

Profile of Pediatric Scrub Typhus in Odisha, India

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Objective: To investigate the distribution and clinical profile of scrub typhus infection among children with acute febrile illness in Odisha. **Methods:** Children (<15 y) presenting with acute fever (>5 days) in 4 agro-climatic zones from June to November 2017 were evaluated. Patients were screened for malaria, leptospira, dengue, typhoid and scrub typhus. Scrub typhus was confirmed by IgM ELISA and PCR. **Results:** Out of 413 cases examined, 48.7% were positive for scrub typhus, and 5.5% of them developed systemic complications. Eschar was found in 17.9% of cases. Five days treatment of Doxycycline and/or Azithromycin was clinically effective against scrub typhus. **Conclusion:** Our study highlights that scrub typhus is one of the causes of high morbidity in children during rainy months in Odisha.

Keywords: Acute encephalitis syndrome, Acute febrile illness, Etiology, Rickettsia.

Scrub typhus, caused by *Orientia tsutsugamushi* is rife in Southeast Asian region and re-emerging as a major cause of acute febrile illness (AFI) in Indian subcontinent, especially among children [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, acute kidney injury (AKI), myocarditis leading to heart failure, hepatitis and multi organ dysfunction (MOD). A late presentation, delay in diagnosis and treatment causes overall 11.1% deaths in children below 10 years because of low index of suspicion, and non-specificity of signs and symptoms [2]. Recently majority of the cases in frequently occurring acute encephalitic syndrome (AES) / JE outbreaks in Gorakhpur, Uttar Pradesh among children (<15 years), have been reported to be due to scrub typhus [3,4]. Odisha is on the Eastern Ghat and has been reporting seasonal AES outbreaks since 2009 at specific interval [5]; but the etiology has not been established. On the basis of the Gorakhpur report, when we did serological analysis of 30 AES archived samples collected from hospitalized children during the 2016 epidemic, we found that 23.3% (7/30) of the JE suspected cases were positive for scrub typhus. This prompted us to carry out this pilot study to investigate the burden of pediatric scrub typhus in this part of the country.

METHODS

This study was conducted from June to November 2017 among children attending OPD of health clinics situated in

four agro-climatic zones of the state. Patients below 15 years of age with acute fever (>5 days) and suspected to be rickettsial infections were included in the study. While patients diagnosed to have some other associated infection were excluded. Data on clinical features and demographics of each patient were collected and 1 mL of venous blood collected aseptically. Malaria, dengue and leptospira were screened by rapid diagnostic kit (SD Standard Diagnostic Inc, South Korea) and typhoid by Widal test. Diagnosis of scrub typhus was done based on test result of IgM ELISA (In Bios International Inc., Seattle, WA). Subjects having optical density of >0.5 at 450 nm were considered positive for scrub typhus. Further diagnosis of scrub typhus was confirmed by PCR in all cases having eschar, as described by Furuya, *et al.* [6]. All patients were treated by the local physician as per standard guidelines. This study was approved by the Institutional Human Ethics Committee of the ICMR-Regional Medical Research Centre, Bhubaneswar and State Ethics Committee, Department of Health and Family Welfare, Government of Odisha. Informed written consent for voluntary participation was taken from the guardian/ parents of the children included in the study.

All statistical analyses were performed using SPSS software version 16.0 (SPSS Inc., Chicago, IL). P value of 0.05 or less was considered statistically significant.

RESULTS

During the study a total of 413 children [Mean (SD) age,

5.4 (3.8)] with >5 days of acute fever were evaluated. Out of the total samples analyzed, 201 (48.7%) were diagnosed to be positive for scrub typhus by IgM ELISA, 16 (3.9%) for malaria (*P. falciparum*: 10; *P. vivax*: 6), 4 (0.97%) each for dengue and leptospira, and 53 (12.8%) for typhoid. Out of 16 malaria positive cases, 6 (47.5%) were found to be co-infected with scrub typhus. The diagnosis of scrub typhus was further confirmed by PCR in 36 eschar samples. The study showed a male preponderance ($P=0.03$) and 10.8 fold higher incidence of scrub typhus infection in rural areas compared to urban areas (**Table I**). Further, the number of suspected/positive cases was observed to be more in the month of August to October suggesting seasonality of transmission. The most important environmental risk factors were living close to forests, bushes or crop fields, and cattle shed as seen in 158 (78.6%) of positive patients (RR 11.6, $P<0.001$).

TABLE I SOCIO-DEMOGRAPHIC AND CLINICAL FEATURES OF SCRUB TYPHUS POSITIVE PATIENTS (N=201), JUNE TO NOVEMBER, 2017, ODISHA

Study variables	No (%)
<i>Age groups (y)</i>	
<1	12 (6.0)
1-5	91 (45.3)
6-10	79 (39.3)
11-15	19 (9.5)
Male sex	124 (61.7)
<i>Geographic location</i>	
Northern plateau	172 (85.6)
Coastal belt	21 (10.4)
Eastern ghat	8 (4.0)
Rural locality	184 (91.5)
<i>Clinical features</i>	
Fever >7 days	70 (34.8)
Myalgia	98 (48.8)
Cough	147 (73.1)
Headache	97 (48.3)
Nausea/vomiting	25 (12.4)
Abdominal pain	13 (6.5)
Rash	39 (19.4)
Puffiness of face	117 (58.2)
Pedal edema	43 (21.4)
Icterus	20 (9.9)
Hepatosplenomegaly	67 (33.3)
Lymphadenopathy	149 (74.1)
Eschar	36 (17.9)

All of the 201 positive cases had a history of long duration of fever ranging from 6-18 days with a median of 12 days. High grade fever (>101°F) was recorded in 177 (88.1%) children. Other common symptoms/signs were cough (73.1%), myalgia (48.8%), headache (48.3%), cervical lymphadenopathy (74.1%), puffiness of face (58.2%), hepatosplenomegaly (33.3%), pedal oedema (21.4%) and maculopapular rashes (19.4%). Eschar, which is an important pathognomonic sign, was seen in 17.9% of cases (**Web Fig. 1**). The most common site of eschar was inguinal region and axilla (33.2%) followed by back and abdomen (16.7%), umbilicus (12.8% each), shoulder, hand, arm and popliteal region (5.5% each) and genitalia (4.5%). Hematological analysis revealed anemia (<11g/dL) in 109 (54.2%), thrombocytopenia (platelets <150 x 10⁹/L) in 43.9%, elevated ESR in 79.81%, and raised liver enzymes in serum (AST in 81.8%, ALT in 73.3% and ALP in 56.1% of cases).

Amongst the enrolled positive cases, 11 (5.5%) children developed complications (ARDS 6; myocarditis 4; and encephalopathy 1) and all recovered after appropriate treatment. Doxycycline was used in 85.5% children and azithromycin in 14.5%.

DISCUSSION

In this study, 48.7% of the cases with acute febrile illness in children <15 year was found to be due to scrub typhus and around 5.5% of them developed systemic complications. High grade fever (>101°F) with cough, cervical lymphadenopathy and puffiness of face were the most common clinical features. Raised ESR and elevated liver enzymes were the most important laboratory findings. However, the limitation of the study is the sampling criteria, as the samples analyzed were only of suspected rickettsial infections.

So far pediatric scrub typhus has been reported from 21 states/union territories and those are mostly restricted to complicated cases admitted to the hospital with pyrexia of unknown origin (PUO) [7-11]. However, we have recruited pediatric patients attending primary care hospitals with prolonged fever, where we have confirmed that scrub typhus is an important cause of acute febrile illness among children in this part of the country in rainy months (August to October) conventionally the peak transmission season for dengue, malaria, leptospira and other viral diseases exhibiting same type of symptoms. Hence early identification of such co-infections is crucial as their treatments differ drastically and also to avert complications and mortality. A high index of clinical suspicion, exploring the history of environmental exposure, and vigilant search for the eschar are crucial for diagnosis as we have observed eschar in 17.9% of cases,

WHAT THIS STUDY ADDS?

- Scrub typhus is an important cause of acute febrile illness and acute encephalitic syndrome among children in Odisha.

but absence of eschar does not rule out the diagnosis. In spite of lack of community based data the increasing number of both uncomplicated and complicated cases indicate that scrub typhus is a fast emerging public health threat in the country and it needs targeted preventive interventions like health education and personal protection among the high risk groups [12]. Additionally, sensitization of the physicians at the PHC level hospitals should be done to use DHR–ICMR guideline for diagnosis and management of the disease [13].

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WEB FIG. 1 Photograph showing Eschar, upper left panel: pinnacle; upper right panel: umbilicus; lower left panel: vulva and lower right panel: abdomen of selected patients.