ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Changing paradigm of scrub typhus infection in children: A study from a tertiary care center of Eastern India

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Submission: 05-06-2024 Revision: 29-08-2024 Publication: 01-10-2024

ABSTRACT

Background: Scrub typhus, a zoonotic disease, is transmitted to humans by the bite of larval trombiculid mite. Keeping in view the morbidity and mortality associated with undiagnosed cases (due to both lack of specific diagnostic tests and ignorance about the disease), the disease deserves a special mention. **Aims and Objectives:** The aims and objectives of the study were to assess complications and atypical manifestations of scrub typhus fever in this subpopulation and to assess the prognosis of patients presenting with atypical manifestations/complications. **Materials and Methods:** This is a longitudinal observational study on the basis of clinical and laboratory evidence at Department of Pediatrics, Calcutta-National-Medical College and Hospital, Kolkata, West Bengal, from March 2021 to February 2022. Children between >28 days and <12 years with atypical manifestations of scrub typhus who were scrub immunoglobulin (Ig)M positive (Serum and/or cerebrospinal fluid) were included in the study. **Results:** Of the 120 scrub typhus IgM-positive patients admitted in 1 year, complications present in 35%. These patients developed encephalitis, encephalomyelitis, neurological deficits, myocarditis, disseminated intravascular coagulation, acute kidney injury, atypical pneumonia, acute respiratory distress syndrome, acute encephalitis syndrome (23.8%), myocarditis with/without heart failure (14.3%), and multi-inflammatory syndrome in children with/without severe acute respiratory syndrome coronavirus 2 IgG (14.2%). There is a statistically significant association between the duration of fever at admission and pediatric intensive care unit (PICU) admission, the longer the fever duration at admission, the higher the rate of complications and thus PICU admission. **Conclusion:** Scrub typhus infection has expanded its various forms, presenting in various atypical manifestations alongside the common clinical features. Multiple cases of multiorgan involvement in the form of multi-inflammatory syndrome and hemophagocytic lymphohistiocytosis have been reported in the background of COVID-19 infection, alongside a significant percentage of scrub typhus infection reported in infancy. Thus, early detection is important to start intervention.

Key words: Scrub typhus in children; Atypical manifestations, Eastern India

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i10.66432

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Scrub typhus has emerged as a leading cause of public health concern globally as well as in India. One billion people are at risk worldwide and about 1 million cases occur every year.[1] This is endemic in the tsutsugamushi triangle which covers a huge 13 million km^2 triangular area in the eastern world extending from Japan in the East and includes India, Pakistan, and Afghanistan. A large part of North and East India (Kashmir, Himachal Pradesh, Assam, Sikkim, and Darjeeling of West Bengal) and some parts of South India (Eastern and Western Ghats) are affected.[2] It is transmitted to humans by the bite of the larva of trombiculid mites (chigger). *Orientia tsutsugamushi* replicates within the human monocyte macrophages and endothelial cells, leading to the release of inflammatory

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cytokines such as tumor necrosis factor and interleukin 1 beta. Perivasculitis of small vessel occurs, resulting in multiorgan involvement and a varied clinical presentation. The disease can affect people across the globe who have visited regions of endemicity. Varied hypotheses have been proposed for the increasing trend of scrub typhus infection throughout the world. The world population explosion and increased urbanization which have resulted in changed land use are major drivers. Furthermore, specific tests are now available for diagnosis, leading to more and rapid case detection. Furthermore, of note is the thriving ability of chiggers in hot and humid weather created by overall global warming.[3] There have also been changes in antimicrobial prescription practices. Antimicrobials such as fluoroquinolones and second and third-generation cephalosporins were widely used in the early 1900s but were ineffective. No licensed vaccines for scrub typhus are available to date. Furthermore, vector control efforts are not well in many places. Scrub typhus infections are seen across all age groups and both genders alike.[4]

Clinical features

The incubation period of scrub typhus infection in humans is usually 10–12 days and can vary between 6 and 21 days. It usually presents as an acute illness, with fever of high grade, malaise, headache, and cough. Generalized lymphadenopathy may also be present. The characteristic clinical feature of scrub typhus is the presence of an eschar at the site of the bite of the trombiculid mite. Areas such as axilla, waist, groin, nape of neck, and other covered parts of the body are affected. Later, in the 1st week, a rash, mostly maculopapular starting on the trunk and spreading centrifugally to the limbs may be seen. In individuals with untreated or advanced disease, multisystemic manifestations of the disease have been found. This ranges from various central nervous system manifestations such as acute diffuse encephalomyelitis, encephalopathy, meningitis, cranial nerve palsies, and several ocular manifestations.[5-7] Meningoencephalitis is the more severe form, characterized by altered sensorium and seizures and ultimately leading to multiorgan dysfunction syndrome (MODS) with an increased case-fatality if not treated promptly. Cardiovascular manifestations may range from non-fatal rhythm abnormalities to features of congestive heart failure.[8,9] The renal system may also be affected which might result in acute renal failure. Interstitial pneumonia and acute respiratory distress syndrome may herald the involvement of respiratory system involvement. There may also be involvement of the gastrointestinal system, which can manifest as pancreatitis, alteration in liver functions, and diarrhea.[10-12]

Objectives

The objective of our study is to assess complications and atypical manifestations of scrub typhus fever in this subpopulation and to assess the prognosis of patients presenting with atypical manifestations/complications.

MATERIALS AND METHODS

A prospective observational descriptive study was conducted at the Department of Pediatrics, Calcutta National Medical College and Hospital, Kolkata, West Bengal, spanning 1 year from March 2021 to February 2022. The study focused on children aged >28 days to <12 years presenting at a tertiary care facility. It involved the total enumeration of all suspected scrub typhus patients exhibiting atypical manifestations who tested positive for scrub immunoglobulin (Ig)M (in serum and/or cerebrospinal fluid [CSF]). The total sample size for our study was 42.

Inclusion criteria

1. Children 28 days age up to 12-year age
2. Scrub IgM-positive (blood and/or CSF)
3. Fever high grade >100.4°F
4. Any atypical manifestation with clinical suspicion of scrub typhus.

Exclusion criteria

Scrub typhus patients with typical presentation and children >12 years and <28 days.

Data collection and interpretation

All treatment decisions were made at the clinical judgment of the treatment provider. A detailed history and results of a thorough physical examination were entered on a standard data collection sheet. Data included patient demographics, vital signs, pulse oximetry, and findings on thorough physical examinations. Clinical features at admission, complications occurring during stay, treatment, and outcome.

Laboratory investigations parameters

- Routine blood examination
- Liver function test
- Renal function test
- Test for dengue fever, malaria, and enteric fever
- USG (whole abdomen)
- Routine urine examination
- Serum electrolyte measurement
- Scrub IgM test
- C-reactive protein (CRP)
- Chest X-ray, USG-KUB, magnetic resonance imaging (MRI), etc.

Specific tests depend on the multiorgan systems involved and the atypical presentations.

Statistical analysis

The data were organized in Microsoft Excel and analyzed using SPSS version 24 software. Continuous variables were summarized with mean and standard deviation, while categorical variables were described with frequency and percentage. The results were effectively presented using appropriate tables and diagrams.

RESULTS

This observational study was done at a tertiary care center and children below age of 12 years with scrub typhus positivity (IgM enzyme-linked immunosorbent assay [ELISA]) were enrolled in the study. Of the 120 scrub typhus-positive patients admitted in 1 year, 42 patients were considered to have atypical manifestations, that is, 35% show atypical manifestations or rather complications. The atypical conditions of scrub typhus are common in females (69.1%) than males (30.9%), and the mean age group is 7.6±2.5. The demographic profile of patients under study is presented in Table 1. The maximum number of patients were admitted at the month of August (35.7%) followed by July (16.7%) and September (14.3%). The distribution has been shown in Figure 1. The important atypical manifestations have been shown in Table 2. Among the atypical manifestations, acute encephalitis syndrome was 23.8%, myocarditis with and without heart failure was 14.3%, and multisystem inflammatory syndrome in children (MIS-C) with/without severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) IgG was 14.2%. Eschar was present in 19% patients, that is, eight out of 42 patients. Generalized lymphadenopathy was noted in maximum, about 73.8% of patients. About 64.2% of patients had significant hepatomegaly and 42.8% of patients had splenomegaly. Rash was a typical finding in only 45.8% of patients. Thrombocytopenia is the most prominent laboratory finding seen in 39 patients. Furthermore, the patients admitted to pediatric intensive care unit (PICU) had more thrombocytopenia than patients who were treated at the general ward. Mean hemoglobin was 8.58 g/dL, mean white blood cell (WBC) was 9775/cu.mm, and mean value of the aspartate transaminase (AST) levels of PICU patients was significantly higher (P=0.036). Thirteen patients had neurological manifestations of scrub typhus. Seizure was the most common, eight out of 13 (61.5%), and severe headache was noted in seven patients, that is, 53.8% of patients. Four patients had signs of meningeal irritation, like neck rigidity/Kernig's sign/Brudzinski sign. Two patients had complained of ataxia, and one of them diagnosed as acute cerebellitis due to scrub typhus. About 38.5% of scrub typhus patients with neurological manifestation were positive for CSF Scrub IgM. About 92.3% of patients of scrub typhus with neurological manifestations tested positive for serum scrub IgM. One out of 42 had negative serum scrub IgM but a positive CSF scrub IgM-positive report. Among the patients with multisystem involvement, 58.3% of patients were positive for SARS-COV-2 IgG, and ECHO-2D changes

Table 1: Demographic characteristics

Demographics	Values (%)
Age (years)	7.6±2.5
Sex	
Male	13 (30.9)
Female	29 (69.1)
Residence	
East Medinipur	2 (4.7)
Howrah	4 (9.5)
Kolkata	5 (11.9)
Nadia	2 (4.7)
South 24 Pargana	27 (64.3)
Bihar	2 (4.7)
Religion	
Hindu	25 (59.5)
Muslim	17 (40.5)

Table 2: Enumeration of the different atypical manifestations

Final diagnosis	n	%
Acute cerebellitis	1	2.38
Acute encephalitis syndrome	10	23.81
Acute kidney injury	1	2.38
Acute liver failure with hep A coinfection	1	2.38
ALF with hepatic encephalopathy	2	4.76
Kawasaki like phenomenon	4	9.52
Liver abscess	1	2.38
Meningitis	2	4.76
MIS-C	3	7.14
MIS-C with SARS-COV-2 IgG positive	3	7.14
Myocarditis	4	9.52
Myocarditis with heart failure	2	4.76
Polyarthritis	1	2.38
Scrub pancreatitis	1	2.38
Scrub typhus and JE coinfection	1	2.38
Secondary HLH/MAS	2	4.76
Severe pneumonia	2	4.76
Severe pneumonia with ARDS	1	2.38

MIS-C: Multisystem inflammatory syndrome in children, SARS-COV-2: Severe acute respiratory syndrome coronavirus 2, IgG: Immunoglobulin G, HLH: Hemophagocytic lymphohistiocytosis, ALF: Acute liver failure, MAS: Macrophage activation syndrome, ARDS: Acute respiratory distress syndrome

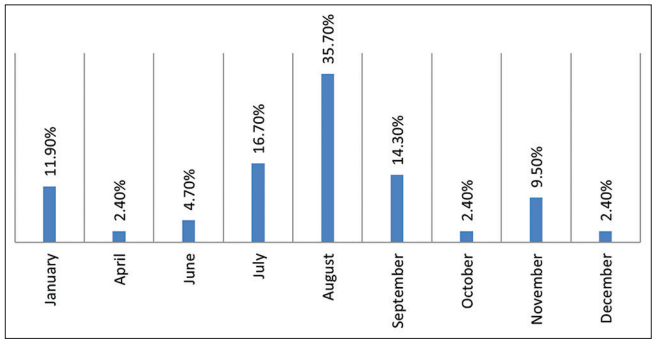

Figure 1: Time of admission of patients with scrub typhus

Table 3: Association between scrub typhus patients requiring PICU admission and statistically significant parameters

Parameter	PICU admission	Mean	SD	P-value
Duration of fever at admission (in days)	Yes No	6.78 4.80	1.78 2.04	0.027*
Platelet/(cubic millimeter)	Yes No	77891.89 142400.00	29362.47 56403.01	<0.001*
AST (IU/L) aspartate aminotransferase (international unit/lite)	Yes No	255.51 117.60	385.41 8.88	0.036*

SD: Standard deviation, AST: Aspartate transaminase, PICU: Pediatric intensive care unit, p<0.05 is statistically significant

were noted in 58.3% of patients. Myocarditis occurred in six out of 42 patients, that is, 14% of patients in my study. Heart failure was evident in 66.7% of patients coming with cardiovascular complications of scrub typhus. Four patients out of 42 had expired, thus the mortality is 9.5%. Fifteen patients, 35.7% of patients, required mechanical ventilator for support during acute course of illness. Table 3 shows that there is a statistically significant association between the duration of fever at admission and PICU admission, the longer the fever duration at admission, the higher rate of complications, and thus, PICU admission. There is a statistically significant association between thrombocytopenia in scrub typhus-infected patients and PICU admission. Furthermore, the higher the AST level, the higher rate of admission in PICU.

DISCUSSION

This longitudinal observational study was done at a tertiary care center and children above the age of 28 days–12 years with scrub typhus positivity (IgM ELISA) were enrolled in the study. Of the 120 scrub IgM-positive patients admitted in 1 year, patients with varied spectrum of the disease considered to have atypical manifestations were 42, that is, 35%. These patients developed encephalitis, encephalomyelitis, neurological deficits, myocarditis, disseminated intravascular coagulation, acute kidney injury, atypical pneumonia, acute respiratory distress syndrome, multi-inflammatory syndrome, etc. in the severe form of the disease.

Atypical manifestations have increasingly being described in recent years in patients with scrub typhus. Many a time, they are under-reported, unrecognized, or not related to scrub typhus infection.

The study shows that atypical manifestations or rather complications of scrub typhus are common in females (69.1%) than males (30.9%).

The mean age group is 7.6±2.5 years. It is around 8.3 years in a study from Nepal. Mean age of 8.8 years was observed by both Kumar Bhat et al., from India,[2] and Palanivel et al. from Nepal.[13]

The highest majority of cases were recorded from South 24 Parganas (64.3%), followed by Kolkata (11.9%), then Howrah (9.5%). This ascertains that South 24 Parganas is endemic for scrub typhus fever.

The maximum number of patients were admitted in the month of August (35.7%), followed by July (16.7%) and then September (14.3%), thus indicating monsoons are favorable for scrub typhus infections. January month also recorded a large number of cases. It is similar to the study from Nepal[3] where most cases are recorded around July, August, and November. Post-monsoon surge of cases has been reported by different authors in various texts. More cases are seen during these months because children from rural areas often work and play in fields, where they are exposed to the bites of larval mites.

Among the atypical manifestations of scrub typhus infections, acute encephalitis syndrome (23.8%), myocarditis with or without heart failure (14.3%), and MIS-C with or without SARS-COV-2 IgG (14.2%) were noted in our study.

Vasculitis is the basis of pathogenic mechanism of scrub typhus infection. It is responsible for various manifestations such as skin rash, microvascular leakage, edema, tissue hypoperfusion, and end-organ ischemic injury.

Scrub typhus has varied clinical presentation with fever being the most common symptom. In this study, fever was documented in all patients, with 21 patients having fever >7-day duration at admission, that is, 50%.

Kumar et al., and Palanivel et al.,[13] also demonstrated fever to be present in all cases. Features of capillary leak usually accompany fever.

Eschar was present in 19% of patients, that is, eight out of 42 patients. Site of eschar: Axilla (2), groin region (2), nape of neck (1), back of arm (1), abdomen (1), and anterior chest (1). It is almost similar to 11.8% from the study from Nepal, 11% by Kumar et al. However, according to the textbook of Nelson eschar, it is generally found in 7–68% of patients (Pg 1628).

Generalized lymphadenopathy was noted in maximum, about 73.8% of patients. Lymphadenopathy in scrub typhus patients is regional, to begin with, large lymph nodes occur at the site of the bite and may lead to generalized lymphadenopathy. Likewise, lymphadenopathy was seen in 84.6% of children in the study from Nepal, De Silva et al., from Sri Lanka reported lymphadenopathy (generalized) in 60% of patients.

64.2% of patients presented with significant hepatomegaly and 42.8% of patients had splenomegaly. Rash was a typical finding in only 45.8% of patients. This is in concordance with The study from Nepal by Palanivel et al, where hepatomegaly (65%), and splenomegaly (46%). However, rash is present in only 9.6% of patients in that study. According to Kumar Bhat et al., rash is present in 20% of patients.

Thrombocytopenia is the most prominent laboratory finding seen in 39 patients, that is <1.5 lacs/cu.mm (92.8%). This is similar to a study by Atindra et al., where thrombocytopenia is seen in 90.4%. Six children had platelet count below 50,000/cu.mm (14.2%), and 27 children had platelet counts between 50,000/cu.mm and 1,00,000/cu.mm (64.2%).

Furthermore, the patients admitted to PICU had more thrombocytopenia than patients who were treated at the general ward. It has been seen that a statistically significant ($P<0.05$) difference exists between these two groups.

Mean hemoglobin concentration of the patients came to be 8.58 g/dL. Mean WBC count was 9775/cu.mm.

A statistically significant difference exists between the mean values of AST levels of complicated scrub typhus patients requiring PICU admission and those who did not require PICU admission; the mean value of the AST levels of PICU patients is significantly higher ($P=0.036$).

There were 13 patients who had neurological manifestations of scrub typhus, that is, 30.9%. This is similar to a study by Garg and Manesh, which states that 20–25% of patients have neurological manifestations.

In this study, seizure was the most common symptom among the patients with CNS manifestations, eight out of 13 (61.5%), severe headache was noted in seven patients, that is, 53.8% of patients. Four patients had signs of meningeal irritation, like neck rigidity/Kernig's sign/Brudzinski sign, and two patients had complained of ataxia, one of them had diagnosed acute cerebellitis due to scrub typhus fever.

Meningitis and meningoencephalitis are the most frequent neurological features of scrub typhus. Patients with scrub typhus meningitis present with classical clinical features of meningeal involvement. They report fever, headache, vomiting, neck stiffness, and altered sensorium. Neck stiffness may be reported in up to 67% of patients. The presence of altered sensorium/seizures including status epilepticus and focal deficits is seen in encephalitis. The median duration from the onset of fever may range from 1 to 30 days as per textbook. In one rare case report, hemorrhagic conversion of encephalitis was reported and was postulated to be consequent to vessel wall fragility in vasculitic blood vessels.

In this study, myocarditis was present in 14.3% of the patients with atypical manifestations. Study by Kumar et al., however, reported myocarditis in 34% of children with scrub typhus fever complications. 2D-ECHO was the diagnostic modality for myocarditis in our study.

In this study, 28.5% of patients had multi-organ dysfunction syndrome. This is similar to a study by Varghese et al.,[14] where 34% of children suffered MODS. In one series published in 2010, MODS was reported in one-third of patients (17 out of 50).

Among the patients with multisystem involvement, 58.3% of patients were positive for SARS-COV-2 IgG, indicating an overlapping picture with MIS-C.

Clinical and laboratory parameters of MIS-C mimic Kawasaki disease (KD). KD has been described in association with dengue, scrub typhus, and leptospirosis. In our study, four patients had presented with Kawasaki-like features. However, MIS-C with concomitant infection has rarely been reported in the literature. In our study, six children were diagnosed to have MIS-C. Investigations showed high values of ferritin, D-dimer, elevated erythrocyte sedimentation rate, CRP, thrombocytosis/thrombocytopenia, anemia, and lymphopenia. Scrub typhus IgM was positive. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgG level was also elevated in three out of six patients with MIS-C. A diagnosis of MIS-C with concomitant scrub typhus has been given. Patients were treated with doxycycline, intravenous Ig (IVIG), and methylprednisolone. All six patients responded to treatment and were discharged in favorable condition. This is similar to a study reported by Gupta and Gill. where the patient was treated with azithromycin, IVIG, and methylprednisolone to full recovery.

KD, MIS-C, and macrophage activation syndrome (MAS) represent three distinct phenotypes of hyperinflammation seen in children during coronavirus disease pandemic. Several tropical infections may mimic or coexist with MIS-C which can be a diagnostic challenge for the treating physician. Identification of coexistence or differentiation between the two conditions is important in countries with

high incidence of tropical infections to guide appropriate investigations and treatment.[15]

Among the patients with multisystem involvement, ECHO-2D changes were noted in 58.3% of patients.

About 38.5% of scrub typhus patients with neurological manifestation were positive for CSF scrub IgM. In another study done by Behara et al., the rate of CSF IgM positivity for scrub typhus has been detected as 62.5%.

About 92.3% of patients with scrub typhus with neurological manifestations tested positive for serum scrub IgM.

Only one patient out of 42 patients had a negative serum scrub IgM but a positive CSF scrub IgM-positive report.

White matter lesions have been described in many case reports in patients with scrub typhus, mainly in the subcortical, periventricular, and deep white matter areas. MRI brain findings were present in 46% of patients with neurological manifestations.

In this study, majority of children were treated with doxycycline and showed very good clinical response. Two patients were treated with doxycycline and azithromycin.

Four children could not be saved even after treatment. Two of the deceased patients died within 12 h of admission (1 patient died within 2 h of admission). One patient died due to severe MAS after prolonged suffering before admission. Thus mortality rate in this study came to 9.5%. This is similar to the study from Nepal by Bajracharya et al[17] as well as the study by Rathi et al. (9%).

Limitations of the study

Due to the limited time period of the study, the sample size was also small and hence conclusions drawn cannot be generalized to the entire population.

CONCLUSION

The clinical profile of scrub typhus fever is changing even in the same region and within the same period of time. Primary care physicians must have a high index of suspicion to diagnose and intervene timely in atypical manifestations of scrub typhus as it is no more a rare entity.

ACKNOWLEDGMENT

The authors would like to thank the patients and families, the hospital authority, and the Department of Pediatrics for letting us conduct this study.

REFERENCES

1. Sharma P, Kakkar R, Kaore SN, Yadav VK and Sharma R. Geographical distribution, effect of season and life cycle of scrub typhus. JK Sci. 2010;12(2):63-64.
2. Kumar Bhat N, Dhar M, Mittal G, Shirazi 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(4):387-392.
3. Veerappan I, Ramar R, and Palanisamy S. Antibiotic response to pediatric scrub typhus in south 94 India: Is clinical failure to azithromycin to be worried? J Trop Pediatr. 2021;67(1):fmab013. https://doi.org/10.1093/tropej/fmab013
4. Gupta A and Gill A. Multisystem inflammatory syndrome in a child with scrub typhus and macrophage activation syndrome. J Trop Pediatr. 2021;67(1):fmab021. https://doi.org/10.1093/tropej/fmab021
5. Wang C, Xiao N, Zhan Y and Ma Q. Encephalomyelitis as the first manifestation of scrub typhus. Neurol Asia. 2019;24(2):157-159.
6. Saifudheen K, Kumar KG, Jose J, Veena V and Gafoor VA. First case of scrub typhus with meningoencephalitis from Kerala: An emerging infectious threat. Ann Indian Acad Neurol. 2012;15(2):141-144. https://doi.org/10.4103/0972-2327.95002
7. El Sayed I, Liu Q, Wee I and Hine P. Antibiotics for treating scrub typhus. Cochrane Database Syst Rev. 2018;9(9):CD002150. https://doi.org/10.1002/14651858.CD002150.pub2
8. Griffith M, Peter JV, Karthik G, Ramakrishna K, Prakash JA, Kalki RC, et al. Profile of organ dysfunction and predictors of mortality in severe scrub typhus infection requiring intensive care admission. Indian J Crit Care Med. 2014;18(8):497-502. https://doi.org/10.4103/0972-5229.138145
9. Rathi NB, Rathi AN, Goodman MH and Aghai ZH. Rickettsial diseases in central India: Proposed clinical scoring system for early detection of spotted fever. Indian Pediatr. 2011;48(11):867-872. https://doi.org/10.1007/s13312-011-0141-7
10. De Silva N, Wijesundara S, Liyanapathirana V, Thevanesam V and Stenos J. Scrub typhus among pediatric patients in Dambadeniya: A base hospital in Sri Lanka. Am J Trop Med Hyg. 2012;87(2):342-344. https://doi.org/10.4269/ajtmh.2012.12-0170
11. Garg D and Manesh A. Neurological facets of scrub typhus: A comprehensive narrative review. Ann Indian Acad Neurol. 2021;24(6):849-864. https://doi.org/10.4103/aian.aian_739_21
12. Kumar M, Krishnamurthy S, Delhikumar CG, Narayanan P, Biswal N and Srinivasan S. Scrub typhus in children at a tertiary hospital in southern India: Clinical profile and complications. J Infect Public Health. 2012;5(1):82-88. https://doi.org/10.1016/j.jiph.2011.11.001
13. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R and Ramachandran P. Clinical profile of scrub typhus in children. Indian J Pediatr. 2012;79:1459-1462. https://doi.org/10.1007/s12098-012-0721-0
14. Varghese GM, Janardhanan J, Trowbridge P, Peter JV, Prakash JA, Sathyendra S, et al. Scrub typhus in South India: Clinical and laboratory manifestations, genetic variability, and outcome. Int J Infect Dis. 2013;17(11):e981-e987. https://doi.org/10.1016/j.ijid.2013.05.017
15. Basu A, Chowdhoury SR, Sarkar M, Khemka A, Mondal R,

Datta K, et al. Scrub typhus-associated hemophagocytic lymphohistiocytosis: Not a rare entity in pediatric age group. J Trop Pediatr. 2021;67(1):fmab001.

https://doi.org/10.1093/tropej/fmab001

16. Behera B, Biswal M, Das RR, Dey A, Jena J, Dhal S, et al. Clinico-epidemiological analysis of scrub typhus in hospitalised patients presenting with acute undifferentiated febrile illness: A hospital-based study from Eastern India. Indian J Med Microbiol. 2019;37(2):278-280.

https://doi.org/10.4103/ijmm.IJMM_19_147

17. Bajracharya L. Scrub typhus in children at tribhuvan university teaching hospital in Nepal. Pediatric Health Med Ther. 2020;11:193-202.

https://doi.org/10.2147/PHMT.S253106

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UB- Prepared first draft of manuscript implementation of the study protocol, data collection, and data analysis; **KB**- Review manuscript, literature survey and preparation of figures manuscript preparation and coordination and manuscript revision; **SP- (**2nd author) Concept design, clinical protocol, manuscript preparation, editing and manuscript revision; **SP-** (3rd author) Design of study, statistical analysis, and interpretation and manuscript preparation.

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Source of Support: Nil, **Conflicts of Interest:** None declared.