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

Ruchi Jha*, Anil Kumar Jaiswal

Department of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India

Received: 18 December 2018
Accepted: 28 December 2018

*Correspondence:
Dr. Ruchi Jha,
E-mail: rjsama2021@gmail.com

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.1,2 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.3,4

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 proven, 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 cross-immunity.

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 to 15 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).

| Month   | Number | Percentage |
|---------|--------|------------|
| January | 2      | 6.1%       |
| February| 4      | 10.1%      |
| March   | 14     | 35.6%      |
| April   | 17     | 43.6%      |
| May     | 16     | 40.9%      |
| June    | 1      | 2.5%       |
| July    | 2      | 5.1%       |
| August  | 18     | 45.9%      |
| September| 20  | 50.0%      |
| October | 17     | 43.6%      |
| November| 2      | 5.1%       |
| December| 1      | 2.5%       |

Figure 1: Seasonal variation of scrub typhus.

Table 1: Demographic profile of patients.

| Demographic character | Number | Percentage |
|-----------------------|--------|------------|
| Age                   | Mean age 7.28 | 62.8 |
| 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.
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 pathognomic 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 transaminases.

### 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       |

### 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.1-3 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.4 Relative unawareness of this presentation of Scrub typhus makes the prompt diagnosis difficult, resulting in significant mortality and morbidity.5

The disease is transmitted to humans through the bite of infected chigger, the larval stage of trombiculid mite.6 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.7

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.8 The mean age of presentation was 7.28±2.84. Which is similar to that reported by other authors.9 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.10 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.13 Lymphadenopathy was seen in 46.15% of cases which is reported to be from 28% to 57% in various studies.14 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%.16 Elevated liver transaminases were seen in the study with SGOT elevations more than SGPT.
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.

Funding: No funding sources
Conflicts of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of Patna Medical College and Hospital, Patna

REFERENCES
1. Frequently asked Questions Scrub Typhus published by World Health Organization WHO Regional Office for South East Asia.
2. Chrissal P, Boorugu H, Gopinath KG, Prakash JA, Chandy S, Abraham OC, et al. Scrub typhus: an unrecognized threat in South India—Clinical Profile and Predictors of Mortality. Tropical Doctor. 2010;40(3):129–33.
3. Mahajan SK, Bakshi D. Acute reversible hearing loss in scrub typhus. JAPI. 2007;55:512–4.
4. Mahajan SK, Rolain JM, Kanga A, Raoult D. Scrub typhus involving central nervous system, India, 2004–2006. Emerg Infect Dis. 2010;16(10):1641.
5. Saifuludeen K, Kumar KS, Jose J, Veena V, Gafoor VA. First case of scrub typhus with meningoencephalitis from Kerala: An emerging infectious threat. Annals Indian Acad Neurol. 2012;15(2):141.
6. Somashekar HR, Moses PD, Pavithran S, Grace Mathew L, Agarwal I, et al. Magnitude and features of scrub typhus and spotted fever in children in India J Tropical Pediatr. 2005;52(3):228-9.
7. Joshi R, Punde A, Ohri A. Rickettsial infections seen in rural India. Bombay Hosp J. 2009;51:385-7.
8. Kumar M, Krishnamurthy S, Delhikumar CG, Narayanan P, Biswal N, Srinivasan S. Scrub typhus in children at a tertiary hospital in southern India: clinical profile and complications. J Infection Public Health. 2012;5(1):82-8.
9. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. Indian J Pediatr. 2012;79(11):1459-62.
10. Rathi N, Rathi A. Rickettsial infections: Indian perspective. Indian pediatr. 2010;47(2):157-64.
11. Eswardass PV, Eswardass C. Clinical, Laboratory Findings and Complications of Scrub Typhus-Meningoencephalitis: Case Series (I7-5D). Neurol. 2015;84(14 Supplement):17-5D.
12. Digra SK, Saini GS, Singh V, Sharma KD, Kaul R. Scrub typhus in children: Jammu experience. JK Sci. 2010;12(2):95.
13. Kumar Bhat N, Dhar M, Mittal G, Shiraizi N, Rawat A, Prakash Kalra B, et al. Scrub typhus in children at a tertiary hospital in north India: clinical profile and complications. Iran J Pediatr. 2014;24:387-392.
14. Sirisanthana V, Puthanakit T, Sirisanthana T. Epidemiologic, clinical and laboratory features of Scrub typhus in thirty Thai children. Pediatr Infect Dis J. 2003;990:359-364.
15. Sinha P, Gupta S, Dawra R, Rijhawan P. Recent outbreak of Scrub typhus in north western part of India. Indian J Med Microbiol. 201432:247-250.
16. Singh SP, Singh R, Ahmad N. A study of scrub typhus in a tertiary health care Institute of Uttarakhand, India. Int J Res Med Sci. 2014;2(1):246-9.
17. Pai H, Sohn S, Seong Y, Kee S, Chang WH, Choe KW. Central Nervous System involvement in patients with scrub typhus. Clin Infect Dis. 1997;24:436-40.
18. Booguru H, Chrispal A, Gopinath KG, Chandy S, Prakash JJ, Abraham AM, et al. Central Nervous System involvement in Scrub typhus. Trop Doct 2014;44:36-7.
19. Kim JH, Lee SA, Ahn TB, Yoon SS, Park KC, Chang DI, et al. Central Nervous System

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

| Place     | Present study | Pai et al17 | Boorugu et al18 | Kim et al19 | Varghese et al20 |
|-----------|---------------|-------------|-----------------|-------------|------------------|
| No. of patients | Bihar         | Korea       | South India    | South India | South India      |
| 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     | 38.3           | 118±46      | 83±25.5          |
| 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           |
complications of Scrub typhus. J Clin Neurol. 2008;4:36-9.

20. Varghese GM, Abraham OC, Mathai D, Thomas K, Aaron R, Kavitha ML, et al. Scrub typhus among hospitalised patients with febrile illness in South India: magnitude and clinical predictors. J Infect. 2006;52(1):56-60.

Cite this article as: Jha R, Jaiswal AK. Clinico-laboratory profile of central nervous system infection by scrub typhus at a tertiary care hospital. Int J Contemp Pediatr 2019;6:375-9.