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Original Research Article

SCRUB TYPHUS IN CHILDREN: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, DIAGNOSTIC CHALLENGES, AND TREATMENT OUTCOMES

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ABSTRACT

Background: Scrub typhus, an acute febrile illness caused by *Orientia tsutsugamushi*, is a significant zoonotic infection endemic in many parts of Asia and is transmitted primarily through the bites of infected chiggers. In India, the disease has seen resurgent cases, significantly affecting the pediatric population. **Objective:** The objective was to describe the demographics, clinical profile, treatment and prognosis of scrub typhus in children. This is a prospective Cross-sectional study conducted at Department of Paediatrics, Jhalawar Medical College, Jhalawar. Participants the study included all children aged 1 month to 18 years who were serologically confirmed with scrub typhus who were admitted to the Pediatrics department of the hospital during the study period of one year. Children diagnosed with any other associated infection or other causes of acute febrile illness were excluded from the study. **Materials and Methods:** Demographic, clinical, and laboratory data were retrieved from medical case records and entered into a predesigned case record form. Clinical variables included presenting symptoms and their duration, along with physical examination findings such as eschar, edema, rash, icterus, pallor, lymphadenopathy, organomegaly, meningeal signs, crackles, and wheeze. Laboratory tests included complete blood count, serum electrolytes, renal and liver function tests, and coagulation parameters. The ELISA for scrub typhus IgM antibody was performed using Scrub Typhus Detect IgM ELISA. Treatment-related variables, details of organ-supportive therapies, and hospital outcomes were recorded. **Result:** A total of 90 serologically confirmed cases of scrub typhus were included, with a mean age of 5.3 years. The majority (72.2%) were between 1-7 years old, and 85.6% resided in rural areas. Fever was the most common symptom (100%), followed by rash (87.8%) and eschar (40%). Hepatomegaly (45.6%) and icterus (41.1%) were frequent examination findings. Complications included hepatitis (41.1%), meningoencephalitis (21.2%), acute kidney injury (11.1%), MODS (3.3%), and ARDS (2.2%). All patients received doxycycline, with 19% requiring additional azithromycin. The overall recovery rate was 97.8%, with two fatalities (2.2%) due to severe complications. **Conclusion:** The findings indicate a pressing need for heightened awareness and improved diagnostic strategies for scrub typhus among pediatric patients. Adequate training for healthcare professionals and the development of cost-effective diagnostic tools are essential to reduce the morbidity and mortality associated with scrub typhus in children.

INTRODUCTION

Scrub Typhus, commonly known as tsutsugamushi disease, is an acute febrile illness caused by Orientia tsutsugamushi, a bacteria from the Rickettsiaceae family. This is a tiny Gram negative, obligatory intracellular bacterium [Japanese term tsutsuga ("dangerous"),mushi ("bug")].[1]

It is transmitted to humans through the bite of the larvae of the Leptotrombidiumdeliense group of trombiculid mites (chiggers), which are almost tiny and often beautifully colourful (red). During the wet season, when mites lay eggs, infected chiggers are abundant in areas of dense scrub vegetation, which is why this disease is also known as river/flood fever.[2]

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Scrub typhus was first described from Japan in 1899, and is endemic to a part of the world known as the “tsutsugamushi triangle”, which extends from northern Japan and far–eastern Russia in the north, to northern Australia in the south, and to Pakistan in the west. It is reported to exist throughout India, particularly in the southern and northern regions.

Sero-epidemiological data also indicate that Orientia tsutsugamushi infection is widespread in Asia, with sero-prevalence ranging from 9.3% to 27.9%. South India and northern thailand have recorded case fatality rates of 12.2% and 13.6 percent, respectively, from locations with lower drug susceptibility. Even after receiving effective antibiotic therapy, the death rate in south India approaches 9%.[3,4]

Scrub typhus is characterised by focal or disseminated vasculitis, which develops as a result of endothelial cell loss and perivascular infiltration of leukocytes, with symptoms ranging from a self-limited febrile sickness to a fulminant sepsis-syndrome.[5]

Scrub typhus is characterised by fever, which is one of the causes of "fever of unknown origin" in endemic areas. It's usually accompanied by a rash, myalgia, and widespread lymphadenopathy, and it can progress to organ failure and death. Scrub typhus is diagnosed by a necrotic eschar at the mite's inoculating site. The eschar looks like a cigarette burn on the skin.Scrub typhus complications such as jaundice, renal failure, pneumonitis, ARDS, septic shock, myocarditis, and meningoencephalitis commonly appear after the first week of disease.[6]

Weil Felix test, Indirect Immunofluorescence Assay Test (IFAT), Immunoperoxidase Assay, Enzyme Linked Immunosorbent Assay(ELISA), Immunochromatography or Rapid Diagnostic Test (RDT), and PCR are some of the procedures used to identify Scrub typhus.[7]

Because of the non-specific clinical appearance, lack of appropriate diagnostic facilities, and doctors' low threshold of suspicion, many cases of scrub typhus in India go undetected or misdiagnosed.[8]

Because a delay in diagnosis and treatment can lead to more serious consequences and even death in patients, this study aims to detect scrub typhus quickly and easily so that timely diagnosis and treatment can reduce significant morbidity and mortality. This study aims to address these gaps by systematically investigating the demographics, clinical manifestations, laboratory findings, treatment approaches, and outcomes of scrub typhus in children. By analyzing data from paediatric patients diagnosed with scrub typhus, this study seeks to provide valuable insights into the epidemiology and clinical characteristics of the disease in this vulnerable population.

MATERIALS AND METHODS

This Prospective cross-sectional study was carried out in Department of Paediatrics at Jhalawar medical college and attached Shrimati Heera Kunwar Baa Mahila (SHKBM) Hospital, Jhalawar, Rajasthan over a period of 15 months from September, 2023 to November, 2024 (Data collection period – 12 months & Data analysis period – 3 months).

Inclusion criteria

The study included all children aged 1 month to 18 years who were serologically confirmed with scrub typhus and admitted to SHKBM Hospital.

Exclusion criteria

Children diagnosed with any other associated infection or other causes of acute febrile illness were excluded from the study.

Sampling technique: Complete enumeration (Census)

The study included all children serologically confirmed with scrub typhus who were admitted to the Pediatrics Department at Jhalawar Medical College, Jhalawar, during the study period.

Ethical Issues: Approval from Institutional Ethical Committee of hospital was taken before the start of the study. Written and informed consent taken from the participants before proceeding the study. Each eligible subject was explained about the purpose of the study by the investigator and an informed consent was obtained, prior to inclusion. They were assured of complete confidentiality of information, and the option of withdrawing from the study at any point of time.

Method of Data Collection: This cross-sectional study was conducted in children admitted to the pediatric ward and Pediatric Intensive Care Unit (PICU) of a tertiary care hospital in Jhalawar. Records of children aged 1 month to 18 years who presented with serologically confirmed scrub typhus were included. Common infectious conditions that could clinically mimic scrub typhus were ruled out through tests such as peripheral smear, rapid antigen test for malaria, dengue (NS1 antigen and IgM antibody) test, urine routine and microscopy. Cerebrospinal fluid (CSF) analysis was conducted for selected cases with meningoencephalitis.

Demographic, clinical, and laboratory data were retrieved from medical case records and entered into a predesigned case record form. Clinical variables included presenting symptoms and their duration, along with physical examination findings such as eschar, edema, rash, icterus, pallor, lymphadenopathy, organomegaly, meningeal signs, crackles, and wheeze. Laboratory tests included complete blood count, serum electrolytes, renal and liver function tests, and coagulation parameters. The ELISA for scrub typhus IgM antibody was performed using Scrub Typhus Detect IgM ELISA.

Treatment-related variables, details of organ-supportive therapies, and hospital outcomes were recorded. The criteria for organ system dysfunction, acute respiratory distress syndrome (ARDS), and

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acute kidney injury (AKI) were defined according to standard guidelines.

Definitions: The following criteria were used to define the various complications in scrub typhus:

- **Acute Kidney Injury (AKI):** Rise of serum creatinine by at least 0.3 mg/dl or 50% higher than baseline within a 24–48 hour period, or a reduction in urine output to 0.5 mL/kg per hour for longer than 6 hours.
- **Acute Hepatitis:** Elevation of serum transaminases more than 2 times the normal upper limit.
- **Meningoencephalitis:** Altered sensorium along with signs of meningeal irritation and/or seizures, associated with elevated protein and lymphocytic/neutrophilic cytology with normal or low sugar on CSF analysis.
- **Multiple Organ Dysfunction Syndrome (MODS):** Dysfunction of more than one organ, requiring intervention to maintain homeostasis.

Statistical Analysis: The data were initially checked for completeness, and data was cleaned for errors and missing values. The corrected data was then entered into Microsoft Excel after preparing a Master-chart. Data analysis was done using licensed SPSS software version 24.0 (Chicago, Illinois). Univariate analyses was done initially and the results were presented with the help of tables, text, bar-diagrams and pie-charts. Descriptive statistics were used to calculate frequencies of categorical variables, and measures of central tendencies and dispersion were used to describe continuous variables. Bi-variate analyses was done using the Chi square test/Fisher's Exact test, to determine the association between grades of hyponatremia or final outcome with various socio-demographic variables, clinical history, risk factors and laboratory outcomes. For quantitative variable Anova test was used. P value <0.05 was considered as statistically significant.

RESULTS

A total number of 90 serologically confirmed cases diagnosed with scrub typhus were admitted during the study period of one year. The age ranged from 1 month to 18 years with the mean age of 5.3 years. Out of 90 participants, 65 (72.2%) belonged to age group of 1-7 years. 48(53.3%) were female and 42 (46.7%) were male children. And majority of them were from rural area, i.e. 77 (85.6%).Out of 90 participants 82 had history of shrubs, 31 had history of pet at home and 73 participants had history of outside play. [Table 1]

The most common symptom was fever which was present in all cases, followed by rashes present in 79 (87.8%) cases. Least common symptom was joint pain in 2 cases (2.2%). The mean duration of fever was 6.5 days. [Table 2] mentions all symptoms with their frequency seen in our cases.

On examination, hepatomegaly was present in 41 (45.6%) participants followed by icterus in 41.1%, pallor in 20%, oedema in 22.2%, lymphadenopathy in 26.7% and splenomegaly in 10% of the cases. Eschar which is a pathognomonic finding of scrub typhus was seen in 36 (40%) patients. [Table 2]

Table no.3 shows laboratory findings seen in the cases. Most of the patients showed lymphocytosis and increased level of AST, ALT and ALP. [Table 3]

Out of 90 participants, 37 were developed Hepatitis, 19 were developed Meningoencephalitis, 10 were developed Acute Kidney Injury (AKI), 3 had Multi Organ Dysfunction Syndrome (MODS) and 2 had Acute Respiratory Distress Syndrome (ARDS). Doxycycline was used in all patients (100%) for treatment of scrub typhus followed by combination with Azithromycin in cases unresponsive to doxycycline alone (19%). Out of 90 patients, 2 patients died and 88 were successfully discharged. [Table 4]

Table 1: Demographics

Age group	Frequency	Percent
1-7 years	65	72.2
>7 years	25	27.8
Gender		
Female	48	53.3
Male	42	46.7
Residence		
Rural	77	85.6
Urban	13	14.4
History		
H/o Shrubs	82	91.1
H/o of pet at home	31	34.4
H/o outside play	73	81.1

Table 2: Symptoms and Examination Findings

Symptoms	Frequency	Percent
Fever	90	100
Eschar	36	40
Vomiting	10	11.1
Giddiness	8	8.9
Loose stool	13	14.4

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Pain abdomen	17	18.9
Cough	19	21.1
Joint pain	2	2.2
Headache	17	18.9
Burning micturition	10	11.1
Decreased urine output	10	11.1
Rashes	79	87.8
Rashes on palm and sole	43	47.8
On examination		
Pallor	18	20
Icterus	37	41.1
Oedema	20	22.2
Lymphadenopathy	24	26.7
Hepatomegaly	41	45.6
Splenomegaly	9	10

Table 3: Laboratory Findings

	n	Mean ± SD
Hemoglobin (gm%)	90.00	10.30 ± 1.68
Total leukocyte count (103/µL)	90.00	15256.67 ± 7133.33
Platelet count (103/µL)	90.00	209044.44 ± 130486.46
Urea (mg/dl)	65.00	19.72 ± 8.72
Creatinine (mg/dl)	65.00	0.69 ± 0.20
TB (mg/dl)	42.00	0.67 ± 0.41
DB (mg/dl)	42.00	0.40 ± 0.25
AST (U/L)	42.00	70.14 ± 49.44
ALT (U/L)	42.00	51.26 ± 28.16
ALP (U/L)	42.00	132.40 ± 132.12
TP (g/dl)	42.00	5.99 ± 1.09
Albumin (g/dl)	42.00	3.56 ± 0.77
Sodium (Meq/L)	78.00	129.99 ± 6.91

Table 4: Complication and Outcome

Complications	Frequency	Percent
Hepatitis	37	41.1
Meningoencephalitis	19	21.2
AKI	10	11.1
MODS	3	3.3
ARDS	2	2.2
Treatment(Antibiotics)		
Doxycycline	90	100
Azithromycin	19	21.1
Final outcome		
Discharged	88	97.8
Died	2	2.2

DISCUSSION

This hospital-based, observational, cross-sectional prospective study was conducted in the Department of Paediatrics, Jhalawar Medical College, Jhalawar, Rajasthan. This study aimed to describe the demographics, clinical profile, treatment and prognosis of scrub typhus in children. A complete enumeration was used to enroll the participants in the study.

Scrub Typhus, also known as tsutsugamushi disease is an acute febrile illness caused by bacteria of the family Rickettsiaceae and named Orientia tsutsugamushi. [Japanese word tsutsuga ("dangerous"), mushi ("bug")], which is a small Gram-negative, obligate intracellular organism.

Fever is most common feature of scrub typhus and in endemic areas as it is one of the causes of "fever of unknown origin. it is typically associated with rash, myalgia and diffuse lymphadenopathy. Sometime ranges from organ failure to fatal disease.

A necrotic eschar at the inoculating site of the mite is pathognomic of scrub typhus. The eschar resembles the skin burn of a cigarette butt.

There are a variety of tests to detect Scrub typhus such as Weil Felix test, Indirect Immunofluorescence assay test (IFAT), Immunoperoxidase assay, Enzyme Linked Immunosorbent Assay (ELISA), Immunochromatography or Rapid diagnostic test (RDT), and PCR.[7,8]

The ELISA is a rapid and specific test use for accurate testing of large numbers of sera, often obtained in seroepidemiological investigations. Scrub typhus-specific IgM ELISA has shown almost equivalent sensitivity and specificity to those of IFA gold standard, and it can be performed by most laboratories because it does not require any special equipment, or technical training.[9]

Epidemiological Characteristics: In our study, mean age of study participants was 5.3 years with SD of 3.3 and out of 90 participants, maximum 65 (72.2%) belonged to age group of 1-7 years. In the

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present study, out of 90 participants, 48 (53.3%) were female and 42 (46.7%) were male children. In current study, out of 90 participants, 77 (85.6%) were belongs to rural area and 13 (14.4%) were belongs to urban area.[10,11]

In the study conducted by Das P et al,[12] and similar to the current study, 101 patients admitted over 2-year period with positive IgM were analyzed. The male: female ratio was found to be 1.4:1. The mean age of the patients in their study was 4.83 years, with the maximum age being 14 years and the minimum being 0.25 years. A total of 21 (19.8%) children were from the urban area and 80 (79.2%) were from the rural area. These findings are in support of the current study.[13,14]

Similar data were also reported by Bhat et al,[15] which included a total of 96 children and found that mean age of children was 8.9 years with SD of 5.2 out of which male participants were 59.4%.

A study conducted by Singh S et al,[10] in south India reported that male children were more affected than female while study by Sharma et al,[16] reported that more females were affected than males because they more commonly worked in the fields. Another study from Rajasthan reported that positivity for scrub typhus was significantly higher among females who were suffering from fever of unknown origin in comparison to males.[17]

Our study revealed that Scrub typhus is more common in rural residence with slightly higher incidence among the females. This is probably because Scrub typhus is an acute febrile sickness caused by the rickettsiae, Orientia tsutsugamushi which spread to people by the bite of an infected chigger, which is the larval stage of the trombiculid mite and wild rodents serve as a reservoir for these mites. These are more abundant in rural areas.

Clinical Profile: In our study, out of 90 participants, 82 had history of shrubs, 31 had history of pets at home and 73 participants had history of outside play. The most common symptom was fever seen in all cases, followed by rashes present in 79 (87.8%) children. The mean duration of fever was 6.5 days with SD of 1.7 and out of 90 participants, 55 (61.1%) had duration of fever within the range of 1-7 days while rest had >7 days duration of fever. On examination most common finding was hepatomegaly present in 41 (45.6%) participants followed by icterus in 41.1%, pallor in 20%, oedema in 22.2%, lymphadenopathy in 26.7% and splenomegaly in 10% of cases.

In contrast to our study, Narvencar KP et al,[18] found predominance of gastrointestinal signs and symptoms such as nausea and vomiting, abdominal pain, and loose motions in their study.[14]

In another study by Brummaier et al,[13] the most common symptom was fever 93.8% followed by headache 48.1% and cough 33.1% which were similar to the findings in our study.

A study by Gopalakrisna, et al,[14] found that the common feature in scrub typhus patients were hepatomegaly (96.3%), generalized lymphadenopathy (81.5%), splenomegaly (81.5%), hypotension (59.3%), rash (14.8%) and eschar (7.4%) and complications including hepatitis (14.8%), pneumonia (14.8%), myocarditis (14.8%) meningoencephalitis (3.7%) and MODS (3.7%).16 These findings are similar to our study, however Eschar was found in more cases in our study probably due to the different settings.

Scrub typhus presents as an acute febrile illness with non-specific signs and symptom.[3] It accounts for up to 23% of all febrile episodes in areas of the Asia- Pacific region where scrub typhus is endemic and can cause up to 35% mortality if left untreated. In the past, the clinical diagnosis of scrub typhus was dependent on detecting eschar and rash and on the history of outdoor activity.[19] However, differentiation of scrub typhus from other acute tropical febrile illness, such as dengue fever, leptospirosis, malaria, viral hemorrhagic fever, is difficult because their signs and symptoms are very similar.[20]

AR Chogle, et al. said that the presence of eschar is an important finding for diagnosis of Rickettsial pox, cutaneous anthrax, tick-borne Rickettsiosis and other diseases.[7] Although eschars have high diagnostic value, the lesions are painless and without any itching sensation in most cases, causing the infection to be undetected by most patients. In addition, an eschar is similar to a scab formed after trauma, and its size may be very small, which also hinders detection of eschar in many cases.[21]

This is not suitable for the Indian subcontinent because eschar and rash were seen in less than 10% of cases. Scarcity of primary lesion has been noted in earlier reports from India this may be due to variation in strain types in this area.[21] A study conducted in India by Singh et al. reported that eschar was not seen in any patient.[22] However, Eschar was seen in 36 (40%) patients in the present study.

It is difficult to search for evidence of an eschar unless a thorough examination of the body. The distribution of eschar on body surface might be associated with dressing styles and personal hygiene, as the two factors affect how and where chiggers entered and stayed on the body surface. However, individuals living in rural areas are often reluctant to accept a through body examination because of cultural or other reasons.[19]

Biochemical Profile: In our study, the cases showed lymphocytosis (mean-40256.67) and increased level of liver enzymes (AST, ALT and ALP). Similar to our study, study by Brummaier et al,[13] found thrombocytopenia (66.7%), elevation of SGOT (85.2%) and SGPT (81.5%). However in the present study thrombocytopenia was not found. In another study done by Zhang M et al., abnormal liver function test was the most common laboratory finding. Elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) found in 75.0% and 80.3% of the patients.

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Complication: In our study, out of 90 cases, 19 developed Meningoencephalitis and signs of meningeal irritation (neck rigidity and/or kernig's sign) were present in all, 3 cases had Multi Organ Dysfunction Syndrome (MODS) and 2 cases had findings of Acute Respiratory Distress Syndrome (ARDS).

Verma et al,[11] also found similar kind of results and revealed that 27 (48.1%) patients presented with features of acute encephalitis syndrome (AES) and 10 (19.2%) patients presented with acute respiratory distress presenting with breathlessness.

Hospital Stay, Treatment and Response: In our study, mean hospital stay among the participants was 12.2±2.2 days and out of 90 cases, 62 stayed for 10-14 days followed by 21 cases which stayed for 7-10 days. In the present study, out of 90 participants, ICU admission was required in 19 (21.1%) cases with mean ICU of 5.4±1.3 days. Out of 19 cases which needed ICU admission, 6 stayed for 5 days and remaining 5 stayed for 6 days in PICU.

In our study, all the participants received Doxycycline 2.2 mg per kg per dose twice daily for 10-14 days. 19 participants who developed any complications and needed ICU also received Azithromycin 10 mg/ kg on day 1 followed by 5 mg/ kg from day 2 to day 5 in single dose.

Outcome: Despite our best efforts, two patients (2.2%) succumbed. Both the patients had features of multi organ dysfunction. One patient had severe ARDS requiring mechanical ventilatory support while the other patient developed hemorrhagic stroke. Expiries are attributable to late presentation, delay in diagnosis and presence of complications like as ARDS, meningoencephalitis. Study by Bhat NK et al,[23] also reported mortality in 7.3%. Study by Kumar V et al,[24] and Sinha P et al,[25] reported mortality ranging from 0-15%.

CONCLUSION

Scrub typhus presents as an acute febrile illness with non specific signs and symptoms which mimic clinical features of similar common endemic diseases such as malaria, dengue, typhoid and leptospirosis. The findings of our study suggest that whenever a child presents with community acquired acute febrile illness associated with clinical features like rashes, hepatospleenomegaly, generalized lymphadenopathy, icterus, pallor, and elevated liver enzymes, scrub typhus should be considered as a differential diagnosis. Eschar, if present, is pathognomonic for scrub typhus. In such cases with high index of suspicion, empirical therapy with doxycycline or azithromycin should be started to prevent complications of scrub typhus such as hepatitis, meningoencephalitis, ARDS and MODS.

Our study also indicates a need for increased public awareness through health education, adequate training of healthcare professionals and development of cost effective diagnostic tools for early diagnosis and effective management of scrub typhus in children.

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