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Original Research Article

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

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ABSTRACT

Background: Scrub typhus is an important emerging etiology of febrile illnesses. Most of the studies of scrub typhus in literature have been carried out in adult population. The objective of the study is to obtain data on clinical spectrum, complications and outcome of scrub typhus infection in pediatric patients.
Methods: This is a descriptive observational study, that includes 487 scrub typhus IgM ELISA positive children, conducted over a period of 36 months at Bankura Sammilani medical college and hospital, Bankura- a tertiary care government hospital in southern part of West Bengal. Data were collected in predesigned case record proforma and then analysed.
Results: Highest number of cases were found among 2 to 6 years age group with male predominance, mostly from rural area and during the monsoon season. Fever, rash, headache, vomiting, cough-cold, myalgia, diarrhoea and body swelling were main presenting complaints. Hepatomegaly, lymphadenopathy, splenomegaly, eschar, pallor, edema were main examination findings. Anaemia, thrombocytopenia, leucocytosis, transaminitis were the important laboratory findings. Important complications were- hepatitis, bronchopneumonia, meningoencephalitis, pleural effusion, shock, myocarditis, acute kidney injury, respiratory failure, ARDS, MODS etc. Both azithromycin and doxycycline were effective for treatment of scrub typhus infection. Overall mortality was noted in 7.80%.
Conclusions: Scrub typhus is an important re-emerging etiology of febrile illnesses in children. So, it should be kept in differentials of acute undifferentiated febrile illness in children. If diagnosed early, it is easy to treat with azithromycin and/or doxycycline and complications and mortality can be minimized significantly.

Keywords: Children, Clinical spectrum, Scrub typhus, West Bengal

INTRODUCTION

Scrub typhus is an acute undifferentiated febrile illness endemic in wider areas of South and South East Asia, the Asian Pacific Rim, and Northern Australia ("tsutsugamushi triangle"). Over one billion people are under the risk of acquiring the infection, and on an average one million cases are being reported every year from these regions.[1] It is also known as bush typhus or tsutsugamushi disease. Japanese word "tsutsuga" (dangerous) "mushi" (bug) is an obligate intracellular gram-negative bacterium- Orientia tsutsugamushi, which is transmitted by trombiculid mite i.e., chiggers.[2] The mites act as reservoir of the bacteria by transovarial and transstadial transmission. Humans are the accidental host, whereas rodents are the natural as well as the reservoir host for O. tsutsugamushi.[3] In humans, the infection may manifest as self-limiting disease to fatal illness in 30%-

70% of cases, with multiorgan dysfunction.[4] There is re-emergence of scrub typhus infection in India with first case detected in Kerala in 2009.[5] Due to lack of awareness, low index of suspicion among clinicians, unavailability of confirmatory diagnostics and non-specific clinical features, it mimics other common diseases such as dengue, malaria and leptospirosis. Scrub typhus remains under-diagnosed especially in children. Most of the studies in the literature have been done among adult patients and there is paucity of data of scrub typhus infection among pediatric population. For this reason, this study was done to obtain information on this relatively neglected domain in children.

METHODS

This is a descriptive observational study done over a period of 36 months from August 2018 to July 2021 in Bankura Sammilani Medical College and Hospital, Bankura, a rural based tertiary care government teaching hospital in the southern part of West Bengal, India.

Inclusion criteria

Inclusion criteria for current study were; acute febrile illness of atleast five days duration, age one month to twelve years were included in this study, scrub typhus Serum IgM report positive, guardian gave consent to be a part of the study.

Exclusion criteria

Exclusion criteria for current study were; age less than one month and above twelve years of age, history of fever less than five days, scrub typhus serum IgM negative report, immunocompromised children, neurodegenerative disorder and major congenital anomaly cases, left hospital against medical advice or lost to follow up and not gave consent to be included in the study.

Total 487 Scrub typhus IgM ELISA positive children were included in this study. Malaria, typhoid, dengue, leptospirosis and urinary tract infection cases were excluded by history, clinical examination and laboratory reports. The cases were investigated with the following tests as per need- Complete blood count, erythrocyte sedimentation rate, Malaria slide test and dual antigen, Widal test, Scrub typhus IgM, Dengue NS1 and IgM, Tuberculin test, blood and urine culture and sensitivity test, liver function and kidney function test, serum electrolytes, chest X-ray. Leptospira IgM and HIV-ELISA were done where clinically indicated. Cardiac evaluation including echocardiography and cerebrospinal fluid (CSF) study and neuroimaging was performed for selected cases with suspected myocarditis or meningoencephalitis respectively. Case details recorded in predesigned proforma and then analysed. Written consent was taken from guardian of all the children.

RESULTS

Total 487 scrub typhus positive cases documented from August 2018 to July 2021. Among which 65.70% (N=320) cases were male and 34.29% (N=167) were female. Minimum age of the scrub typhus positive case was 57 days with mean age 5.61±3.58 years. Highest number of cases found in 2 to 6 years age group 43.53% (N=212), followed by 6 to 12 years group 38.39% (N=167).

Table 1: Age and gender-based distribution of scrub typhus cases (n=487).

Gender	Age range in years (%)			
	0-2 (%)	>2-6 (%)	>6-12 (%)	Total N (%)
Male	57	139	124	320 (65.70)
Female	31	73	63	167 (34.29)
Total N (%)	88 (18.06)	212 (43.53)	187 (38.39)	487

Mean duration of illness during hospitalisation was 6.35±2.73days. Most of the cases were from rural areas-83% and 17% from urban areas. Majority of cases reported during the monsoon-63% case, followed by post monsoon- 27% and premonsoon-10% cases.

Table 2: Duration of fever during hospitalisation.

Duration of fever during admission (days)	N (%)
<7	51 (10.47)
≥7-10	335 (68.78)
>10	101 (20.73)

Total 68.78% (n=335) children admitted in between 7th to 10th day of their febrile illness, followed by 20.73% (N=101) cases after 10th day and 10.47% (N=51) cases admitted before 7th day of fever (Table 2).

Table 3: Symptoms in scrub typhus infection.

Symptoms	N (%)
Fever	487 (100)
Cough-cold	382 (78.44)
Headache	322 (66.11)
Myalgia	293 (60.16)
Body swelling	272 (55.85)
Vomiting	259 (53.18)
Diarrhoea	111 (22.79)
Shortness of breath	103 (21.15)
Maculopapular rash	94 (19.30)
Reduced urine	53 (10.88)
Convulsion	47 (09.65)
Bleeding	35 (07.18)
Arthralgia	05 (01.02)

Chronologically most common presenting symptoms were fever (100%), cough-cold (78.44%), headache (66.11%), myalgia (60.16%), body swelling (55.85%), vomiting (53.18%) (Table 3). Some less frequent presenting complaints were diarrhoea (22.79%), shortness of breath (21.15), maculopapular rash (19.30%), reduced urine volume (10.88%), convulsion 9.65% (N=47), bleeding 7.18% (N=35) and arthralgia 1.02% (N=5).

Table 4: Signs in scrub typhus infections.

Signs	N (%)
Hepatomegaly	437 (89.73)
Lymphadenopathy	381 (78.23)
Pallor	362 (74.33)
Splenomegaly	329 (67.55)
Edema and facial puffiness	304 (62.42)
Eschar	217 (44.56)
Altered sensorium	179 (36.75)
Petechiae/purpura	131 (26.89)
Meningeal sings	84 (17.24)
Icterus	76 (15.60)
Gangrene	5 (1)

The most common clinical signs chronologically were hepatomegaly in 89.73% (N=437), lymphadenopathy in 78.23% (N=381), pallor in 74.33% (N=362), splenomegaly in 67.55% (N=329), edema and facial puffiness in 62.42% (N=304), eschar in 44.56% (N=217), altered sensorium in 36.75% (N=179), petechiae/purpura in 26.89% (N=131), meningeal signs in 17.24% (N=84), icterus in 15.60 (N=76) and gangrene of digits and ear lobule noted in 5 children only (Table 4). Anaemia in 87.68% (N=427), leucocytosis in 78.23% (N=381), thrombocytopenia in 77.41% (N=377), twice raised liver enzymes in 57.28% (N=279), Hyponatremia in 37.16% (N=181), Hypoalbuminemia in 31.41% (N=153), CSF pleocytosis in 28.54% (N=139) with 85% lymphocytes, raised plasma creatinine in 24.84% (N=121) and hyperbilirubinemia in 23.61% (N=115) cases (Table 5).

Table 5: Laboratory parameters of scrub typhus infection in children.

Laboratory parameters	N (%)
Anaemia (<11 gm/dl)	427 (87.68)
Leucocytosis (>11000/mm³)	381 (78.23)
Thrombocytopenia (<1.5 Lk/mm³)	377 (77.41)
Raised creatinine (>1.5 mg/dl)	121 (24.84)
Four times raised liver enzymes (AST and ALT) (Normal=35- 45 U/lt)	279 (57.28)
Hypoalbuminemia (<2.5 mg/dl)	153 (31.41)
Hyperbilirubinemia (>1.5 mg/dl)	115 (23.61)
Hyponatremia (<135 meq/lt)	181 (37.16)
CSF Pleocytosis	139 (28.54)

Table 6: Laboratory values of scrub typhus cases.

Laboratory parameters	Value (mean±SD)
Haemoglobin (g/dl)	8.7±4.2
Total Leucocytes(cells/mm³)	9721±6325
Platelets (cells/mm³)	121751±90253
Serum Urea (mg/dl)	39.3±24.7
Serum Creatine (mg/dl)	0.85±0.76
Aspartate aminotransferase (AST) (Unit/lt)	369.73±291.59
Alanine aminotransferase (ALT) (Unit/lt)	327.57±301.34
Serum Albumin (mg/dl)	2.45±0.97
Total Bilirubin (mg/dl)	1.9±1.5
Serum Sodium (mmol/lt)	127.21±26.37
CSF cell count (cells/mm³)	38±9

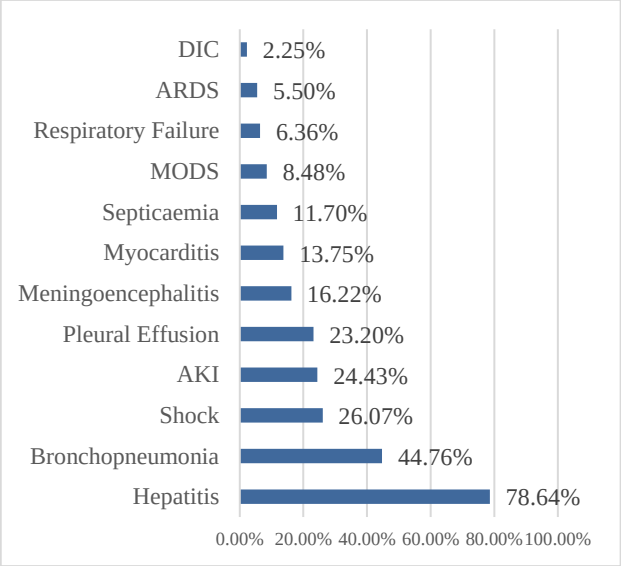

Figure 1: Complications of scrub typhus infection in children.

Mean values of various laboratory parameters found in this study: Hb 8.7±4.2 gm/dl, TLC 9721±6325 cell/mm³, platelets 121751±90253 cells/mm³, serum urea 39.3±24.7mg/dl, serum creatinine 0.85±0.76mg/dl, AST 369.73±291.59 U/Lt, ALT 327.57±301.34 U/Lt, serum albumin 2.45±0.97 mg/dl, total bilirubin 1.9±1.5 mg/dl and serum sodium 127.21±26.37 meq/Lt (Table 6).

Total 43% children were treated with Doxycycline and 67% with Azithromycin. Other antibiotics were also used as and when necessary, on case-to-case basis depending on clinical profile and laboratory parameters. 31.42% (N=153) children needed PICU care. Mechanical ventilation was needed in 7.18% (N=35) and 14.57% (N=71) cases needed inotrope support for treating fluid refractory shock.

Antiepileptics, packed red blood cells and fresh frozen plasma used in cases as per need. Average duration of

hospital stay was 8.63±3.51 days with minimum 5 days and maximum 19 days. Overall mortality of scrub typhus found 5.54% (N=27). Most common complications culminating to death were septic shock, meningoencephalitis, multiorgan dysfunction syndrome (MODS), acute respiratory distress syndrome (ARDS) and disseminated intravascular syndrome (DIC).

DISCUSSION

Scrub typhus is an endemic, re-emerging vector-borne gram negative bacterial illness contributing to 50% of the acute undifferentiated febrile illness reported from many parts of India.[6-9] It is a potentially fatal infection that affects about one million people every year worldwide.[10] It was found to be a major etiology of AES reported from Gorakhpur, UP (63%), and Assam (20%).[11,12] This is an important public health problem in West Bengal as well. This study has been conducted in scrub typhus IgM ELISA positive pediatric cases in pediatric ward and PICU. Vasculitis is the basic pathogenic mechanism in scrub typhus infection and responsible for skin rash, microvascular leakage, edema, tissue hypoperfusion and end organ ischemic injury.[13]

Knowledge of clinical profile of pediatric scrub typhus cases will help the clinician to- identify the suspected scrub typhus cases at the earliest, detect patients with higher risk of needing intensive care and monitor them closely for the early identification of fatal complications and reduce the morbidity and mortality by providing appropriate treatment at time. In this study there were more male children 65.70% (N=320) than female 34.29% (N=167) with male to female ratio 1.91:1, which may be due to higher exposure of boys to chiggers due to their more outdoor activities. This finding is consistent with other researchers.[14-19]

Highest number of cases were found in 2 to 6 years age group 43.53% (N=212), followed by 6 to 12 years group 38.39% (N=167). Minimum age of the scrub typhus positive case was 57 days. Mean age at presentation found 5.61±3.58 years, which is lower than that of other researchers.[16,18] Majority of the cases reported during the monsoon- 63% case, followed by post monsoon- 27% and premonsoon- 10% cases. This finding is similar to many other authors.[16-24] Most of the cases were from rural areas- 83% and 17% cases from urban areas, that is similar to reports by other researchers.[25,26]

Mean duration of illness during hospitalisation was 6.35±2.73days. Majority of the cases 68.78% (N=335) admitted in between 7th to 10th day of their febrile illness.[25] Clinical presentation of scrub typhus is non-specific, so there is high chance of positive cases being missed and often misdiagnosed. Fever was present in 100% cases, that is similar to most of the studies by other researchers.[26,27] Cough-cold found in 78.44% which is nearly similar to study by Rakholia, et al.[28]

In this study headache and myalgia noted in 66.11% and 60.16%, that is considerably higher than that reported by Nowneet et al, Navneet et al but lower than that reported by Rakholia et al.[26-28]

Body swelling and vomiting was found in 55.85% and 53.18% cases respectively that is consistent with the above researcher but much higher than another researcher.[28] In this study maculopapular rash detected in 19.30%, shortness of breath in 21.15, reduced urine volume in 10.88%, convulsion in 9.65%, bleeding in 7.18% and arthralgia in 1.02% cases. All the finding are at per with the reports of other researchers, except reduced urine volume and arthralgia, which found lesser in this study than other authors.[16,25,29-31]

An Eschar, which is a pathognomonic sign of scrub typhus infection found in 44.56% cases in this study. Similar findings reported by many previous studies, and much higher occurrence of eschar reported by some other researchers.[6,16,25,29,30-33]

Hepatomegaly (89.73%), lymphadenopathy (78.23%), pallor (74.33%) and splenomegaly (67.55%) were the common findings in this study. Other studies reported varied occurrence of hepatomegaly (26%-98%) and splenomegaly (17%-88%).[34-36] Anaemia noted in 87.68% cases which is much higher than other authors.[27,37] Thrombocytopenia detected in 77.41% cases, which is much higher than other researchers.[16,21,34-36]

Hepatitis noted in 78.64% cases while four times raised liver enzymes were seen in 57.28% children, which is almost consistent with studies done by other authors.[26,28] Hyperbilirubinemia, hypoalbuminemia, hyponatremia was recorded in 23.61%, 31.41% and 37.16% cases in this study same results were 42%, 20% and 16% in another study.[26] CSF analysis revealed lymphocytic (85%) pleocytosis with mean cells 38±9 cells/mm^3, resembling viral or aseptic meningitis, consistent with reports of another study.[38]

Scrub typhus infection is considered as a potentially life-threatening illness in children. Most of the complications develop in the second week of the disease. When bacteria invade endothelial cells, it produces disseminated vasculitis and perivascular inflammatory lesions. Vasculitis leads to significant micro vascular leakage, edema, tissue hypoperfusion and ensure end-organ ischemic injury.[13]

Most important complications found in our study were hepatitis, bronchopneumonia, septic shock, acute kidney injury (AKI), meningoencephalitis, myocarditis, multiorgan dysfunction syndrome (MODS), acute respiratory distress syndrome (ARDS) and disseminated intravascular coagulation (DIC) etc. Gangrene of ear lobules, pinna and digits were found in five children.

Table 7: Comparison of various complications found in the current study and previous studies.

Complications (%)	Current study	Behera et al.[25]	Kumar et al.[16]	Bhat et al.[27]	Bajracharya et al.[31]	Pathak et al.[30]	Gupta et al.[29]
Hepatitis	78.64	61.76	31	13.6	59.5	34.2	8
Pneumonia	44.76	52.9	3	10.6	25	--	--
Shock	26.07	11.76	--	25.8	--	--	6.7
AKI	24.43	65.8	20	16.7	14.3	65.8	6.7
AMES	16.22	20.58	17	30.3	34.5	14.5	14.7
Myocarditis	13.75	75.4	34	9.1	40.5	72.4	1.3
MODS	8.48	11.76	--	--	19	3.9	--
Respiratory Failure	6.36	--	--	12.1	--	--	--
ARDS	5.50	11.76	9	12.1	15.5	--	9.3
DIC	2.25	--	9	1.5	5.9	--	--
Gangrene	1	--	3	--	--	3.9	--
Death	5.54	0	2.8	7.5	4.8	3.9	--

Limitations

As this is a hospital based, single centred, small scale study involving cases of a particular age group; findings of this study may not be extrapolated to the whole population.

CONCLUSION

In a child with acute febrile illness with maculopapular rash, hepatosplenomegaly, lymphadenopathy, features of capillary leakage and encephalopathy and/or encephalitis and some non-specific features, we must consider scrub typhus infection in the differential diagnosis. An eschar supports the diagnosis. Hepatitis, pneumonia, shock, meningoencephalitis and acute kidney injury are the common complications. In suspected scrub typhus cases, empirical treatment should be started immediately with azithromycin or doxycycline, as delay in initiation of treatment may cause life threatening complications. Therefore, increasing awareness of early diagnosis and treatment will help to decrease mortality and improve prognosis in pediatric age group.

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