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# **Original Research Article**

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# Clinico-laboratory profile of central nervous system infection by scrub typhus at a tertiary care hospital

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### **ABSTRACT**

**Background:** Scrub typhus is an emerging epidemic in India. Its course can be complicated by involvement of Respiratory system, cardiovascular system, gastrointestinal system and central nervous system. Central nervous system involvement can lead to major morbidity and mortality.

**Methods:** It is an observational study conducted in the Department of Pediatrics, Patna Medical College and Hospital, Patna from January 2016 to August 2018. All cases of AES who were serologically proven to be due to scrub typhus were clinically examined, signs and symptoms were noted, and complete blood counts were done. Lumbar puncture was done, and CSF was sent for analysis of cells, sugar and protein, IgM for scrub typhus in CSF, gram staining and CSF culture.

**Results:** Seventy-eight cases were tested positive for scrub typhus. Incidence of scrub typhus among AES cases was 19.4% in the study. Among cases of Scrub typhus, a male predominance and sex ratio was 1.68. Age at presentation ranged from 2 months to 12 years with a mean age of 7.28 years. Most of the cases were seen in the months of September and October with a mini peak in the month of March. Fever and Altered consciousness were present in all the cases. Among laboratory investigations, thrombocytopenia was the most common feature followed by raised Transaminases. CSF Analysis shows mildly increased cell count with lymphocytic predominance and presence of few polymorphs, sugar mildly decreased, and protein mildly raised.

**Conclusions:** Scrub typhus is an important causative agent of AES in the Eastern parts of India. It should be suspected in cases which present as AES with symptoms of hepatosplenomegaly, thrombocytopenia, and elevated liver enzymes in addition to dengue encephalitis which forms its close differential.

**Keywords:** Central nervous system infection, CSF, Scrub typhus, Thrombocytopenia

# **INTRODUCTION**

Scrub typhus is an important cause of acute febrile illness in Eastern parts of India. The causative agent is distinct from, but related to, Rickettsia species. The infection is transmitted via chigger (larval mite) bites and involves many antigenically diverse strains of *Orientia tsutsugamushi*. Most infections in children are acquired in rural areas. In India, scrub typhus is an emerging cause of acute fevers of unknown origin. Infections are most

common during rainy months, usually June through November. Reported cases in boys are higher than in girls.<sup>3,4</sup>

O. tsutsugamushi is transmitted via the bite of the larval stage (chigger) of a trombiculid mite (Leptotrombidium), which serves as both vector and reservoir. Transovarial transmission (passage of the organism from infected mites to their progeny) is the major mechanism for maintenance in nature. Because only the larval stage

takes blood meals, a role for horizontal transmission from infected rodent hosts to uninfected mites has not been proved, but transmission among cofeeding larval mites is a possibility. Multiple serotypes of *O. tsutsugamushi* are recognized, and some share antigenic cross reactivity; however, they do not stimulate protective crossimmunity.

Acute encephalitis syndrome (AES) has emerged as a major epidemic in Bihar and is associated with high mortality. Owing to the increasing burden of disease and its associated morbidity and mortality, studies were undertaken to evaluate specific etiology of AES. One of the studies conducted by the Department of Microbiology of Patna Medical College, Patna along with King George's Medical University, Lucknow, observed that the positivity rates of Scrub typhus IgM or PCR was 25%, followed by IgM positivity for Japanese encephalitis 8.1%, West Nile virus (6.8%), dengue virus (6.1%), chikungunya virus (4.5%).

#### **METHODS**

The study was conducted in Patna Medical College and Hospital, Patna, Bihar. Case presenting with clinical diagnosis of AES who were serologically proven to be due to Scrub typhus, from January 2016 to August 2018, admitted in Patna Medical College were enrolled in the study.

#### Inclusion criteria

- Serologically proven cases of scrub typhus
- Age between 1-month to15 years
- Acute onset of fever
- Change in mental status
- Seizures
- Neurologically normal before the onset of fever.

# Exclusion criteria

- Known case of seizure disorder
- Fever for longer duration
- Febrile convulsion
- Cerebral palsy.

It is an observational study conducted in the Department of Pediatrics, Patna Medical College and Hospital, Patna from January 2016 to August 2018. All cases of AES who were Serologically proven to be due to scrub typhus were clinically examined, signs and symptoms were noted, and complete blood counts were done.

After clinical stabilization and fundoscopy, lumbar puncture was done, and CSF was sent for analysis of cells, sugar and protein, IgM for scrub typhus in CSF, gram staining and CSF culture. Samples were sent, and cerebral malaria and typhoid encephalopathy were ruled out. ADEM was ruled out based on MRI findings.

#### **RESULTS**

Out of 397 cases admitted with the provisional diagnosis of AES, 78 cases were tested positive for scrub typhus. Incidence of scrub typhus among AES cases was 19.4% in the study.

Among cases of scrub typhus, 49 were males and 29 were females, having a male predominance and sex ratio was 1.68. Age at presentation ranged from 2 months to 12 years with a mean age of 7.28 years (±2.84 years).

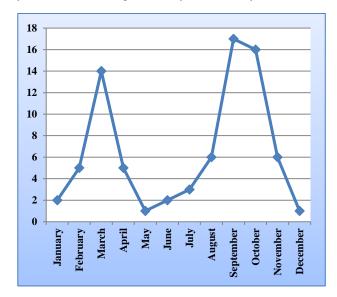


Figure 1: Seasonal variation of scrub typhus.

Figure 1 shows the seasonal distribution of scrub typhus. Most of the cases were seen in the months of September and October having 17 and 16 cases respectively, with a mini peak in the month of March having 14 cases.

Table 1: Demographic profile of patients.

Demographic character	Number	Percentage
Age		
Mean age	7.28	
Standard deviation	2.84	
Sex		
Male	49	62.8
Female	29	37.1
Background		
Rural	45	57.6
Urban	33	42.3

Table 1 demonstrates the demographic characters of the patients of AES due to scrub typhus. Mean age of presentation was 7.28 years (±2.84 years). 49 cases were males and 29 cases were females having a male to female ratio of 1.68. 45 patients were from rural background and 33 were from urban background. Rural predominance is expected because of close proximity of dense vegetations, ticks and human inhabitation.

**Table 2: Clinical presentation of the cases.** 

Signs and symptoms	Number	Percentage
Fever	78	100
Altered consciousness	78	100
Convulsion signs of meningeal	62	79.4
Irritation	18	23.07
Pain abdomen	42	53.8
Vomiting	28	35.89
Lymphadenopathy	36	46.15
Hepatosplenomegaly	48	61.5
Rash	22	28.2
Eschar	15	19.2
Pallor	48	61.5
Icterus	02	2.5
Edema	38	48.7
Thrombocytopenia	66	84.6
Raised SGOT/SGPT	54	69.2

As per the case definition of AES, Fever and Altered consciousness were present in all the cases. Convulsion was the most common CNS symptom, having an incidence of 79.4%. Signs of meningeal irritation was seen in 23.07% of the cases. Among GIT symptoms, pain abdomen was the most common prodromal symptom (53.8%) followed by vomiting (35.89%). Among clinical signs, lymphadenopathy and hepatosplenomegaly was seen in 46.15% and 61.5% respectively. Rash, predominantly maculopapular rash was seen in 28.2% cases. Eschar, which is pathognomonic of scrub typhus was seen only in 15 cases. (19.2%). Pallor, icterus and edema was seen 61.5%, 2.5% and 48.7% cases respectively. Thrombocytopenia was the most common laboratory finding followed by raised transamiases.

Table 3: CSF analysis.

Parameters	Highest value	Lowest value	Mean
Cell	148	12	58±24.43
Polymorphs	28%	09%	16±8.35
Lymphocytes	91%	72%	82±12.4
Sugar	189	43	76±46.8
Protein	114	54	84±45.5

CSF analysis shows mildly increased cell count with lymphocytic predominance and presence of few polymorphs, sugar mildly decreased, and protein mildly raised.

#### **DISCUSSION**

Scrub typhus is a well-known mite borne disease in the Eastern States of India and is emerging public health problem in India.<sup>1-3</sup> Although available medical literatures mention many of the complications of scrub

typhus, Central Nervous System involvement in the form of Acute Encephalitis Syndrome has seldom been highlighted.<sup>4</sup> Relative unawareness of this presentation of Scrub typhus makes the prompt diagnosis difficult, resulting in significant mortality and morbidity.<sup>5</sup>

The disease is transmitted to humans through the bite of infected chigger, the larval stage of trombiculid mite.<sup>6</sup> The bacteria multiply at the inoculation site with the formation of a papule that ulcerates and becomes necrotic, evolving into eschar, with regional lymphadenopathy that may progress to generalized lymphadenopathy within a few days. Vasculitis is the basic pathogenic mechanism in scrub typhus. It is responsible for skin rash, microvascular leakage, edema, tissue hypo perfusion and end organ ischemic injury.<sup>7</sup>

In this study, authors described the clinico- laboratory profile of scrub typhus causing Acute Encephalitis Syndrome in a Tertiary care hospital in Bihar. The majority of the cases occurred between the months of September and November, which follow the rainy season and coincide with the peak growth of vegetations and mite population. Similar observations have been recorded by other authors. The mean age of presentation was 7.28±2.84. Which is similar to that reported by other authors. There were more male patients than female patients with a male to female ratio of 1.68, which was probably due to the higher exposure to chiggers among boys, who like to play outdoors. Similarly, a higher incidence was noted in rural population due to exposure to vegetations and close contact with domestic animals.

Among the clinical manifestations, fever and altered sensorium, were present in all the cases as they formed the case definition for Acute Encephalitis Syndrome. Convulsion was seen in 79.4% cases. This is slightly more than Eswaradass and Eswaradass in 2015 which was 66.6%. 11 Signs of meningeal irritation was present in 23.07% of cases which ranges from 20% to 50% in various other studies. 12 Pain abdomen and vomiting was present in 53.8% and 35.89% respectively. A study from South India has reported the incidence 51% and 34% respectively.<sup>13</sup> Lymphadenopathy was seen in 46.15% of cases which is reported to be from 28% to 57% in various studies.<sup>14</sup> Incidence of hepatosplenomegaly in present study was 61.5% which ranges from 18% to 88%. 15 28% of the patients had rash with a reported incidence ranging from 23 to 100 % in the above studies.

The presence of Eschar is a valuable clinical clue in the diagnosis of scrub typhus, but its absence does not rule out the disease. Thrombocytopenia was a major laboratory finding observed in present study with a reported frequency in literature of 22% to 78%. <sup>16</sup> Elevated liver transaminases were seen in the study with SGOT elevations more than SGPT.

	Present study	Pai et al <sup>17</sup>	Boorugu et al <sup>18</sup>	Kim et al <sup>19</sup>	Varghese et al <sup>20</sup>
Place	Bihar	Korea	South India	South India	South India
No. of patients	78	25	39	17	16
Mean CSF TC (total count)	73±24.43	54±21.8	47.3	96±54.2	83±34.6
Range	12-148	0-110	2-450	7-387	24-124
Mean lymphocyte%	82±12.4	74±16.6	85.3	118±46	831±2.5
Range	72-91%	11-80	30-100	68-100	38-128
Mean glucose (mg/dl)	76±46.8	54±22.6	67.6	84±42.4	81±44.5
Range	43-189	47-84	35-209	34-160	36-167
Mean protein (mg/dl)	94±45.5	74±56.5	90.6	118±46.6	107±66.7
Range	54-189	10-110	14-360	32-340	28-178

Table 4: Comparison of CSF analysis of meningitis due to scrub typhus with other studies.

## **CONCLUSION**

Scrub typhus is an important causative agent of AES in the Eastern parts of India. It should be suspected in cases which present as AES with symptoms of hepatosplenomegaly, thrombocytopenia, and elevated liver enzymes in addition to Dengue Encephalitis which forms its close differential. Unless, there is a high index of suspicion to this condition, timely treatment could not be initiated which could lead to high mortality and morbidity among survivors.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Patna Medical College and Hospital, Patna

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