RESEARCH

STUDY OF CLINICAL FEATURES OF RICKETTSIAL FEVER IN PEDIATRIC AGE GROUP

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Abstract

Background: Rickettsial infections are emerging tropical infectious diseases caused by obligate intracellular pleomorphic gram negative cocco-bacilli. Rickettsial fever is difficult to diagnose early due to low index of suspicion and widely variable sensitive and specific serological tests. Present study was aimed to study clinical features of rickettsial fever in pediatric age group. **Materials and Methods:** Present study was single-center, prospective, observational study, conducted in children, age 2 months to 15 years, admitted with fever of more than five days duration and had clinical suspicion of scrub typhus, all hospitalized children with clinical features suggestive of Rickettsial disease (fever, generalized rash) who tested ELISA positive for IgM against Scrub Typhus. **Result:** During study period 45 children satisfying study criteria were evaluated. Majority were male (57.78 %), from 6-10 years age group (35.56 %) & 2-5 years age group (33.33 %). Common symptoms reported were fever (100 %), maculopapular rash (57.78 %), headache (42.22 %), difficulty in breathing (33.33 %), abdominal distension (28.89 %), convulsions (26.67 %), altered sensorium (24.44 %), eschar (13.33 %) & gangrene (2.22 %). On clinical examination, common findings were hepatomegaly (82.22 %), edema (60 %), lymphadenopathy (44.44 %) & splenomegaly (20 %). Laboratory findings noted were thrombocytopenia (95.56 %), hypoalbuminemia (93.33 %), hyponatremia (93.33 %), anemia (64.44 %) & leucocytosis (40 %). Common complications observed were hepatitis (15.56 %), meningoencephalitis (13.33 %), pneumonia (11.11 %), pleural effusion (6.67 %), MODS (6.67 %), vasculitis (4.44 %), acute kidney injury (4.44 %) & myocarditis (2.22 %). Death was observed in all 3 cases of MODS (6.67 %). **Conclusion:** Definitive treatment should be instituted on the basis of clinical and epidemiological clues as early as possible to avoid severe disease and fatal outcome.

INTRODUCTION

Rickettsial infections are emerging tropical infectious diseases caused by obligate intracellular pleomorphic gram negative cocco-bacilli.[1] Infection is acquired by transmission through arthropod vectors (ticks, fleas, mites, and lice) or by direct exposure to the reservoir animal harboring rickettsial organisms (rodents, dogs, cattle and mice).[2] Rickettsial fever has been reported to be endemic in the Himalayan belt, Maharashtra and Karnataka in India among the adult population.[3]

Rickettsial fever is difficult to diagnose early due to low index of suspicion and widely variable sensitive and specific serological tests.[4] The lack of proper clinical diagnostic techniques in low-income settings such as India further contributes to a delay in starting treatment. Conventional diagnostic tests such as the Weil-Felix test are insensitive and non-specific. The recently introduce serological test IgM antibody against scrub typhus (done by is ELISA or immunofluorescence assay) is considered as the gold standard, not widely available in India.[2]

These diagnostic deficiencies result in physicians relying on clinical suspicion alone to begin treatment, and point to a need for the development of newer, cost-effective diagnostic assays. Doxycycline is the drug of choice and treatment should begin promptly without waiting for confirmatory laboratory results.[5] Delay in diagnosis and initiation of appropriate treatment can result in severe complications such as acute respiratory distress syndrome (ARDS), septic shock and multisystem organ failure resulting in mortality.[6] Present study was aimed to study clinical features of rickettsial fever in pediatric age group.

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MATERIALS AND METHODS

Present study was single-center, prospective, observational study, conducted in Department of Paediatrics, at JJMMC, Davanagere, India. Study duration was of 2 years (January 2020 to December 2021). Study was approved by institutional ethical committee.

Children, age 2 months to 15 years, admitted with fever of more than five days duration and had clinical suspicion of scrub typhus, all hospitalized children with clinical features suggestive of Rickettsial disease (fever, generalized rash) who tested ELISA positive for IgM against Scrub Typhus parents willing to participate in study were considered for present study.

Study was explained to parents & written consent was taken for participation. Children with high-grade intermittent fever and having five out of the following eight clinical features, such as: headache, myalgia, regional lymphadenopathy, generalised lymphadenopathy, hepatomegaly, splenomegaly, eschar, and rash.

A thorough history, meticulous physical examination findings, hospital course, complications (if any), and outcome were recorded in a proforma. Basic laboratory studies such as complete blood count, urine routine and microscopic examination, liver and renal function tests, and chest X-ray were performed in all cases. If required cerebrospinal fluid (CSF) examination, echocardiography, and radiological imaging, such as ultrasound of the abdomen and CT scan of the brain, were performed.

Blood and urine culture, Quantified Buffy Coat (QBC) testing for malaria parasite, and serology for dengue and leptospirosis were done to exclude some prevalent diseases. Serum IgM ELISA was performed in all suspected cases using scrub typhus (In Bios International Inc. [country of manufacture]) as per the manufacturer's instructions. Detection of IgM antibody in ELISA for O. tsutsugamushi in serum samples with optical density (OD) more than 0.5 was considered to be a positive result for typhus and was recorded as a confirmed case of scrub typhus.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

During study period 45 children satisfying study criteria were evaluated. Majority were male (57.78 %), from 6-10 years age group (35.56 %) & 2-5 years age group (33.33 %). [Table 1]

Common symptoms reported were fever (100 %), maculopapular rash (57.78 %), headache (42.22 %), difficulty in breathing (33.33 %), abdominal distension (28.89 %), convulsions (26.67 %), altered sensorium (24.44 %), eschar (13.33 %) & gangrene (2.22 %). On clinical examination, common findings were hepatomegaly (82.22 %), edema (60 %), lymphadenopathy (44.44 %) & splenomegaly (20 %). [Table 2]

Laboratory findings noted were thrombocytopenia (95.56 %), hypoalbuminemia (93.33 %), hyponatremia (93.33 %), anemia (64.44 %) & leucocytosis (40 %). Weil-Felix test suggestive of scrub typhus (OX-K) (75.56 %), Spotted fever (OX-19, OX-2) (17.78 %) & Other typhus (6.67 %). [Table 3]

In present study, common complications observed were hepatitis (15.56 %), meningoencephalitis (13.33 %), pneumonia (11.11 %), pleural effusion (6.67 %), MODS (6.67 %), vasculitis (4.44 %), acute kidney injury (4.44 %) & myocarditis (2.22 %). Death was observed in all 3 cases of MODS (6.67 %). [Table 4]

Table 1: Demographic details of the study population.

Parameter	Frequency	Percentage
Age		
≤1 year	2	4.44%
2-5 years	15	33.33%
6-10 years	16	35.56%
11-15 years	12	26.67%
Gender		
Male	26	57.78%
Female	19	42.22%

Table 2: Clinical features

Parameter	Frequency	Percentage
Symptoms		
Fever	45	100.00%
Maculopapular rash	26	57.78%
Headache	19	42.22%
Difficulty in breathing	15	33.33%
Abdominal distension	13	28.89%
Convulsions	12	26.67%
Altered sensorium	11	24.44%
Eschar	6	13.33%
Gangrene	1	2.22%
Clinical examination		
Hepatomegaly	37	82.22%

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Edema	27	60.00%
Lymphadenopathy	20	44.44%
Splenomegaly	9	20.00%

Table 3: Laboratory findings.

Laboratory derangements	Frequency	Percentage
Thrombocytopenia	43	95.56%
Hypoalbuminemia	42	93.33%
Hyponatremia	42	93.33%
Anemia	29	64.44%
Leucocytosis	18	40.00%
Weil-Felix test		
Scrub typhus (OX-K)	34	75.56%
Spotted fever (OX-19, OX-2)	8	17.78%
Other typhus	3	6.67%

Table 4: Complications and mortality.

Parameter	Frequency	Percentage
Hepatitis	7	15.56%
Meningoencephalitis	6	13.33%
Pneumonia	5	11.11%
Pleural effusion	3	6.67%
MODS	3	6.67%
Vasculitis	2	4.44%
Acute kidney injury	2	4.44%
Myocarditis	1	2.22%
Death	3	6.67%

DISCUSSION

Rickettsial Diseases are dangerous among children, due to atypical presentations and complications, as increasing trends in India since last many years.[7,8] Scrub typhus and other rickettsial infections are grossly underdiagnosed in India because of their non-specific clinical presentation, low index of suspicion among clinicians, limited awareness about the disease and lack of diagnostic facilities.

Clinical spectrum of the disease ranges from mild flu like illness to multi organ dysfunction like pulmonary edema, meningoencephalitis, renal failure and shock. Rash or eschar (a black necrotic area at the site of initial tick bite) may not be always present, making diagnosis difficult. Gastrointestinal symptoms including nausea, vomiting, diarrhea and pain abdomen occur frequently (39–63 %) early in the course of disease.[9,10]

The infection clinically manifests as non-specific febrile illness, which is accompanied by headache, myalgia, occasional rash, often accompanied by gastrointestinal, respiratory, or central nervous system (CNS) symptoms, which may lead to severe multi-organ dysfunction in untreated cases.[11,12]

Judy V J et al,[13] studied 340 subjects, 241 (70.88%) children were aged >48 months. Male participants were 187 (55%) and remaining 153 (45%) were females. Out of 340 subjects, 48 (14.12%) participants were positive for scrub typhus. The common clinical features seen were fever, abdominal pain, cough, vomiting and hepatosplenomegaly in the decreasing order of frequency. The seroprevalence of scrub typhus rickettsial infection was 14.12%, which was quite high.

Mallesh K et al,[14] studied 49 patients, common age group affected was 1-5 years (32.7 %), from rural background (78 %). Most common presentation being fever (100 %), 81.6% of patients had significant Rathi-Goodman-Aghai score of >14. Weil felix showed significant titres (1:80) in 97.9% out of which serology suggestive of scrub typhus was found in 79.6% patients. There was no statistical significance between rickettsial score and Weil-Felix test (p value= 0.736). 26.5% of the cases required respiratory support and 2% cases required dialysis. 10.2% cases succumbed and 89.8% cases improved.

Sandeep K et al,[15] studied 139 children diagnosed to have rickettsial disease, mean age was 7.2 ± 4.56 years. Common clinical manifestations were fever (100%), vomiting (46.8%), hepatosplenomegaly (39.5%), isolated splenomegaly (38.7%), pallor (35.5%), headache (31.5%), myalgia (30.6%), breathlessness (4.8%), edema (33.9%), abdominal pain (22.6%), conjunctival congestion (21%), cough (19.4%), skin rash (18.5%), eschar (17%), seizures (9.7%), altered sensorium (8.9%), and lymphadenopathy (8.9%). Complications seen were meningitis/meningoencephalitis (9%), pneumonia (5%), acute respiratory distress syndrome (ARDS) (4%), gangrene (2%), myocarditis (1.6%), acute kidney injury (AKI) (1.6%) and stroke (1.6%). Common laboratory features were elevated liver enzymes (60.5%), thrombocytopenia (54%), hypoalbuminemia (53.2%), anemia (47.6%), elevated CRP (46%), leucocytosis (41.9%), and hyponatremia (38.7%). There was no mortality and all recovered.

Vinod HR et al,[16] studied 36 children, male: female ratio was 1:1, mean age of presentation was 5.6 years. The most common clinical symptoms/signs

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were fever 36 (100%), rash 20 (55%), hepatomegaly 25 (69%), splenomegaly 18 (50%), pallor 18 (50%), pedal oedema 14 (38%) and ascites 6 (16%). Among the laboratory profile thrombocytopenia was seen in 27% cases, hyponatremia in 71.4% cases. No mortality was noted.

Kalal BS et al,[17] studied 103 children with clinical features suggestive of rickettsial illness, ELISA test confirmed 53 cases for scrub typhus, 23 cases for spotted fever group and 14 with mixed infection. The average age was 7.3 (±3.9) years and 44 (71.0%) children were male. Majority of cases were from Karnataka (50%), Andhra Pradesh (32.3%) and Tamil Nadu (17.7%). Common clinical features included fever (100%, average duration 11 days), nausea and vomiting (44%), rash (36%); eschar was rare. Compared to the ELISA test, Weil-Felix test (OX-K titer of 1:80) had a sensitivity and specificity of 88.7% and 43.9%, respectively. Treatment with chloramphenicol or doxycycline was given to most of the children. Complications included meningoencephalitis (28%), shock (10%), retinal vasculitis (10%) and purpura fulminans (7%).

Even if suspected by clinician, therapy is empirical as serological tests for diagnosis become positive around a week after onset of fever and early diagnostic test like polymerase chain reaction is not freely available.

Larger multicenter studies may be carried out to ascertain the endemicity, variation in clinical manifestations, prognostic indicators, and predictive value of signs and symptoms in different age groups. Further research must focus on preventive strategy against scrub typhus including vector control and availability of a vaccine soon.

CONCLUSION

Definitive treatment should be instituted on the basis of clinical and epidemiological clues as early as possible to avoid severe disease and fatal outcome. High index of clinical suspicion is required for the diagnosis of rickettsial diseases. Awareness about different clinical presentations of these infections may assist in early diagnosis, especially in areas where no diagnostic facilities are available.

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