was 1.36:1. The mean age at presentation was 3.6 years, which is less than that reported by other studies<sup>[2,7]</sup> while the youngest patient was 53days. Hence adults who are at risk of exposure to mites should take the following steps to prevent disease spread to the infants

1. Vector control: controlling rodents and cutting, burning vegetations/ spraying of insecticides such as lindane.
2. Preventing vector bite:
  - Avoid exposure to vector infested habitats wearing closed protective clothes
  - Permethrin based sprays (on cloths) and 20-50% DEET (N, N-diethyl-m-toluamide) based (on skin) insect repellants should be used.
  - Hot water washing and hot drying of cloths before touching infants
  - Pets should be protected with medications or tick collars
3. Prompt removal of attached ticks: useful strategy as ticks need minimum 4-6 hours of attachment before they transmit infection<sup>[31]</sup>

Most studies have found to have maximum number of cases in monsoon<sup>[2,7,9,10,13,15,16,20]</sup> during the months of August – September, whereas a study from Taiwan found the greatest number of cases during May and August which corresponds with our study<sup>[7]</sup>

The clinical manifestations of scrub typhus in children are non-specific. Most common symptoms include fever, headache, myalgia and cough and symptoms of capillary leak which was found in other studies as well<sup>[2,7,14]</sup>. Eschar, a characteristic cigarette burn like lesion provides helpful clinical clue in diagnosing this disease and differentiation it from dengue<sup>[20,26]</sup>. Some studies have shown eschars to be present in 50-80% of cases<sup>[15]</sup>. In our study we found 23% of patients to be having eschars which corresponds to other studies<sup>[4,16]</sup>.

We found puffiness of face in 61.5% in the present study, which is similar to a previous study<sup>[2]</sup>. Other common features such as myalgia(69.2%), vomiting (55.7%), headache (38.4%) was also found in other studies<sup>[2,14]</sup>.

We observed hepatomegaly and splenomegaly in 82% and 34% of cases, respectively, whereas other authors have reported hepatomegaly in 59% to 98% and splenomegaly in 82% to 88% respectively<sup>[2,14,23]</sup>. The presence of splenomegaly is an important sign to distinguish scrub typhus from dengue fever, since splenomegaly is uncommon in the latter<sup>[20,26]</sup>. Tender lymphadenopathy was observed in 34% of cases in the present study. Other authors have reported lymphadenopathy in 18% to 62% without mentioning about tenderness<sup>[9,13,14,22]</sup>. Thrombocytopenia was found in 71.1% of our cases. other studies have reported a frequency of 22% to 78%<sup>[2,14,16,23]</sup>. Thrombocytopenia without an elevated hematocrit, is an important clue which helps to differentiate scrub typhus from dengue fever.

Scrub typhus can be life-threatening if left undiagnosed and untreated. The potential complications we found in our studies are Meningoencephalitis (in 19.3% cases), followed by hepatitis (19.3% cases) and myocarditis (13.4% cases). Rickettsial diseases should be considered in the differential diagnosis of every patient with aseptic meningitis or meningoencephalitis or acute encephalitic syndrome with compatible epidemiological history<sup>[28,29,30]</sup>. We found 9.6% of patients to be in shock most of them responded well to fluids with only 3.8% cases requiring inotropic support. The incidence of AKI in scrubs typhus has been found to vary among different studies with some studies showing absence of AKI<sup>[6]</sup> while others showing figures as high as 20%<sup>[2]</sup> We had 2 cases (3.8%) with AKI which responded well to conservative management and did not require dialysis.

Hypotension requiring inotropic support (shock) was observed in 25.8% of cases against 45% reported in a previous study<sup>[14]</sup>. Another common complication was AKI, which was found in 16.7% of cases. Rickettsial infections have often been overlooked as a cause of AKI, especially in children. A retrospective study from central India did not report any case of AKI in children with rickettsial infections<sup>[6]</sup>. Three previous studies based on pediatric scrub

typhus have reported lower incidences of AKI ranging from 2 to 10%<sup>[9,14,23]</sup>, whereas another study from south India has reported a higher frequency of 20%<sup>[13]</sup>. In adult studies, AKI has been described in 12-22% of cases<sup>[4,5]</sup>. Multiorgan failure and intra-vascular fluid depletion is thought to be the major factors for AKI in scrub typhus.

In our study we found 9.6% of children having pneumonia. Other studies have also found pneumonia to be in range of 5-20%<sup>[2,4,14]</sup>. One study has found myocarditis to be in much higher numbers (34%)<sup>[2]</sup>. A study from Meghalaya reported acute hepatitis (16.7%), pneumonitis (15.6%) and AKI (12.2%) as their common complications with 38.5% (n=5) death due to MODS<sup>[26]</sup>. This suggests that the complication rate in children are much higher when compared to adults with scrub<sup>[27]</sup>. The high incidence of shock, acute kidney injury and myocarditis observed in the present study have diagnostic and therapeutic implications since these can also be seen in dengue infection. However the presence of splenomegaly, lymphadenopathy, eschars and absence of rise in hematocrit can help in differentiating scrubs from dengue. Most of the patients in this study demonstrated an excellent clinical response to azithromycin or doxycycline as in other studies<sup>[8,9,13-17,20]</sup>. This dramatic response has also been used as a diagnostic test<sup>[4,15-17]</sup>.

Mortality rate in our study was nil which is lower than the study conducted by Kamarasu et al (15%) and Rathi et al (9%)<sup>[19,20]</sup>.

## 6. Limitations

IgM ELISA were used for serological diagnosis because the indirect immunofluorescence assay, the gold standard confirmatory test is not available in our institute.

## 7. Conclusion

Our study showed that scrub typhus results in a significant burden of cases in this part of the country. In our study we found several young infants suffering from scrub typhus, the youngest being 53 days old, which have not been reported in any previous studies which signifies the transmission of ticks from adults/pets.

Any case of acute febrile illness, maculopapular rash, hepatosplenomegaly, tender lymphadenopathy, thrombocytopenia and features suggestive of capillary leak, diagnosis of scrub typhus must be suspected even in very young infants and an eschar further helps in pointing towards the diagnosis. As scrub typhus is treatable with specific antimicrobials, an early and accurate diagnosis essential for reducing risks of severe complications and death.

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