

Scrub Typhus in Children at a Tertiary Care Hospital in Odisha: A Study on Clinical, Laboratory Profile, Complications and Its Outcome.

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ABSTRACT

Background: To study the clinical profile, laboratory parameters, complications and outcome of scrub typhus in children. **Methods:** One hundred children with undiagnosed febrile illness admitted to our hospital from Aug 2014 to Nov 2014 were included in the study. All children were tested for scrub typhus using a commercial ELISA kit for specific IgM antibodies against *Orientia tsutsugamushi*. **Results:** Out of 100 children admitted to our hospital, only 50(50%) patients had positive IgM antibodies against *O. tsutsugamushi*. 30(60%) cases had fever of 5 to 10 days duration and 20(40%) cases had fever of more than 10 days duration. Vomiting with abdominal pain was reported in 20 (40%) cases, Lymphadenopathy in 18 (36%), hepatosplenomegaly in 35 (70%), generalized edema in 18 (36%) patients. Eschar was seen in 25(50%) patients. Most common abnormal laboratory parameters were raised SGOT, thrombocytopenia, raised bilirubin, raised CRP, leukocytosis and anemia. Most common complications were shock and electrolyte disturbances. **Conclusion:** In children Scrub typhus should be considered in the differential diagnosis of acute febrile illness associated with gastrointestinal symptoms, hepatosplenomegaly and lymphadenopathy. Prompt antibiotic treatment for scrub typhus should be given in cases with strong clinical suspicion to prevent morbidity and mortality.

Keywords: Eschar, *Orientia tsutsugamushi*, hepatosplenomegaly.

INTRODUCTION

In past few years no of scrub typhus, cases have increased and posed a challenge to diagnosis and management particularly in children. Not suspecting scrub typhus has increased morbidity and mortality in children. Scrub typhus is a rickettsial disease, which is transmitted by the larval mites of *leptotrombidium deliense* group.

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Scrub typhus is caused by *Orientia tsutsugamushi*. It is a strict intracellular bacterium endemic to a geographically distinct region including Japan, Taiwan, China, South Korea.^[1] In India scrub typhus had occurred among troops during world war two in eastern and northeastern region including Assam and West Bengal. Subsequently scrub typhus was reported from all states in India.^[2] Scrub typhus affects people of all age groups including children and has become endemic

in few regions in India.^[3] Worldwide approximately 1 million infections occur each year. It is estimated that more than 1 billion children are at risk.^[4] Infections are more common during rainy season. Scrub typhus is characterized by focal or disseminated vasculitis and perivasculitis, which affects almost all major organs like lungs, heart, liver, spleen and central nervous system. Scrub typhus has a broad clinical spectrum with variable presentation ranging from undifferentiated mild febrile illness to severe complicated disease with multi organ dysfunction with significant morbidity and mortality particularly in children. Mortality rate in undiagnosed and untreated children ranges from 0 to 30%^[5]. Commonly it presents with fever with chills, rash, myalgia, vomiting, lymphadenopathy and hepatosplenomegaly. Scrub typhus is commonly associated with presence of an eschar.^[6] Complications such as pneumonitis, meningoencephalitis, jaundice, renal failure and Myocarditis develops in severely affected patients. Few cases of Scrub typhus has been reported presenting as hemophagocytic histiocytosis in children.^[7] As the disease has similar signs and symptoms of that of many acute febrile illnesses, it is difficult to diagnose the cases clinically. The

diagnosis of Scrub typhus is mainly based on serological tests.^[8] Indirect immuno-florescent antibody test is the gold standard test for scrub typhus. ELISA to detect scrub typhus IgM can be used for quick diagnosis and treatment as it has good sensitivity and specificity. Scrub typhus responds to common antibiotics like doxycycline, azithromycin and tetracycline. So clinical suspicion with laboratory confirmation by serology and prompt treatment can significantly reduce the morbidity and mortality in children. There is paucity of studies on scrub typhus in children. So we have conducted the study to assess clinical, laboratory profile, complications and outcome of scrub typhus in children.

MATERIALS AND METHODS

This prospective observational study was conducted in a tertiary care teaching hospital in Bhubaneswar, Odisha from August 2014 to November 2014. After getting the approval from institutional ethical committee and informed consent of parents, pediatric patients from 1 yr to 14 year age group presenting with febrile illness were evaluated. All cases presenting with fever lasting for more than 5 days were included in the study. Common causes of fever such as malaria, dengue fever, pharyngitis, enteric fever, urinary tract infection were excluded after detail history, clinical examination and appropriate laboratory investigations such as urine analysis, complete blood count, smear for malarial parasite, QBC test for malaria, dengue Elisa, Widal test and blood culture and urine culture. Chest X-ray, abdominal ultrasonography, cerebrospinal fluid (CSF) examination, renal function tests and liver function tests were done as and when necessary. Specific IgM antibodies against *O. tsutsugamushi* was done by ELISA. ELISA test was based on detection of IgM antibodies against 56 Kda antigen. Children with positive IgM antibodies against *O. tsutsugamushi* were diagnosed as having scrub typhus. Complications such as hepatitis, meningitis, meningoencephalitis, hypotension, myocarditis, acute renal failure and shock were noted. Despite administration of isotonic intravenous fluid bolus >60 ml/kg in 1 hour; decrease in blood pressure (BP) <5th percentile for age or systolic BP < 2 standard deviation (SD) below normal for age or requiring vaso-active drug to maintain BP was labeled as shock. Meningitis was defined as altered sensorium with signs of meningeal irritation associated with elevated proteins and cells on cerebrospinal fluid (CSF) analysis. In laboratory parameters, leukocytosis was considered when white cell count (WBC) was more than 12000 cells/cmm and leucopenia was defined as WBC < 4000 cells/cmm.

Thrombocytopenia was considered when platelet count was < 150,000 cells/cmm. Raised SGOT > 40IU/L, raised SGPT >55IU/L and raised bilirubin was > 1 mg/dl were considered as abnormal liver function.^[9] The children who were serologically diagnosed of having scrub typhus or those with strong clinical suspicion of scrub typhus, were given doxycycline (in children > 8 years of age, in critically ill patient and those who did not respond to azithromycin). Azithromycin was given orally or parenterally in children < 8 years of age. All other supportive measures like transfusion of blood components, inotropic support were given as and when required. Clinical and laboratory parameters and complications associated with scrub typhus were analyzed.

RESULTS

A total of 100 children with undiagnosed fever were included in the study. 50 children (50%) had positive IgM antibody against scrub typhus. Mean age of presentation was 60 months with age range of 12 months to 14 years. Male: Female ratio was 2:1.80% of scrub typhus cases were from rural area. Out of 50 children, 8 were undernourished and 42 were with normal nutritional status. The common clinical features are shown in [Table 1] and laboratory parameters are shown in [Table 2]. Complications are shown in [Table 3]. Pneumonitis was seen in 2(4%) children and hypotension in 10 (20%) children out of which 8 children needed inotropic support. Meningoencephalitis was seen in 1 (2%) cases. Hepatosplenomegaly (75%) was the most common presentation followed by fever (60%), eschar (50%), nausea/vomit /pain abdomen (40%), lymphadenopathy (36%), oedema (36%), and pneumonitis (4%). Only one child with meningoencephalitis died in the hospital. All the remaining children recovered within 1 to 5 days of starting treatment. Azithromycin was given in 30 children and Doxycycline in 20 children.

Table 1: Clinical presentation of scrub typhus

Clinical features	No. of patients [n=50] (%)
Fever (5-10 days)	30 (60%)
Fever (>10 days)	20 (40%)
Hepatosplenomegaly	35 (70%)
Hepatomegaly only	15 (30%)
Nausea/Vomiting/pain abdomen	20 (40%)
Lymphadenopathy	18 (36%)
Eschar	25(50%)
Cough	12(24%)
Altered sensorium	6(12%)
Pedal/generalized edema	18 (36%)
Headache	10 (20%)
Meningeal signs	1 (2%)
Rash	3(6%)

Table 2: Laboratory abnormalities in scrub typhus

Laboratory parameter	No. of patients [n=50(%)]
Raised SGOT	27(54%)
Hb(<11 gm%)	25(50%)
Thrombocytopenia	16 (32%)
Raised SGPT	8(16%)
Leukocytosis	16 (32%)
Raised Bilirubin	4 (8%)
CRP(>1mg/dl)	50(100%)

Table 3: Complications of scrub typhus

Complications	No. of patients [n=50(%)]
Electrolyte disturbances	8(16%)
Acute renal failure	2(4%)
Shock	10 (20%)
Meningoencephalitis	1(2%)
Pneumonitis	2 (4%)
G.I bleed	2(4%)

DISCUSSION

In last few years several reports of scrub typhus outbreaks has been reported from all over India.^[10] More than half of patients of scrub typhus were found among pediatric age group. The present study was conducted in the rainy season for which we have detected large no of cases. Monsoon and post monsoon surge of scrub typhus has been reported previously^[11] In our study fever was the common presentation in all cases. Fever was associated with hepatosplenomegaly, lymphadenopathy, vomiting and pain abdomen. The pathognomonic feature of scrub typhus is an eschar at the site of bite of the mite. Eschar was seen in 50% of cases in our study, which is similar to other studies.^[12] Lymphadenopathy is one of the most common presentation in scrub typhus with similarity to our study.^[13] Lymphadenopathy can be a differentiating feature from other common febrile diseases like dengue and malaria where organomegaly is a common finding. Usually *O. tsutsugamushi* infects vascular endothelium leading to vasculitis, capillary leak and organ dysfunction.^[14] In our study Serum transaminases were elevated in large number of patients which is similar to few other studies.^[15] So in all children suffering from fever of unknown origin with deranged liver function, we should take scrub typhus as a differential diagnosis.^[16] Anemia, Leukocytosis and thrombocytopenia and low serum albumin and raised CRP are other laboratory findings thought to be associated with severe scrub typhus^[16]. Serious complications of scrub typhus include gastro intestinal bleed, myocarditis, meningitis, meningoencephalitis, pneumonitis and acute kidney injury which can increase morbidity and mortality in children.^[17] The gold standard of diagnosis in scrub typhus is serology. The gold standard serological tests are immunofluorescence

antibody test or indirect immunoperoxidase assay.^[18] Weil-Felix test is a cheaper test with high specificity, but it lacks sensitivity.^[19] In the present study, we used ELISA testing for IgM antibodies against *O. tsutsugamushi* for diagnosis. ELISA testing for IgM has a good sensitivity and specificity of 90%.^[20] Complications in scrub typhus develop after first week of illness due to increased blood load of *O. tsutsugamushi*.^[21] Khandelwal et al has studied clinical and laboratory manifestation of scrub typhus in 183 children with fever and opined that scrub typhus should be considered in the differential diagnosis of acute febrile illness with hepatosplenomegaly, lymphadenopathy and gastro intestinal symptoms.^[22] Mahesh kumar et al^[23] and Devarajan et al^[24] in their respective studies suggested that scrub typhus should be considered in all hospitalized children with eschar, splenomegaly and thrombocytopenia. Further Mahesh Kumar also reported higher incidence of myocarditis and acute kidney injury in his study.^[23] Murli Krishnan studied 100 children and opined that high index of suspicion of scrub typhus should be made and prompt antibiotic therapy should be started accordingly.^[25]

The recommended treatment regimen for scrub typhus in children > 8 yrs is doxycycline (4 mg/kg/day PO or IV divided every 12 hours, maximum 200 mg/day) and azithromycin (10 mg/kg/day) for 7 days. Alternative regimens include tetracycline (25-50 mg/kg/day PO divided every 6 hours, maximum 2 gm/day) or chloramphenicol (50-100 mg/kg/day divided every 6 hours IV, maximum 4 g/24 hr). Therapy should be continued for a minimum of 5 days and until the patient has been afebrile for ≥ 3 days to avoid relapse.^[26]

CONCLUSION

Although incidence and prevalence of Scrub typhus is less common in comparison to other diseases we must suspect and investigate it. Scrub typhus should be suspected in all cases presenting with fever, hepatosplenomegaly, lymphadenopathy and other nonspecific symptoms like pain abdomen, nausea, vomiting particularly where no other definite diagnosis could be made. Specific tests like IgM ELISA should be done to confirm the diagnosis in suspected cases. Any delay in diagnosis and treatment may lead to complications like shock, gastro intestinal bleed, pneumonitis, meningoencephalitis and acute renal failure with significant morbidity and mortality in children. High index of clinical suspicion with prompt empirical antibiotic treatment is needed for complete recovery and better outcome.

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