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Original Research Article

A study on clinico-epidemiological profile of scrub typhus in rural Bengal and therapeutic response to known drugs

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ABSTRACT

Background: Scrub typhus is an important cause of fever in South and East Asia and the Pacific, but is grossly underdiagnosed due to lack of awareness. This was a prospective observational study to study the clinical profile of scrub typhus in paediatric population in a tertiary care hospital in Rural Bengal of Malda district.
Methods: The study was conducted from May 2021 to November 2021 among children presenting to OPD and admitted in IPD of Malda Medical College and Hospital in the Deparment of Paediatrics. Children under the age of 12 years presenting with signs and symptoms suggestive of scrub typhus were included in this study and serological diagnosis was confirmed by Scrub IgM ELISA with a positive titre >0.5.
Results: Out of the 178 cases enrolled in our study, 136 were confirmed positive by ELISA. All the cases were admitted with fever (100%), other symptoms were vomiting (77.9%), cough (68.3%), abdominal pain (57.3%), maculopapular rash (52.9%), headache (49.2%), myalgia (41.1%), oedema (30.8%), conjunctival congestion (23.5%). Hepatomegaly (91.1%), splenomegaly (83.8%) and lymphadenopathy (75%) were the most common signs. Oral doxycycline in doses of 5 mg/kg/day in 2 divided doses were given in half the cases (68) and azithromycin (10 mg/kg/day) were given in 34 cases, while 34 cases were given oral chloramphenicol (75 mg/kg/day). Doxycycline and chloramphenicol were equally effective with defervescence in maximum cases within 48 hrs. Azithromycin response was poor with fever persisting in 80% cases after 48 hrs.
Conclusions: Scrub typhus must be included in the differential diagnosis of acute febrile illness in children with or without eschar for its early detection and prompt treatment leading to favourable outcome. Doxycycline or Chloramphenicol were equally effective in treatment while Azithromycin showed poor response.

Keywords: Scrub typhus, Prevalence, Rural Bengal, Antibiotic response

INTRODUCTION

The causative organism of scrub typhus is *Orientia tsutsugamushi*, which is distinct from other spotted fever group and typhus group rickettsiae. It is transmitted by the bite of the larval stage (chigger) of a trombiculid mite. The mite acts both as vector and reservoir. Transovarial transmission of the organism occurs in the mite. After entry into the host organism it infects the endothelial cells and causes vasculitis which is the predominant clinicopathological feature of the disease. End organ damage resulting from the vascular compromise most commonly manifests in the brain and the lungs.[1]

The disease is characterised by diverse clinical manifestations ranging from a mild self-limiting state to variable severity like acute respiratory distress syndrome (ARDS), meningoencephalitis, acute kidney injury (AKI), myocarditis leading to heart failure, hepatitis, and multi organ dysfunction (MOD). A late presentation, delay in diagnosis and treatment causes overall 11.1% deaths in children below 10 years because of low index of

suspicion,and non-specificity of signs and symptoms.[2] Recently majority of the cases in frequently occurring acute encephalitis syndrome (AES)/JE outbreaks in Gorakhpur among children less than 15 years have been reported to be due to scrub typhus.[3,4] The study was conducted to evaluate the varying clinical profile, complications and outcome of serologically confirmed scrub typhus cases at a tertiary care medical college in rural Bengal.

METHODS

The study was conducted in department of paediatrics, Malda medical college located in rural Bengal setting over a period of 7 months in the rainy season from May to November 2021. Children with fever >5 days and sign symptoms suggestive of scrub typhus were enrolled in the study. Out of total 178 child included in the study, 136 were found positive. Serological diagnosis was confirmed by immunoglobulin (IgM) ELISA technique.

Titre >0.5 was taken as positive and <0.5 was considered negative. Clinical presentation, laboratory findings, complications and outcome of the enrolled cases were recorded on Microsoft excel sheet. Data regarding age, sex, residence and history of going to fields were recorded and thorough search for eschar was done in all cases. MPDA (malaria dual antigen), typhi dot IgM, dengue serology (IgM, IgG) and blood/urine cultures were sent to exclude other infections. Complete blood count, chest X-ray, LFT, RFT, Urine R/E, M/E, C/S and electrolyte study were sent for confirmed cases. ECHO was done for suspected myocarditis cases and CSF study was sent for meningoencephalitis cases. 7 days course of antibiotics (doxycycline 5 mg/kg/day or azithromycin 10 mg/kg/day, or chloramphenicol 75 mg/kg/day) were given in all confirmed scrub typhus cases.

RESULTS

Out of the 178 cases enrolled in our study, 136 were confirmed positive by ELISA. 76 were male (55.88%) and 60 were female. All the cases were from rural areas, 60 from Malda district, 34 from North Dinajpur, 26 from South Dinajpur, 16 from Jharkhand. Age of the cases ranged from 7 month to 12 years with mean being 73.6 months. Most of the cases were from Malda district (44.1%), followed by North Dinajpur (25%), South Dinajpur (19%) and Jharkhand (11.7%). All the cases were admitted with fever (100%), followed by vomiting (77.9%), cough (68.3%), abdominal pain (57.3%), maculopapular rash (52.9%), headache (49.2%), myalgia (41.1%), oedema (30.8%), conjunctival congestion (23.5%). Other symptoms were generalised tonic clonic seizures (GTCS), altered sensorium and jaundice. Hepatomegaly (91.1%), spleenomegaly (83.8%) and lymphadenopathy (75%) were the most common signs. Necrotic eschar which is considered to be the most definitive sign of scrub typhus was present only in 32 (23.5%) cases.

Table 1: Clinical profile and demographic data of patients.

Clinical manifestations	N	%	Demographic data	N	%
Fever	136	100	**Age (years)**		
Vomiting	106	77.9	6 months 2 years	28	20.5
Abdominal pain	78	57.3	2-8 years	56	41.1
Headache	67	49.2	9-12 years	52	38.2
Cough	93	68.3	**Gender**		
Myalgia	56	41.1	Male	76	55.8
Oedema	42	30.8	Female	60	44.2
Maculopapular rash	72	52.9	**Residence**		
GTCS	20	14.7	Malda	60	44.1
Conjunctival congestion	32	23.5	North Dinajpur	34	25
Altered sensorium	23	16.9	South Dinajpur	26	19.1
Eschar	32	23.5	Jharkhand	16	11.7
Jaundice	38	27.9			
Hepatomegaly	124	91.1			
Splenomegaly	114	83.8			
Lymphadenopathy	102	75			
Pallor	128	94.1			
Ascites	44	32.3			

All the patients received inj. ceftriaxone till the serology results confirmed the cases. Oral doxycycline in doses of 5 mg/kg/day in 2 divided doses were given in half the (68) and azithromycin (10 mg/kg/day) were given in 34 cases, while 34 cases were given oral chloramphenicol (75 mg/kg/day). The cases were given different drugs to find out relative efficacy of the drugs in our region. Doxycycline and chloramphenicol were equally effective with defervescence in maximum cases within 48 hrs. Azithromycin response was poor with fever persisting in

80% cases after 48 hrs. 56 patients developed complications, with meningoencephalitis being the most common (N47), pneumonia in 6 patients, pleural effusion in 5, empyema in 4, hemophagocytic lymphohistiocytosis (HLH) in 10, myocarditis in 3, disseminated intravascular coagulation (DIC) in 2. PICU admission was required in 33 cases. Few of the cases had more than one complication. Mortality was seen in 3 cases.

Table 2: Laboratory findings of patients.

Laboratory findings	N (%)
Anaemia <10 g/dl	120 (88.2)
Leucocytosis >15000/cc	94 (60.9)
Leucopenia <5000/cc	42 (30.8)
Thrombocytopenia <1.5l/cc	68 (50)
Albumin <2.5 g/dl	103 (75.7)
AST >40IU/l	58 (42.6)
ALT >40I U/l	60 (44.1)
Creatinine >1.5 mg/dl	96 (70.5)
Urine RBC >5/hpf	34 (25)
CSF pleocytosis	28 (20.5)
Hyponatremia (<135 meq/l)	45 ((30)
Raised bilirubin	
Direct (>2 mg/dl)	36 (26.4)
Indirect (1.2 mg/dl)	88 (64.7)

DISCUSSION

We decided to conduct this study because although there are a few studies from north and south India, there is no study from this part of West Bengal regarding incidence and prevalence of scrub typhus in paediatric population. Being a rural area, there is lack of awareness rewarding rickettsial disease and lack of diagnostic facilities.

We found a slight male preponderance (55:45) similar to other studies probably due to higher prevalence of outdoor activities among boys and consequently higher chances of exposures to chiggers.

We chose the study period around rainy season when there is maximum activity of the mites and breeding season of the rodents. Mean age of presentation was 73.6 months with the minimum age of presentation being 7months. This is the lowest reported age of presentation in any study. Previous reported lowest age of presentation was 4.1 years.[10]

All the cases presented with fever (100%) with mean duration being 8.2 days. The other common symptoms were vomiting (77.9%), cough (68.3%), abdominal pain (57.3%), maculopapular rash (52.9%), headache (49.2%), myalgia (41.1%), oedema (30.8%), conjunctival congestion (23.5%).

Table 3: Clinical response to antibiotics.

Time taken to become afebrile after starting antibiotic (hours)	Among patients treated with doxycycline (n=68) Frequency (%)	Among patients treated with azithromycin (n=34)	Among patients treated with chloramphenicol (n=34)	Total number of patients (n=136)
<24	11 (16)	1 (2.9)	12 (35)	24 (17.2)
24 to <48	43 (63)	5 (14.7)	17 (50)	65 (47.8)
48 to <72	14 (20.5)	8 (23.5)	5 (15)	27 (19.8)

These findings are comparable to other studies. Eschar was found in 23.5% cases which is higher than that reported by Kumar et al and Sankhayan et al but eschar was absent in high majority of cases (76.5%) and so its absence does not rule out diagnosis.

Common sites of eschar were perineum, axilla and buttocks.[11,12] Hepatomegaly was reported in 91.1% with hepatic dysfunction in nearly half of these cases (42.6%) and splenomegaly in 83.8% cases, which is similar to other studies but lymphadenopathy was present in 75% cases which is higher than all the studies.

Anaemia (88%) and hypoalbuminemia (75.7%) reported in our study is higher compared to other studies. Thrombocytopenia was noted in 50% cases. Meningoencephalitis was the most common complication (34.5%) with CSF picture of aseptic meningitis, similar to study done by Kumar et al.[5] Respiratory complications, viz pneumonia, pleural effusion, empyema was the second most complications. Secondary HLH was seen in 10 patients with 3 patients requiring IV methylprednisolone pulse therapy. Shock, CCF, DIC, HLH, myocarditis was the life-threatening complications requiring PICU admission. Most of the patients were revived but unfortunately 3 patients succumbed due to delayed presentation.

A recent Cochrane review concluded that tetracycline, doxycycline, azithromycin and rifampicin are effective drugs available for treatment of scrub typhus and suggested that there may be little or no difference between these as treatment options.[13] But our study found significantly poor response to azithromycin and chloramphenicol to be as effective as doxycycline in management of scrub typhus. Cases treated had nearly 80% defervescence in first 48 hours as compared to azithromycin (17-18%). Mortality rate (2.2%) was lower as compared to study conducted by Kamarasu et al (15%) and Rathi et al (9%).[11-15]

Table 4: Comparative analysis of our study with other studies.

Feature	Our study	Kumar et al	Sankhayan et al	Dass et al	Digra et al	Rajendran et al
Male:female	76:60	20:15	9:6	54:46	11 ;10	12.6
Mean duration of fever (days)	8.2	-	7	8.4	8	10
Mean age (month)	73.6	75.6	78	112.8	-	104.4
Headache	67 (49.2)	11	-	25	-	17
Vomiting	106 (77.9)	49	67	20.8	-	44
Altered sensorium	23 (16.9)	23	73	16.6	19	-
Seizure	20 (14.7)	11	60	12.5	-	28
Cough	93 (68.3)	51	33	35.7	-	34
Conjunctival congestion	32 (23.5)	-	33	8.3	46	61
Abdominal pain	78 (57.3)	34	-	25	23.8	-
Oedema	42 ((30.8)	60	60	-	57	-
Rash	72 (52.9)	20	67	-	100	22
Eschar	32 (23.5)	11	13	41.7	-	72
Lymphadenopathy	102 (75)	37	40	12.5	61.9	61
Hepatomegaly	124 (91.1)	91	93	33.3	76.2	72
Splenomegaly	114 (83.8)	60	87	45.8	76.2	88
Meningeal irritation	47 (34.5)	6	33	29.2	19	0
Anemia	120 (88.2)	-	-	-	100	44
Leucocytosis	94 (60.9)	37	47	25	28.6	28
Thrombocytopenia	68 (50)	31	47	26	38.1	55
Transaminitis	58 (42.6)	31	100	58.3	14.3	88
Hyponatremia	45 (30)	17	53	66.7	-	-
Hypoalbuminemia	103 (75.7)	54	100	52.2	-	72

Limitations

Limitation of the study was that many cases came to us after receiving empirical antibiotic therapy and they were started on ceftriaxone till the serology results were available. Being a tertiary care referral hospital, many cases reported late when complications like MOD had already set in.

CONCLUSION

Scrub typhus is a very frequent cause of fever in this part of Bengal but grossly under diagnosed due to lack of awareness and availability of diagnostic facilities. High clinical suspicion and diagnosis with prompt treatment with either doxycycline or chloramphenicol leads to excellent outcome. Azithromycin has poor response in this geographic area may be due to resistance acquired by overuse of this drug in Acute respiratory infections.

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