# An Emerging Infection "Scrub Typhus"– A Detailed Clinical Profile and Complications among Children in a Tertiary Hospital

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**Abstract**

**Objectives:** To study the clinical profile and complications of **Scrub typhus** in children.

**Methods:** This descriptive study conducted in Siddhartha Medical college, Vijayawada, among children less than 12 years for a period of one year(December 2020-November 2021).A total of 49 children who are serologically/ clinically diagnosed cases of Scrub typhus.

**Results:** Scrub typhus mainly occurred in school going children with male predominance. Fever being the single most clinical presentation in most of the cases(95.9%) associated with pallor, hepatosplenomegaly. Co infection was documented in 14.2% cases with 85.7% cases showing increased morbidity and mortality. Mortality rate is more in infants.

**Conclusions:** Among cases of Acute febrile illness, Scrub typhus accounts for 9.8% of cases. Main clinical features were persistent fever, hepatosplenomegaly, thrombocytopenia, anemia along with capillary leak signs like edema with or without eschar.

**Infants** are at high risk for complications and mortality.

**Keywords:** Scrub typhus, anemia, thrombocytopenia, hypotension.

## Introduction

Scrub typhus is an **Emerging infectious** disease that is caused by *Orientia tsutsugamushi* from chigger bite. It is common in Asia-Pacific countries especially in India[1]. The disease is characterized by diverse clinical manifestations ranging from a mild, self-limiting state to variable severity like acute respiratory distress syndrome(ARDS), meningoencephalitis[2].

Scrub typhus and other rickettsial infections are **grossly under-diagnosed** in India because of their non-specific clinical presentation, low index of suspicion among clinicians, limited awareness about the disease and lack of diagnostic facilities.[3]

Hence a high degree of suspicion and knowledge on clinical features is needed for early diagnosis and treatment[4]. So that significant morbidity and

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mortality can be avoided in Children.Use of empirical antibiotics have been recommended, pending serology to prevent life threatening complications.[5]

A cross sectional observational study was conducted, to study the clinical features and complications of pediatric scrub typhus. The aim of the study is to determine the clinical profile and risk factors in children presenting with scrub typhus and various clinical and laboratory clues to diagnose clinically, for the early diagnosis and treatment to prevent complications and mortality

## Aims and Objectives

**Primary Objective:**

1. To study the clinical profile of scrub typhus in children.
2. To study the complications of scrub typhus.

**Secondary Objective:**

1. To find out the laboratory clues for early diagnosis.
2. To identify the risk factors for complications in scrub typhus infection.

## Methods and Methodology

Study type: cross –sectional / observational/ institutional study.

- Place of study: department of pediatrics/old government general hospital, vijayawada affiliated to siddhartha medical college.
- Duration of the study: 1 year (December 2020 to November 2021)
- Sample unit: all children aged less than 12 years either positive scrub typhus
- Serology or clinically diagnosed scrub typhus cases(response to treatment).
- Sample size: 49 children meeting inclusion and exclusion criteria.
- Sampling technique: purposive sampling technique.

**Inclusion Criteria:**

All Children of Age Group From Birth to 12 years With

1. Positive scrub typhus serology
2. Clinically diagnosed cases where serology was not feasible(based on treatment response-Standard therapy of Doxycycline(oral or IV) 4-5mg/kg/day or Azithromycin(oral or IV) 5mg/kg/day.

**Exclusion Criteria:**

Isolated other proven causes of acute febrile illnesses.

Serologically negative cases.

## Results

Totally **49 children** were diagnosed with Scrub typhus either serologically**(35)** or clinically**(14).** It comprised of about **9.8%** of cases with acute febrile illnesses. Scrub typhus affects mainly of **school going age group** (27(55%)) followed by preschool age group(9(18.4%)), toddlers (8(16.4%)) and infants (5(10.2%)) **Fig 1**. Affecting mainly boys(30(61.2%)) than girls(19(38.7%))**Fig 2**.

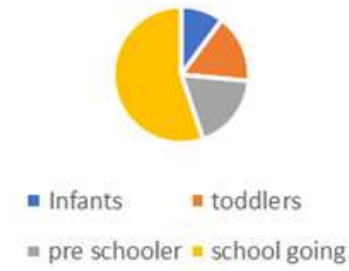


**Fig 1: Age Distirbution**

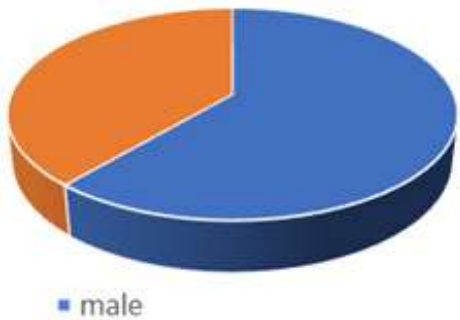


**Fig 2: Gender Distirbution**

**Clinical Presentation:**

All 49 cases had a history of fever for a duration of <7days in 20(40%) cases, 7-14days in 22(45.8%) cases,>14 days in 6(12.2%) cases. So most cases are presented with history of fever for 1 to 2 weeks without diagnoses. Gastrointestinal symptoms were present in 25(51%) cases which includes vomiting(14(28.5%)), abdominal pain(10(20.4%)), loose stools 1(2%)), abdominal distension(2(4%)) and jaundice(2(4%)).

**Clinical Features(Table1):** Respiratory symptoms in 20(40.8%) cases which includes cough(11(22.4%)) and breathing difficulty (9(18.3%)).Central nervous system involvement in 15(30.6%) cases.Vascular leak symptoms like facial puffiness,hypotension in 4(8%) cases. Clinical signs includes altered sensorium in 5(10.2%) cases, tachypnea in 11(22.4%), tachycardia in 9(18.3%), hypotension and rash noted in 2(4%) cases, pallor in 35(71.4%) cases, icterus in 2(4%) cases, lymphadenopathy in 11(22.4%) cases, edema in 4(8%) cases. The most pathognomonic finding of scrub typhus, eschar is seen in 13(26.5%) cases. Hepatosplenomegaly was documented in 35(71.4%) cases.

**Table 1: Clinical Profile: Symptoms and signs of Scrub typhus**

| SYMPTOMS | FREQUENCY (n) | PERCENTAGE (%) | SIGNS | FREQUENCY | PERCENTAGE (%) |
|---|---|---|---|---|---|
| FEVER | 49 | 100 | FEBRILE STATE | 45 | 91.8 |
| <7 DAYS | 20 | 40 | ALTERED SENSORIUM | 5 | 10.2 |
| 7-14DAYS | 24 | 45.8 | PALLOR | 35 | 71.4 |
| >14DAYS | 6 | 12.2 | ICTERUS | 2 | 4 |
| GASTRO INTESTINAL SYMPTOMS | 25 | 51 | LYMPH ADENOPATHY | 11 | 22.4 |
| VOMITING | 14 | 28.5 | EDEMA | 4 | 8 |
| ABDOMINAL PAIN | 10 | 20.4 | ESCHAR | 13 | 26.5 |
| LOOSE STOOLS | 1 | 2 | ISOLATED HEPATO MEGALY | 7 | 14.3 |
| ABDOMINAL DISTENSION | 2 | 4 | ISOLATED SPLENO MEGALY | 2 | 4 |
| JAUNDICE | 2 | 4 | HEPATO SPLENOMEGALY | 35 | 71.4 |
| RESPIRATORY SYMPTOMS | 20 | 40.8 | TACHYPNEA | 11 | 22.4 |
| COUGH | 11 | 22.4 | TACHYCARDIA | 9 | 18.3 |
| BREATHING DIFFICULTY | 9 | 18.3 | ASCITES | 3 | 6 |
| CNS SYMPTOMS | 15 | 30.6 | HYPOTENSION | 2 | 4 |
| HEADACHE | 10 | 20.4 | RASH | 2 | 4 |
| CONVULSION | 5 | 10.2 | | | |
| VASCULAR LEAK SYMPTOMS | | | | | |
| FACIAL PUFFINESS | 4 | 8 | | | |

**Co infection;** was noted in 7(14.2%) cases which includes malaria in 4 cases, dengue positive in 2 cases and leptospirosis in 1 case. Acute rheumatic fever criteria positive in one case of scrub typhus serology positive case. 6 out of 7 cases with co infection showed significant morbidity(85.7%) with one mortality.

**Complications;** like moderate to severe Anemia noted in 5(10%) cases, thrombocytopenia in 40(81.6%),which is another important clue in diagnoses of scrub typhus. Hypotension noted in 3(6.1%) cases, transient hypertension in 1 case. Pneumonia in 8(16.3%) cases, meningoencephalitis in 7(14.2%) cases, myocarditis, hepatitis and shock in 2 cases each. Other complications includes seizure, bradyarrhythmias, CCF, pleural effusion, ARDS, Acute Kidney injury &DIC.

**Mortality** is seen in 3 cases(6.1%).Causes of death being ARDS, Cardiogenic shock, encephalopathy.

## Discussion

Out of 49 children, 35 cases were diagnosed serologically and 14 cases were diagnosed clinically

based on criteria formulated by Rathi et al[6].Scrub typhus constitutes about 9.8% of cases with acute febrile illnesses.

**Distribution**

Mean age of infection in my study is 6 years which is school going age group and most commonly affects boys of rural population. All these findings are similar to studies like Bhat NK et al, Kalal BS et al[8], Kumar M,et al, Thomas R et al[1], Rathi N,Rathi A et al[6]. The seasonal period in which scrub typhus infection occurred in my study is between August to January similar to studies like Thomas R et al[1] and Rathi N et al[6].

**Symptomatology**(TABLE 2)

Fever is present in 91.8% of patients at the time of admission whereas history of fever is present in all the patients. Lymphadenopathy documented in 22.4% cases which is lower than the cases reported in studies like Rathi N et al(41%)[6],Bhat NK et al(38%) [7],Kalal BS et al[8] (49%), and similar to the study done by Thomas R et al[1].

Eschar is documented in 26.5% of cases similar to studies like Bhat Nk et al[7],Kalal BS et al[8].Rash is uncommonly present in my study(4%) which is in contradiction with the studies done by Thomas R et al[1] where rash is reported in 50% of cases and Rathi N et al[6] which reported 59% of cases with rash.

**Table 2: Comparison Of Various Studies For Symptomatolgy**

| STUDY | Rathi N, Rathi A (2009)[6] | Bhat NK, Dhar M, et al (2011-2012) [7] | Kalal BS et al., (2011-2012) [8] | Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011) [9] | Thomas R, Puranik P,, et al (2008-2012) [1] | MY STUDY |
|---|---|---|---|---|---|---|
| Fever | 100% | 100% | 100% | 100% | 100% | 95.9% |
| Lymph adenopathy | 41% | 38% | 49% | 37% | 21.8% | 22.4% |
| Eschar | 7% | 20% | 36% | 11% | 5.7% | 26.5% |
| Rash | 59% | 20% | 26.4% | 20% | 50% | 4% |

**CLINICAL PRESENTATION(TABLE 3)**

My study ,similar to other studies showed commonly hepatomegaly(82.7%),but it is associated with or isolated splenomegaly is present in 75.5% cases which is higher than other studies like Bhat NK et al[7], Vivekanandan M et al[3] studies.Anemia(85.5%) and or thrombocytopenia(81.6%) is documented in my study which is higher than other studies like Rathi N et al[6], Bhat NK et al[7],Vivekanandhan M et al[3]. Hyponatremia is noted in my study,similar to other studies.

**TABLE 3: COMPARISON OF VARIOUS STUDIES FOR CLINICAL PRESENTATION**

| STUDY | Bhat NK, Dhar M, et al (2011-2012) [7] | Vivekanandan M, Mani A, Priya YS, et al (2011-2012) [3] | Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011) [9] | Thomas R, Puranik P, et al (2008-2012) [1] | Rathi N, Rathi A (2009) [6] | MY STUDY |
|---|---|---|---|---|---|---|
| Hepatomegaly | 82% | 67.9% | 91% | 87% | 99% | 82.7% |
| splenomegaly | 59% | 32.1% | 60% | 50% | Not included | 75.5% |
| Anemia | 62% | 69.8% | Not mentioned | 68.7% | 71% | 85.5% |
| Thrombocytopenia | 53% | 66.7% | 31% | Not included | 68% | 81.6% |
| Electrolyte imbalance | Not documented | Hyponatremia (<125meq/dl) 5.6% | Hyponatremia 17% | Hyponatremia 11.5% | 64% hyponatremia | 36.7% Hyponatremia (20.4%) Hypocalcemia (24.4%) |
| Average no of hospital day | 7 days | 7 days | 6 days | 7 days | 7 days | 7 days |

**COMPLICATIONS(TABLE 4)**

61.2%(n=30) cases showed complications. Severe anemia(<6gm/dl) is seen in 4% cases which is less when compared to studies like Thomas et al[1]. Bhat NK et al[7]. Severe thrombocytopenia (<50,000) is seen in 42.7% which is less than the study done by Kalal BS et al[8],more than the studies like Bhat NK et al[7],Kumar M et al[9]. Meningoencephalitis is documented in 14.2% cases which is similar to the study by Rathi N[6] et al,Kala BS et al,Kumar M et al[9].Pneumonia is seen in 16.3% which is higher than studies done by Kumar M et al[9], Thomas R et al[1]. Hypotension is seen in 6.1% cases in my study which is higher than studies like Thomas M et al[1], Rathi N et al[6] but lower than the studies like Kalal BS et al[8] and Kumar M et al[9]. Other rare complications are transient hypertension(2%).simple febrile seizures(2%), Diffuse cerebral atrophy(2%), myocarditis(4%), transient bradyarrhythmias(2%), Congestive cardiac failure(2%), pleural effusion(2%),ARDS(2%), Renal impairment(2%), Hepatitis(4%), DIC(2%), shock(4%). Mortality is seen in 3 cases(6.1%) due to ARDS, Cardiogenic shock and encephalopathy respectively which is similar to studies like Rathi N et al[6], Bhat NK et al[7] and higher than the studies done by Kumar M et al[9] and Thomas R et al[1].

In addition to these findings,my study documented co infection of scrub typhus with other infections in total of 7 cases (14.2%). Co infection with malaria in 4 cases,dengue in 2 cases and leptospirosis in 1 case. One peculiar finding is that one of the serologically positive case showed features of Acute rheumatic fever which was diagnosed based on Modified Jones criteria and the case died due to cardiogenic shock despite the necessary cardiac support.6 out of 7 cases with co infections showed severe morbidity and mortality.

One more important finding includes even the infants(n=5) can acquire scrub typhus, despite less outdoor activities and they are prone to develop severe complication which is 80%(n=4) and mortality in 40%(n=2) mainly due to endothelial damage and vascular leaking. Combination of all these features with capillary leak signs especially in endemic areas, diagnosis of Scrub typhus must be considered and treatment to be initiated early[10].

**TABLE 4: COMPARISON OF VARIOUS STUDIES FOR COMPLICATIONS:**

| COMPLICATIONS | Bhat NK, Dhar M, et al (2011-2012) [7] | Kalal BS et al., (2011-2012) [8] | Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011) [9] | Thomas R, Puranik P,, et al (2008-2012) [1] | Rathi N, Rathi A (2009) [6] | MY STUDY |
|---|---|---|---|---|---|---|
| SEVERE ANEMIA (<6g/dl) | 6.1% | (<11g/dl) 69.8% | Not included | 68.7% | 71% (<9g/dl) | 4% |
| SEVERE THROMBOCYTOPENIA (<50000) | 27.2% | 66.7% | 31% (<1,00000) | Not included | Not included | 42.7% |
| HYPOTENSION | Not mentioned | 10% | 34% | 1% | 3% | 6.1% |
| HYPERTENSION (TRANSIENT) | Not mentioned | 0 | 0 | Not included | 0 | 2% |
| MENINGO ENCEPHALITIS | 30.3% | 17% | 17% | 28% | 15% | 14.2% |
| SIMPLE FEBRILE SEIZURE | Not mentioned | 15% | 0 | Not included | 0 | 2% |
| DIFFUSE CEREBRAL ATROPHY | Not mentioned | 0 | 0 | Not included | 0 | 2% |
| MYOCARDITIS | 9.1% | 0 | 34% | Not included | 5% | 4% |
| TRANSIENT BRADYARRHYTHMIA | Not mentioned | 0 | 0 | 0 | 0 | 2% |

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| | | | | | | |
|---|---|---|---|---|---|---|
| CONGESTIVE CARDIAC FAILURE | Not mentioned | 0 | 0 | 0 | 0 | 2% |
| PNEUMONIA | 10.6% | 0 | 3% | 6.1% | 21% | 16.3% |
| PLEURAL EFFUSION | 9.1% | 0 | 14% | Not included | 0 | 2% |
| ARDS | 12.1% | 0 | 9% | 1% | 5% | 2% |
| HEPATITIS | 13.6% | 81.1% | 31% | 0 | Not included | 4% |
| RENAL IMPAIRMENT | 16.7% | 0 | 20% | 0.4% | 5% | 2% |
| SHOCK | 25.8% | 10% | 34% | 1.9% | 5% | 4% |
| DIC | 1.5% | 0 | 9% | Not included | 5% | 2% |
| MORTALITY | 7.5% | 0% | 2.8% | 1.9% | 8% | 6.1% |

## Conclusions

1. In cases of Acute febrile illness especially after monsoon season ,consider the diagnosis of Scrub typhus,
2. Consider empirical treatment with Doxycycline as delay in the treatment after complications may lead to serious morbidity and mortality.
3. Main clinical clues includes persistent fever, hepatosplenomegaly, thrombocytopenia, anemia along with leak signs like edema with or without Escher ,in endemic area consider the first differential diagnosis as Scrub typhus.
4. In resource limited settings,consider starting Doxycycline if the clinical clues points towards Scrub typhus as drastic response will be seen.
5. Although duration of fever doesn't correlate with the complications, delay in treatment may lead to serious complications.
6. Like other hemorrhagic fever**, Infants** are high risk group for complication and mortality as 80% of them showed complications and 66% mortality. Other risk factor includes **co infections** (14.2%).Consider doing investigations for other infections also for better outcome.

**Conflict of Interest:** None

**Source of Funding:** NIL

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