International Journal of Contemporary Pediatrics
Vaishnav P et al. Int J Contemp Pediatr. 2024 Sep;11(9):1209-1217
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20242287

Original Research Article

Clinical profile, complications, outcome and predictors of intensive care for paediatric scrub typhus: a tertiary hospital-based study from southern Rajasthan, India

Prerna Vaishnav[1]*, Deepak Shivpuri[2]

[1]Department of Paediatrics, American International Institute of Medical Sciences, Udaipur, Rajasthan, India
[2]Department of Paediatrics, Surya Hospitals, Jaipur, Rajasthan, India

Received: 20 July 2024
Accepted: 09 August 2024

***Correspondence:**
Dr. Prerna Vaishnav,
E-mail: drprerna1987@gmail.com

ABSTRACT

Background: Scrub typhus is an endemic acute febrile zoonotic disease and one of the most neglected tropical illnesses. In 2019, its outbreak was reported from Mewar region of Rajasthan, India. It is caused by *Orientia tsutsugamushi* which is intra cellular gram-negative coccobacilli.
Methods: It is retrospective descriptive study conducted on children diagnosed positive for scrub typhus by IgM enzyme-linked immunosorbent assay (ELISA) admitted in ward and paediatric intensive care unit at tertiary care centre during 1 year of study period from April 2023 to March 2024. Clinical profile, laboratory parameters, course of illness and outcome data were collected in predesigned case records proforma for analysis.
Results: Mean age of presentation was 10.5±3.2 years with female preponderance (F:M 1.21:1). 78.5% belong to rural areas. Environmental exposure was living close to forests, bushes in 38%, crop fields in 26% and cattle shed with pets in 30%. All cases had fever (100%, n=42) followed by vomiting (62%), cough-cold (42.8%), myalgia (40.4%), altered sensorium (35.7%), breathlessness (31%), oliguria (16.6%), conjunctival redness (11.9%). Most common signs were temperature >101'F (90.4%), hepatomegaly (62%), hypotension (21.4%), edema (23.8%), meningeal signs (14.2%). Tachypnoea (n=14) (p value <0.0001), CRT>3 seconds (n=13) (p value <0.0003), altered sensorium (n=15) (p value=0.0003) and SpO_2 <90% (n=7) (p value=0.004) were found significant predictors of pediatric intensive care unit (PICU) admission. Eschar and rash seen in 3 cases (7.1%). 16 (38%) children requiring intensive care unit admission had statistically significant anaemia (85.7%) (p=0.013), thrombocytopenia (78.5%) (p=0.042) and raised C-reactive protein (CRP) (50%) (p<0.0001).
Conclusions: Scrub typhus is common in Rajasthan and should be suspected in any child with acute febrile encephalopathy, signs of shock, breathlessness, hepatomegaly, anaemia and thrombocytopenia in the monsoon season with the history of exposure. Early diagnosis and prompt treatment with doxycycline can prevent mortality.

Keywords: Children, India, ARDS, Shock, Intensive care, Scrub typhus

INTRODUCTION

Scrub typhus is potentially fatal infection that affect one million people every year worldwide. It is endemic re-emerging vector borne disease caused by gram-negative coccobacilli, *Orientia tsutsugamushi*.[1] It persists by transovarial transmission in trombiculid mites (chiggers or berry bugs). These chiggers (stage to transmit disease) inoculate organisms into the skin. It is endemic in India due to its location in "*tsutsugamushi triangle"* which includes Japan, Taiwan, China on north, India on west, Australia on south.[2] It has become a pan-Indian phenomenon. Epidemics of scrub typhus have been reported from North, East, West and South India.[3-7] It was

first reported from Alwar district in 2011. Scrub typhus was found to be a major aetiology of acute encephalitis syndrome (AES) reported from Gorakhpur, Uttar Pradesh (63%), Assam (20%).[8] The presence of one or more organ failures with overlapping clinical features at the onset poses a challenge in differentiation of scrub typhus from other tropical infections. Mortality rate in untreated cases ranges from 10-30%.[9]

Mewar is a region in the south-central part of Rajasthan, India. It was bordered by Aravali Range to the north-west, Ajmer to the north, Gujrat region to south and Hadoti region to east.[10] The region has forest, covering mostly hilly tracts. This forest cover is highly dense during the monsoon. The main contributing factor to its endemicity is houses in dense forest and bushy areas, cattle shed, farming in crop fields, rearing livestock, outside cooking and lack of indoor sanitary facility. Very few studies have been conducted in Rajasthan on paediatric scrub typhus.[11] The purpose of this study is to determine clinical profile, complications and predictors of paediatric critical care (PICU) admission in scrub typhus infection from Mewar region of Rajasthan.

METHODS

This is a retrospective descriptive study conducted in children admitted in ward and PICU of paediatric unit of department of American International Institute of Medical Sciences (AIIMS) College and GBH-General Hospital (a tertiary care hospital) located at Udaipur, Rajasthan, India. All children between 1 year to 18 years age group, presenting between April 2023 to March 2024 (12 months duration) with clinically compatible signs and symptoms and tested positive for IgM enzyme-linked immunosorbent assay (ELISA) scrub typhus, were included in this study. Children with undifferentiated fever who were positive for scrub typhus with coinfection, such as dengue, malaria and enteric fever were excluded from the study.

Demographic, clinical and laboratory data were retrieved from medical case records and entered in a pre-designed case record form. Laboratory tests include complete blood count (CBC), renal and liver functions test, serum electrolytes, quantitative C-reactive protein (CRP), and coagulation parameters. Radiological investigations such as chest-X-ray, abdominal ultrasound, magnetic resonance imaging (MRI) brain was done in few indicated cases. Lumber puncture was done in few cases for cerebrospinal fluid (CSF) analysis. Times needed for defervescence after starting doxycycline was recorded. Treatment using drugs (doxycycline or azithromycin), organ supportive therapy such as inotropes (noradrenaline or dobutamine), oxygen, invasive or non-invasive ventilation, osmotherapy (3% NaCl or mannitol), length of hospital stay and hospital outcome were recorded. The recovery of child, death or sequalae was considered for assessing the outcome of disease. Descriptive statistics including frequency, mean, median, interquartile range (IQR) and standard deviation (SD) were calculated for demographic data and laboratory parameters. The data were analysed using statistical package for the social sciences (SPSS) software version 22.0. The Chi-square test was used to compare dichotomous variable. The associations of clinical signs and laboratory parameters with the outcome were analysed by univariate logistic regression. For all tests, a p value 0.05 or less was considered statistically significant.

The study was approved by Institutional Ethics Committee. The complications of scrub typhus were defined as follows. ARDS was diagnosed on the basis of the American-European Consensus Committee also known as the Berlin criteria - acute onset: within one week of a known insult or new/worsening respiratory symptoms; chest radiograph showing bilateral lung infiltrates which are not explained by other lung pathology; non-cardiogenic pulmonary edema and; severe hypoxia with a decreased partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2), regardless of the level of positive end expiratory pressure (mild ARDS: 201-300 mm Hg, moderate ARDS: 101-200 mm Hg and severe ARDS: ≤100 mm).[12]

Shock was identified by capillary refilling time >3 seconds or hemodynamic compromise that required vasopressor (dobutamine or noradrenaline). Hypotension was defined as a systolic blood pressure below the 5th percentile for the corresponding age, sex and height. Hepatitis was diagnosed when liver transaminases were found to be more than three times elevated (>40 U/l) or total serum bilirubin >1 mg/dl. Acute kidney injury (AKI) was defined according to kidney disease: improving global outcomes (KDIGO) classifications.[13] Myocarditis was diagnosed when left ventricular dysfunction identified by echocardiography or elevated CPK-MB or troponin levels in blood.

RESULTS

In this study, a total of 42 cases (Scrub typhus IgM ELISA positive) from April 2023 to March 2024 were enrolled. Mean age was 10.5±3.2 years with a range of 4-18 years and female: male ratio of 1.21:1 with female preponderance. Highest number of cases were found in 10-18 years age group 57.1% (n=24) followed by 5-10 years group 33.3% (n=14) and least in 1-5year 9.5% (n=4). Majority were from rural habitat 78.5% and 21.4% were from urban habitat. Living close to forest, bushes and crop fields were major environmental risk factors in 68% followed by 30% living in cattle shed with pets (Table 1).

Forty patients (95%) presented during monsoon months (July to October) and post monsoon months (November to February) of Rajasthan as depicted in Figure 1.

The demographic data and clinical parameters of the study populations were depicted in Tables 1 and 2 respectively. The median (IQR) duration of hospital stay was 7 (5-8 days) with a range of 4 to 20 days. Among children who had complications, it was 14 days. Median (IQR) duration

of PICU stay was 4 (3,7). Fever was present in all the cases (100%, n=42) followed by vomiting (62%), cough-cold (42.8%), myalgia (40.4%), breathlessness (31%), abdominal pain (23.8%), headache (16.6%), oliguria (16.6%), conjunctival redness (7.1%), rash (7.1%).

Table 1: Demographic variables of scrub typhus cases.

Demographic data	N	%
Gender		
Male	19	45.2
Female	23	54.7
Age in years		
1-5	4	9.5
5-10	14	33.3
10-18	24	57.1
Habitat		
Rural	33	78.5
Urban	9	21.4
Exposure		
Forest, bushes	16	38
Cattle shed	12	30
Crop fields	10	26

Common examination findings as summarized in Table 2 were hepatomegaly (62%), tachypnoea (33.3%), hypotension (21.4%), pallor (26.1%), splenomegaly (21.4%), crackles/wheeze (21.4%), edema (23.8%), eschar (7.1%). Sites of eschar were axilla and groin. Most of the cases presented with hepatomegaly while about one-fourth presented with splenomegaly. Lymphadenopathy was not seen in any case. Tachypnoea was seen in 33.3% while pulse oximetry saturation <90% was observed in 16.6%. Capillary refilling time >3 seconds was present in 30.9%. Icterus was present in only 9.5%. High grade fever (>101'F) at admission was recorded in 90.4% (38). CNS symptoms such as altered sensorium and convulsions were observed in 35.7% and 9.5% while meningeal signs such as kernig sign and brudzinski signs were present in 14.2%.

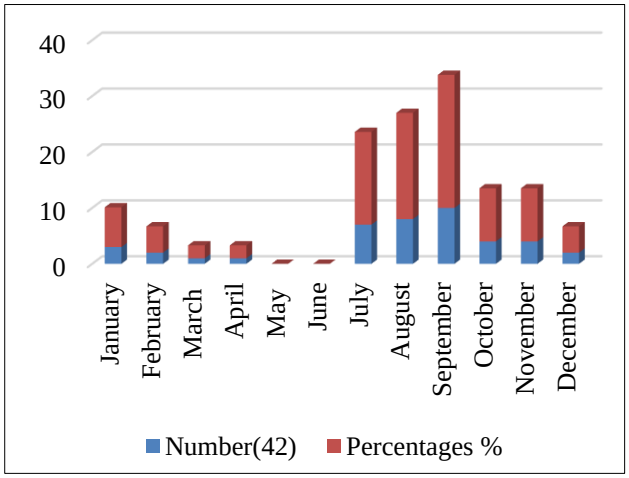

Figure 1: Graphical representation of seasonal variation of scrub typhus in children.

Table 2: Clinical parameters (signs and symptoms) of 42 children with scrub typhus.

Symptoms	No.(%)	Signs	No. (%)
Fever (days)	42 (100)	Temperature>101'F	38 (90.4)
<7	24 (57.1)	Hepatomegaly	26 (62)
>7	18 (42.8)	Tachypnoea	14 (33.3)
Vomiting	26 (62)	CRT>3 seconds	13 (30.9)
Cough cold	18 (42.8)	Hypotension	9 (21.4)
Myalgia	17 (40.4)	Pallor	11 (26.1)
Altered sensorium	15 (35.7)	Crackles/wheeze	9 (21.4)
Breathlessness	13 (31)	SpO_2<90%	7 (16.6)
Abdominal pain	10 (23.8)	Pedal edema	10 (23.8)
Headache	7 (16.6)	Meningeal signs	6 (14.2)
Oliguria	7 (16.6)	Splenomegaly	9 (21.4)
Conjunctival redness	5 (11.9)	Icterus	4 (9.5)
Convulsion	4 (9.5)	Eschar	3 (7.1)
Rash	3 (7.1)	Lymphadenopathy	0 (0)

CRT - Capillary refilling time, SpO_2 - oxygen saturation

Anaemia 36 (85.7%) and thrombocytopenia 33 (78.5%) were characteristic laboratory parameter with mean (SD) haemoglobin 8.7 (2.5) gm/dl and median (IQR) platelets 71,000 (25,000, 1,24,750 cells/mm^3). Others were leucocytosis 28 (66.6%), leukopenia 5 (11.9%), deranged international normalized ratio (INR) 9 (21.4%), hyponatremia 5 (11.9%%), three times raised liver enzymes serum alanine transaminase (SGPT/ALT) 15 (35.7%), aspartate transaminase (SGOT/AST) 11(26.1%), raised serum creatinine 9 (21.4%), hypoalbuminemia 6 (14.2%), hyperbilirubinemia 4 (9.5%) as depicted in Table 3. Severe thrombocytopenia (platelets <50,000/mm^3) were seen in 15 (35.7%) cases. The median (IQR) of CRP was 85.7 (30.4, 255) mg/l.

Table 3: Laboratory profile of 42 children with scrub typhus infection.

Investigations (normal range)	N (%)
Haemoglobin (11-14 gm/dl)	
Anaemia (<11 gm/dl)	36 (85.7)
Total leucocyte counts (4-11×10^3/mm^3)	
Leucocytosis	28 (66.6)
Leukopenia	5 (11.9)
Platelets (150-500 cell/mm^3)	
Thrombocytopenia (<150×10^3/mm^3)	33 (78.5)
C-reactive protein (<8 mg/l)	
Raised CRP (>8 mg/l)	21 (50)
SGOT/AST (15-37 U/l)	
SGPT/ALT (0-41 U/l)	
Three times raised SGOT and SGPT	10 (23.8)
Serum albumin	
Hypoalbuminemia (<3.5 gm/dl))	12 (28.5)
Serum bilirubin	
Hyperbilirubinemia (>1 mg/dl)	5 (11.9)
Serum sodium	
Hyponatremia (<130 mEq/l)	5 (11.9)
Serum creatinine	
Raised serum creatinine (>1.2 mg/dl)	4 (9.5)
INR	
Coagulopathy (>1.5)	4 (9.5)
CSF Pleocytosis	5 (11.9)

Predictors of the need of intensive care admission were compared between PICU group and non-PICU group as depicted in Table 4. On univariate analysis, tachypnoea (n=14) (p value <0.0001), CRT>3 seconds (n=13) (p value <0.0003), altered sensorium (n=15) (p value=0.0003) and oxygen saturation SpO_2 <90% (n=7) (p value=0.004) were found statistically significant predictors of PICU admission in our study. Statistically significant laboratory parameters were anaemia (85.7%) (p=0.013) and thrombocytopenia (78.5%) (p=0.046) and raised CRP (50%) (p<0.0001) in Table 4.

Complications were observed in 16 cases (38%). Shock was most common complication seen in n=14, 33.3% cases as depicted in Figure 2. ARDS (n=13, 23.8%), hepatitis (n=9, 21.4%), meningoencephalitis (n=5, 11.9%), AKI (n=4, 9.5%), DIC (n=4, 9.5%), MODS (n=3, 7.1%), and myocarditis (n=1, 2.3%). Sixteen (38%) children required PICU admission. Intensive care needs include invasive ventilation in severe ARDS in 6 (14.2%) cases, vasoactive drugs for hemodynamic support in 14 (33.3%), osmotherapy therapy to treat raised intra-cranial tension in 9 (21.4%).

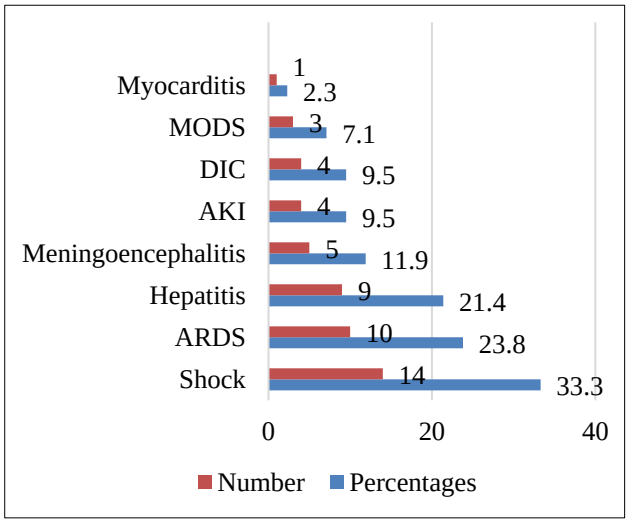

Figure 2: Complications of scrub typhus infection in children.

Table 4: Predictors of PICU admission (logistic regression model) in children with scrub typhus with or without need of intensive care.

Variables	Intensive care admission		Univariate analysis
	PICU-group (n=16)	Non-PICU group (n=26)	P value
Clinical signs			
Tachypnoea (14)	12	2	0.0001
CRT >3 seconds (13)	11	2	0.00032
Altered sensorium (15)	12	3	0.00031
SpO_2 <90% (7)	6	1	0.0044
Hepatomegaly (26)	10	16	0.950
Hypotension (9)	5	4	0.223
Laboratory investigations			
Anaemia (36)	11	25	0.013
Leucocytosis (28)	10	18	0.653
Thrombocytopenia (33)	10	23	0.046
Raised CRP (21)	15	6	0.0001
Raised SGOT/SGPT (10)	5	5	0.374
Hypoalbuminemia (12)	7	5	0.087
Hyponatremia (5)	3	2	0.282

Doxycycline is drug of choice given at dose of 4.4 mg/kg/day in two divided doses for 7 days intravenously. Azithromycin was also given in critically ill children. Doxycycline was given in all 42 cases and azithromycin was given in 16 cases. Rifampicin was added in those critical cases not responding to doxycycline. 32 children (77%) became afebrile within 48-72 hours after initiating doxycycline. The mean (SD) for defervescence after starting doxycycline was 2.32 (1.54) days.

Doxycycline is drug of choice given at dose of 4.4 mg/kg/day in two divided doses for 7 days intravenously. Azithromycin was also given in critically ill children. Doxycycline was given in all 42 cases and azithromycin was given in 16 cases. Rifampicin was added in those critical cases not responding to doxycycline. 32 children (77%) became afebrile within 48-72 hours after initiating doxycycline. The mean (SD) for defervescence after starting doxycycline was 2.32 (1.54) days.

A total of 39 (92.8%) patients had survived to discharge with case fatality rate of 7.1% (3). Out of 3 cases, two died due to severe ARDS, refractory shock, AKI and MODS and one died due to meningoencephalitis, septic shock and respiratory failure. 38 cases (90.4%) were discharged with complete recovery and one case had motor impairment and 6th nerve palsy as sequalae due to meningoencephalitis, ARDS, secondary HLH.

10-year-old girl with high grade fever for 7 days, vomiting, convulsion and altered sensorium at admission with signs of tachypnoea, shock (CRT >3 seconds), meningeal signs (neck stiffness and brudzinski sign) and hepatomegaly, admitted in paediatric ICU and in view of acute febrile encephalopathy, IgM-ELISA for scrub typhus was sent and tested positive. Laboratory findings at admission were Hb-9.2 gm/dl, wbc-22,000/mm^3, platelets-45000/mm3, CRP-200, Na+ 129 mEq/l, S. creatinine-1.7 mg/dl, SGOT-480 U/l, SGPT-120 U/l, albumin-1.9 gm/dl, bilirubin-2.2 mg/dl.

Blood gas analysis showed pao2/fio2=90, suggestive of severe ARDS for which started on invasive mechanical ventilation with IV fluids, inotropes support of noradrenaline and dobutamine for septic shock started. Antiepileptics given injection doxycycline (4.4 mg/kg/day bid) was given. CSF pleocytosis with lymphocytosis seen in CSF analysis. 3% NaCl infusion started in view of Meningoencephalitis with raised Intracranial tension. On 5th day she developed AKI and DIC (INR-2.1).

Injection vitamin K with FFP transfusion given. Injection azithromycin was also added. On further evaluation, she had pancytopenia, hypofibrinogenemia (120 mg/dl) with hyperferritinemia (657 ng/ml) and triglyceridemia (250 mg/dl). Diagnosis of hemophagocytic lymphohistiocytosis (HLH) secondary to scrub typhus was made. She was discharged from ward after 20 days and referred to rehabilitation centre for sequalae of motor impairment, speech difficulty, 6th nerve palsy, respiratory illness.

DISCUSSION

Scrub typhus is presenting as acute febrile illness with or without eschar and its outbreak was reported from Mewar region of Rajasthan, in 2019.[14] Since then, there have been annual outbreaks affecting children during the monsoon and post-monsoon months with the most affected districts of Mewar region being Dungarpur, Rajsamand, Chittorgarh, Banswara, Bhilwara, Pratapgarh and rural Udaipur. A study by Vyas et al, from Rajasthan denoted that scrub typhus is common in adults of Mewar region and should be considered as differential diagnosis with high index of suspicion, as early diagnosis may reduce mortality.[14] Early diagnosis of scrub typhus is challenging due to its overlapping clinical features with many other tropical fevers such as dengue, malaria, typhoid, viral encephalitis and viral hepatitis.[15] Vasculitis is basic mechanism in scrub typhus. When bacteria invade endothelial cells, it produces disseminated vasculitis, causing microvascular leakage, perivascular inflammation, edema, tissue hypoperfusion and end-organ ischemic injury.[15] Despite the severity of illness and high prevalence of multiorgan failure, early treatment with doxycycline and supportive care had shown favourable results.

It is a retrospective descriptive study similar to other Indian studies by Nallasamy et al, Muthukrishnan et al, Behera et al, Masand et al, Shrikiran et al, Loganathan et al, whereas studies were commonly prospective.[3,5,7,16-20] Mean age at presentation was 10.5±3.2 years (range 1-18 years) which was higher than that of other studies.[3,6] Female preponderance (F:M ratio=1.21:1) seen in our study was not consistent with other Indian studies.[3,17] Incidence was higher in adolescent female due to their activities under cattle shed rearing livestock. A study from Nepal also noted female preponderance.[20] M: F ratio of 1:1 was seen in study by Muthukrishnan et al.[7] In this study we observed clustering of cases in monsoon followed by post-monsoon months trends similar to other studies.[7,17] Children presented from adjoining districts of Mewar region showing both forest exposure, growth of secondary vegetations (scrubs) in rainy season and rural habitat as risk factor.

In concordance to a study from north India, the median (IQR) duration of hospital stay was 7 (5-8 days) with a range of 4 to 20 days.[3] 58% presented with fever for more than 7 days. In a study from south India by Aroor et al, 62.5% had fever >7 days and in a study by Kumar et al, 60% had fever for 7-14 days prior to admission.[6,21] Fever at presentation was high grade (>101'F) in 90% children in our study which was 89% in a south Indian study.[7]

Vomiting (62%), cough-cold (42.8%), myalgia (40.4%), breathlessness (31%), abdominal pain (23.8%) and headache (16.6%) were common symptoms in our study. A study from south India, Pondicherry by Kumar et al, also reported these symptoms in 49%, 51%, 26%, 37%, 34% and 11% respectively.[21]

Table 5: Comparative analysis of complications with previous Indian studies.

Authors	Bhat et al[19]	Kabiraj et al[5]	Kumar et al[21]	Behera et al[16]	Masand et al[17]	Aroor et al[6]	Nallasamy et al[3]	Muthukrishnan et al[7]	Present study
Sample size	66	487	35	374	30	88	160	84	42
Place of study	Dehradun	West Bengal	Pondicherry	Odisha	Rajasthan	Karnataka	Chandigarh	Chennai	Rajasthan
Year	2011-2012	2018-2021	2010-2011	2016-2019	2013	2018-2019	2013-2015	2012-2019	2023-2024
Age range	8 months-18 years	1 month-12 years	1.5-12 years		3-16 years	0.9 months-12 years	3 months-12 years	1 month-18 years	1-18 years
Mean age, years (SD)	8.8	5.61 (3.58)	6.3	6.4 months (3.6)	8.56 (3.43)	7.2 (4.5)	6.8 (3.2)		10.5 (3.2)
Study design	Prospective	Prospective	Prospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Complications, %									
ARDS	12.1	5.5	9	11.76	6.6	12.5	11	16	23.8
Shock	25.8	26.07		11.76		37.5	17	30	33.3
Hepatitis	13.6	78.6	31	63.6	60	100	4		21.4
AKI	16.7	24.4	20	65.8	3.3	6.25	16	11.3	9.5
Myocarditis	9	13.7	34	75		12.5	3		2.3
Meningoencephalitis	30.3	16.2	6	20.5		37.5	29	11.3	11.9
MODS		8.48		11.76		6.25		6.4	7.1
DIC	1.5	2.2	9			6.2	13	3.2	9.5
Anemia	62	87.6		80	60	40.9	45		85.7
Thrombocytopenia	53	77.4	61	50	26	54.5	82.5	27.3	78.5
Mortality	7.5	5.54	2.8	0	6.6	2.2	8.8	5	7.1

ARDS-Acute respiratory distress syndrome, AKI-acute kidney injury, MODS-multisystem organ dysfunction, DIC-disseminated intravascular coagulation

Oliguria and pedal edema observed in 16.6% and 23.8% in the present study and other studies have reported their higher incidence.[19,21] Conjunctival redness seen in 11.9% children in our study was seen in 13% children in a study from Chandigarh.[3] Altered sensorium and convulsions present in 35.7% (15) and 11.9% (5) in our study compared to 24% and 26% in a study by Nallasamy et al.[3] Presence of eschar and rash which is considered specific, was present in only 7.1% (3) cases each in present study which is similar to an earlier study from Rajasthan by Masand et al (eschar in 3.3% and rash in 10%).[17] The reported incidence for eschar varied from 11 to 80% in most case series.[4-7] Variation in cutaneous immunity has been suggested as one of the reasons for absent eschar, however it can be easily missed if not examined carefully.[17] Absence of lymphadenopathy and presence of eschar and rash in only 3 cases was unusual. This is similar to a Thai study which reported absence of lymphadenopathy and eschar in their cases.[22]

Laboratory findings was anemia in 85.7% cases and thrombocytopenia in 78.5% cases. This finding was almost consistent with studies done by other authors.[17,19] In about half it was severe thrombocytopenia (below 50,000 cells/mm3). In previous studies, the incidence of anemia has ranged from 41 to 87 % and thrombocytopenia has ranged from 26 to 83% (Table 4). Hepatitis with three times raised transaminases seen in 21.4% cases in the present study ranges from 13.6% to 78.6% in previous studies.

Tachypnoea, CRT >3 seconds and SpO_2 <90% and altered sensorium were significant clinical findings and anemia, thrombocytopenia and raised CRP were significant laboratory parameters while comparing PICU and non-PICU group ($p<0.05$) (Table 5). Hence these parameters are indicators for the need of intensive care admission. A retrospective observational study conducted by Nallasamy et al from Chandigarh, India also observed the presence of lymphadenopathy, respiratory distress, shock, altered sensorium and thrombocytopenia as independent predictors for need of PICU.[3] Although leucocytosis was not found statistically significant but there was trend towards higher leucocytes counts in intensive care group. Behera et al in his study in infants also reported thrombocytopenia as significant indicators of PICU admission, although hypoalbuminemia and transaminitis significant in his study were not significant in the present study.[16] CSF analysis revealed lymphocytic pleocytosis with mean cells 28±9 cells/mm^3 consistent with reports of other studies.[19] Hypoalbuminemia, hyperbilirubinemia and hyponatremia was found in 28.5%, 11.9% and 11.9% cases in present study, which is lesser than other studies.[5,21]

A study from Vellore, India concluded that ARDS remains dreaded complication in children.[18,23] ARDS due to interstitial pneumonitis and non-cardiogenic pulmonary edema driven by vasculitis is peculiar feature of scrub typhus which help to discriminate it from other undifferentiated fever.[23] According to previous study by Muthukrishnan et al from Chennai, ARDS and shock was reported in 16% and 30% children among 84 cases.[7] Shock was most common complication present in 14 (33.3%) cases in this study and sepsis was aggravating factor causing vasculitis, tissue hypoperfusion and end organ ischemic injury. A study from West Bengal, India by Kabiraj et al reported shock in 26% cases and gangrene in 1% cases.[5] Gangrene was not seen in any case in present study. Encephalitic presentation has been increasingly recognised in recent literature with reported incidence ranging from 6% to 37.5% (Table 4). In this study meningoencephalitis reported in 5 (11.9%) cases and they underwent CSF examinations showing CSF pleocytosis with 85% lymphocytes. Scrub typhus was found to be a major aetiology of acute encephalitis syndrome (AES) in previous studies.[6,19]

All of our patients received doxycycline and the mean (SD) for defervescence after starting doxycycline was 2.32 (1.54) days, a trend similar to other studies.[21,24] In a retrospective study by Loganathan et al from Vellore, 10 required non-invasive ventilation, 9 were delivered continuous positive pressure ventilation via nasal cannula, 14 were started on humidified high-flow oxygen.[18] Non-invasive respiratory support (NRS) work by stabilizing chest wall, maintaining functional residual capacity (FRC) to prevent atelectasis and maintain patency of airways. NRS helps to avoid complications such as ventilator-induced lung injury, infections and airway edema.[25] In the present study, non-invasive support was required in 4 (9.5%) cases in the form of positive pressure ventilation via BiPaP in one case, oxygen via face mask in one case and non-rebreathing mask in 2 cases. Non-rebreathing mask delivers 60-100% FiO_2 at 10-15 l/min oxygen flow.

Though rare, secondary hemophagocytic lympho-histiocytosis (HLH) has been reported as well recognized complication of scrub typhus in children.[26] Only one child in our study was diagnosed with HLH secondary to scrub typhus and was discharged with sequalae. The case-fatality rate in the present study was 7.1%. ADEM was also reported as complication of scrub typhus in a recent study from India.[27] Mortality from paediatric scrub typhus has ranged from 2.2% to 11% in previous Indian reports as shown in Table 5.

CONCLUSION

This study concluded that scrub typhus is re-emerging as acute febrile illness in children of Rajasthan and is typically underdiagnosed. This differential should be kept in mind by clinicians. The present study found that disease is more prevalent in female gender with age group of ten to eighteen years. Shock and ARDS were common complications. Due to limited recognizance, low index of suspicion among clinician and lack of diagnostic facilities most cases were referred from primary health centre (PHC) at late stage, which leads to complications.

Suggestions that can be made are ensuring the availability of testing (IgM against *O. tsutsugamushi*) in all health care facilities, prompt referral following administration of first dose of anti-scrub medications, environmental modification strategies, vector control measures and investing in vaccine research.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Jeong YJ, Kim S, Wook YD, Lee JW, Kim KI, Lee SH. Scrub typhus: clinical, pathologic, and imaging findings. Radiographics. 2007;27(1):161-72.
2. Lalchhandama K. Orientia tsutsugamushi, the agent of scrub typhus. Wiki J Med. 2019;6(1):1-2.
3. Nallasamy K, Gupta S, Bansal A, Biswal M, Jayashree M, Zaman K, et al. Clinical profile and predictors of intensive care unit admission in paediatric scrub typhus: a retrospective observational study from North India. Indian J Crit Care Med. 2020;24(6):445.
4. Goswami D, Hing A, Das A, Lyngdoh M. Scrub typhus complicated by acute respiratory distress syndrome and acute liver failure: a case report from Northeast India. Int J Infect Dis. 2013;17(8):e644-5.
5. Kabiraj B, Saha S, Maiti S, Sit SP, Pal AC. A study on clinical spectrum, complications and outcome of scrub typhus infection in children admitted in pediatric department of a tertiary care hospital in West Bengal, India. International Journal of Contemporary Pediatrics. 2022 Oct;9(10):927
6. Aroor S, Mundkur S, Kumar S. Clinical profile and predictors of severity in children with scrub typhus admitted to paediatric intensive care unit. Int J Contemp Pediatr. 2023;10(7):1027-32.
7. Muthukrishnan K, Tarikere S, Sivaraman RP, Sankaranarayanan S, Prabaharan K, Kothandam BT. Clinical profile and predictors of outcome for pediatric scrub typhus at a tertiary care hospital. Arch Pediatr Infect Dis. 2021;9(1).
8. Thangaraj JW, Mittal M, Verghese VP, Kumar CG, Rose W, Sabarinathan R, et al. Scrub typhus as an etiology of acute febrile illness in Gorakhpur, Uttar Pradesh, India, 2016. Am J Trop Med Hygiene. 2017;97(5):1313.
9. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (Orientia tsutsugamushi). PLoS Negl Trop Dis. 2015;9(8):e0003971.
10. Todarwal R. Flora of Aravalli Range in Rajasthan. Flora. 2022;9(5).
11. Khandelwal S, Meena JK, Sharma BS. Scrub typus in children: clinical profile and complications. Pediatr Oncall J. 2015;12(4):95-8.
12. Kogan A, Segel MJ, Ram E, Raanani E, Peled-Potashnik Y, Levin S, et al. Acute respiratory distress syndrome following cardiac surgery: comparison of the American-European consensus conference definition versus the Berlin definition. Respiration. 2019;97(6):518-24.
13. Sethi SK, Bunchman T, Chakraborty R, Raina R. Pediatric acute kidney injury: new advances in the last decade. Kidney Res Clin Pract. 2021;40(1):40.
14. Vyas A, Lakum A, Bansal A, Sharma A. Outbreak of Scrub typhus in Mewar Region. Global J Res Analysis. 2020;9(12):2277-8160.
15. Rathi NB, Rathi AN, Goodman MH, Aghai ZH. Rickettsial diseases in central India: proposed clinical scoring system for early detection of spotted fever. Indian Pediatr. 2011;48:867-72.
16. Behera JR, Sahu SK, Mohanty N, Mohakud NK, Lal A. Clinical manifestations and outcome of scrub typhus in infants from Odisha. Indian Pediatr. 2021;58(4):367-9.
17. Masand R, Yadav R, Purohit A, Tomar BS. Scrub typhus in rural Rajasthan and a review of other Indian studies. Paediatr Int Child Health. 2016;36(2):148-53.
18. Loganathan SK, Jaybhaye A, Dash N, Punnen A, Ghosh U, Rose W. Acute respiratory distress syndrome in paediatric scrub typhus. Trop Doctor. 2021;51(4):514-7.
19. Bhat NK, Dhar M, Mittal G, Shirazi N, Rawat A, Kalra BP, et al. Scrub typhus in children at a tertiary hospital in north India: clinical profile and complications. Iranian J Pediatr. 2014;24(4):387.
20. Bajracharya L. Scrub typhus in children at Tribhuvan University teaching hospital in Nepal. Pediatr Health Med Therap. 2020;193-202.
21. 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 Infect Public Health. 2012;5(1):82-8.
22. Sirisanthana V, Puthanakit T, Sirisanthana T. Epidemiologic, clinical and laboratory features of scrub typhus in thirty Thai children. Pediatr Infect Dis J. 2003;22(4):341-5.
23. Force AD, Ranieri VM, Rubenfeld GD, Thompson B, Ferguson N, Caldwell E, et al. Acute respiratory distress syndrome. JAMA. 2012;307(23):2526-33.
24. Palanivel S, Nedunchelian K, Poovazhagi V, Raghunadan R, Ramachandran P. Clinical profile of scrub typhus in children. Indian J Pediatr. 2012;79:1459-62.
25. Gupta S, Bansal A, Biswal M, Jayashree M, Zaman K, et al. Clinical profile and predictors of intensive care unit admission in paediatric scrub typhus: a retrospective observational study from North India. Indian J Crit Care Med. 2020;24(06):445-50.
26. 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.

27. Jana JK, Mandal AK, Gayen S, Mahata D, Mallick MS. Scrub typhus in children: A prospective observational study in a tertiary care hospital in Eastern India. Cureus. 2023;15(7):e41976.

Cite this article as: Vaishnav P, Shivpuri D. Clinical profile, complications, outcome and predictors of intensive care for paediatric scrub typhus: a tertiary hospital-based study from southern Rajasthan, India. Int J Contemp Pediatr 2024;11:1209-17.