

Original research paper

Outcome of rickettsial infections in children aged less than 12 years: Clinical descriptive study

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Abstract

Rickettsial infections are one of the important causes of pyrexia of unknown origin (PUO) and these needs to be differentiated from other febrile illnesses. Rickettsial infections are grossly under-diagnosed in India. All children aged less than 12 years admitted in paediatric ward with fever without an identifiable source of infection and one or more of the following clinical features: rash, oedema, hepatosplenomegaly, Lymphadenopathy, an Eschar and a tick bite or tick exposure were suspected to have rickettsial infection. All suspected cases were subjected to rickettsial IgM/IgG ELISA test and tests to exclude other diseases. Scrub typhus and Indian tick typhus elisa positive (mixed infection) noted in 14% of cases. Complications like meningoencephalitis (5.8%), shock (5.8%), DIC (2.9%) was observed in the study. There was good clinical response on initiation of doxycycline within 48hrs of initiation of treatment. Case fatality rate of rickettsial disease in this study was 5.8% (n=2). Rickettsial diseases are difficult to diagnose, unless suspected but treatment is easy, affordable and often successful with dramatic response to antimicrobials.

Keywords: Rickettsial infection, ELISA, childrens

Introduction

Rickettsial diseases are one of the most re-emerging infections of the present time, which are often failed to diagnose. Untreated cases can have fatality rates as high as 30-35% but when diagnosed properly, they are often easily treatable ^[1]. It is one of the most important causes of pyrexia of unknown origin (PUO) and this needs to be differentiated from other febrile illnesses like Enteric fever, Malaria, Dengue, Infectious mononucleosis, Kawasaki disease, Collagen vascular diseases. Rickettsial infection is a zoonotic acute febrile illness caused by small, non-flagellated, obligate intracellular, pleomorphic gram-negative coccobacilli from the genera Rickettsia, Orientia, Ehrlichia, Neorickettsia and Anaplasma and they are transmitted by arthropod vectors. 35, 37 they are primary parasites of arthropods like lice, fleas, ticks and mites, in which they are found in the alimentary canal ^[2].

Rickettsial infections are grossly under-diagnosed in India. As no single laboratory test is

specific for early diagnosis, treatment needs to be started empirically on clinical and epidemiological suspicion. In view of low index of suspicion, nonspecific signs and symptoms, and absence of widely available sensitive and specific diagnostic test, these infections are extremely difficult to diagnose but treatment is easy, affordable and often successful with dramatic response to antimicrobials^[3,4].

The National Centre for Disease Control (NCDC, formerly National Institute of Communicable Disease) has played important role in providing serological evidence of rickettsial diseases in India in various States like Jammu & Kashmir, Himachal Pradesh, Uttarakhand, Haryana, Rajasthan, Assam, West Bengal, Maharashtra, Tamil Nadu, Kerala, Karnataka, Sikkim, and Manipur in the last decade. 1, 2, 4 Batra has reported high magnitude of scrub typhus, spotted fever Indian tick typhus^[5].

Weil-Felix antibody testing should not be performed, because it lacks both sensitivity and specificity. Definitive diagnosis is most often accomplished by serology, which is retrospective, because a rise in titre is not seen until after the first week of illness. Orientia tsutsugamushi serologic tests such as indirect fluorescent antibody assay are approximately 90% sensitive with 11 or more days of fever. Infections from Indian tick typhus can be confirmed by immunohistologic or immunofluorescent or demonstration of seroconversion by 4 fold rise in serum antibody titres^[6].

IgM and IgG ELISA: ELISA techniques, particularly immunoglobulin M (IgM) capture assays are probably the most sensitive tests available for rickettsial diagnosis and the presence of IgM antibodies, indicates recent infection with rickettsia. Immunofluorescence assay (IFA) is a gold standard for diagnosis of rickettsial infection^[7].

The majority of studies regarding rickettsial infections in India and other parts of the world are based on adult populations and on scrub typhus. There is a paucity of studies regarding the incidence and clinical profile of rickettsial disease in children from the Indian subcontinent and majority of published studies are retrospective or sporadic case reports. 11, 36 hence this study aims to study the clinical features and outcomes of paediatric rickettsial disease^[8].

Methodology

All children aged less than 12 years admitted in pediatric ward with fever without an identifiable source of infection and one or more of the following clinical features: rash, edema, hepatosplenomegaly, lymphadenopathy, an eschar and a tick bite or tick exposure were suspected to have rickettsial infection. The purpose of the study was explained to the parents or guardians of the child and an informed consent was taken from them enrolling the child in study group. All suspected cases were subjected to rickettsial IgM/IgG ELISA test and tests to exclude malaria-thick and thin peripheral smear, WIDAL for enteric fever and NS 1 and IgM Mac ELISA for dengue fever. Patients were treated according to the hospital protocol. All rickettsial IgM/IgG positive cases were followed up through hospital stay and outcomes were noted. The ELISA kit used in this study was Scrub typhus IgM/IgG from INBIOS international from USA and Rickettsia Conorii ELISA IgM/IgG VIRCELL from Spain.

Chest X-rays, tests for renal and liver function, serum electrolyte, ultrasonography (USG), neuroimaging, cerebrospinal fluid analysis (CSF) were done as and when required.

A predesigned proforma was used to collect data regarding age, gender, residential area, exposure to animals. Clinical data, including the duration of the fever, associated symptoms, vital signs, general and systemic examination findings, complications, investigations, treatment and defervescence time were recorded.

Inclusion criteria

- All children up to 12 years of age will be considered.
- All children aged less than 12 years admitted in pediatric ward with fever without an identifiable source of infection and one or more of the following clinical features: rash, edema, hepatosplenomegaly, lymphadenopathy, an eschar and a tick bite or tick exposure were suspected to have rickettsial infection along with positive serology test for Rickettsial IgM/IgG ELISA.

Exclusion criteria: Cases with other established causes of infection.

Results

Table 1: Blood Parametres

Parameters	No. of patients (n)	%
Hemoglobin(g/dl)		
<9	7/34	20.6
>9	27/34	79.4
TLC (cumm)		
Normal	27/34	79.4
Leucopenia	3/34	8.8
Leukocytosis	4/34	11.7
Platelet counts		
<1.5 lakh/cumm	12/34	35.2
>1.5 lakh/cumm	22/34	64.8
S. Sodium (mEq/L)		
Normal	9/30	30
Hyponatremia	21/30	70
S. AST (U/L)		
Normal	12/16	75
Elevated	4/16	25
S. ALT (U/L)		
Normal	12/16	75
Elevated	4/16	25
Total Bilirubin (mg/dl)		
Normal	15/16	93.75
Elevated	1/16	6.25
Total protein (gm/dl)		
Normal	11/16	68.75
Decreased	5/16	31.25
Albumin (gm/dl)		
Normal	14/16	87.5
Decreased	2/16	12.5
S. Creatinine (mg/dl)		
Normal	25/25	100

TLC: Total leukocyte count. S. AST: Serum Aspartate transaminase, S.ALT: Serum Alanine transaminase.

Considering hematological parameters, 20.6% (n=7) had hemoglobin <9g%, 8.8% (n=3) had leucopenia and 11.7% (n=4) had leukocytosis. Thrombocytopenia (<1.5 lakh/cumm) was present in 12 cases (35.2%).

Renal function test, liver function tests, were done as and when required.

Out of 30 cases, 9 cases had normal serum sodium levels. Hyponatremia (S. Sodium

<135mEq/L) was present in 21 cases (70%). 4 out of 16 cases had elevated serum transaminase level (AST and ALT elevated twice the normal value). Elevated bilirubin (>2mg/dl) was present in 1 out of 16 cases. Hypoalbuminemia was seen in 2 out of 16 cases. 25 out of 34 cases had renal function test done, all had normal serum creatinine levels. Two cases had neuroimaging (CT Brain) done, both reported normal. USG was done on 18 children. One children enlarged hypoechoic liver with splenomegaly and one children had hepatosplenomegaly. Sixteen children USG Abdomen scanning was normal. CSF analysis was done in only one patient, which showed features of aseptic meningitis (Cell count 20 cells, Cell type 70% lymphocytes 30% neutrophils, glucose-59, protein-22 and chloride-98. ZN stain-Neg, Gram stain-Neg, C/S-no growth).

Table 2: Day of initiation of doxycycline and duration of therapy (n=34)

	No. of patients (n=34)	%
Day of initiation of doxycycline		
< 72 hrs	33	97.1
> 72 hrs	1	2.9
Duration of therapy		
7 days	30	88.2
10 days	2	5.9

Out of 34 cases, Doxycycline was initiated within 72 hours of admission in 33 (97.1%) cases. Duration of therapy was given for 7 days in 30 cases (88.2%) for 10 days in 2 cases (5.9%). 2 cases died within 48 hrs of admission.

Table 3: Response to doxycycline (n=32)

Asymptomatic from day of starting doxycycline	No. of patients (n=32)	%
<48 hrs	26	81.25
>48 hrs	6	18.75

Out of 32 cases who improved after starting doxycycline therapy, 26(81.25%) responded within 3 days whereas 6(18.75%) cases took more than 3 days to respond.

Table 4: Duration of hospitalization (n=34)

Duration	No. of Patients	%
≤ 5 days	18	52.9
6-10 days	15	44.1
≥11 days	1	2.9
Total	34	100.0

Out of 34 cases 2 case died accounting for a case fatality rate of 5.9%. Cause of death was

1. Meningoencephalitis with Shock.
2. Rickettsial vasculitis with DIC with Shock.

Discussion

In our study 8.8% (n=3) had leucopenia. Similar findings was noted in other studies like Takhar *et al.* ^[9] (15%), Kumar S *et al.* ^[10] (9.6%) and Ratageri VH *et al.* ^[11] (8.3%). Leukocytosis was present in 11.7% in the current study. While Takhar *et al.* ^[9] (30%), Kumar S *et al.* ^[10] (38%) and Ratageri VH *et al.* ^[11] (38.8%) reported leukocytosis in higher number of patients.

Thrombocytopenia (<1.5 lakh/cumm) was noted in 35.2% of children in our study. Ratageri

VH *et al.* ^[11] reported Thrombocytopenia in 27.7% of patients and Digra SK *et al.* ^[12] in 38% of patients.

Out of 30 cases, 9 cases had normal serum sodium levels. Hyponatremia (S. Sodium <135mEq/L) was present in 21 cases (70%). Similar findings were noted by Ratageri VH *et al.* ^[11] (71.4%).

Scrub Typhus and Indian Tick Typus Elisa Positive (mixed infection) noted in 14% of cases, similar finding noted in Kalal BS *et al.* ^[13].

The most common complication observed in this study was meningoencephalitis in 5.89% (n=2) of cases. Similar findings were noted in studies by Rathi NB *et al.* ^[14] and Palanivel S *et al.* ^[15] reporting meningoencephalitis in 5% and 6% of patients respectively. In a study by Reddy BK *et al.* ^[16] on Rickettsial meningoencephalitis conducted in IGICH, Bangalore observed meningoencephalitis in 31.1%.

Other complications like shock were observed in 5.89% in this study. Rathi NB *et al.* ^[14] and Kalal BS *et al.* ^[13] reported shock in 5% and 10% of cases respectively.

DIC was observed in 2.9% of cases in our study. Palanivel S *et al.* ^[15] Kumar S *et al.* ^[10] and Rathi NB *et al.* ^[14] reported DIC in 1.5%, 1.7% and 5% of cases respectively.

There were no renal or cardiac complication seen in this study, unlike study done by Kumar M *et al.* ^[17] where in myocarditis with cardiogenic shock in 34%, acute kidney injury in 20% of cases noted which was attributed to late referrals.

All the 34 cases in our study received treatment with Doxycycline, of which 32 cases (94.11%) was improved. 81.25% responded to the treatment within 48 hrs and 18.75% of cases responded after 48 hrs.

Kumar M *et al.* ^[17] has demonstrated that good response to Doxycycline (97%).

Rickettsial disease is known to produce serious complications and has a mortality rate of 30% ^[18]. Deaths were attributable to late presentation, delayed diagnosis and drug resistance.

A mortality of 12% was reported by Palanivel S *et al.* ^[15] 2.8% by Kumar M *et al.* ^[17] and 9% by Rathi NB *et al.* ^[14] In this study there was mortality of 5.9% (n=2).

Conclusion

- Indian tick typhus is the most common rickettsial fever noted in this part of Karnataka.
- Rickettsial diseases are difficult to diagnose, unless suspected but treatment is easy, affordable and often successful with dramatic response to antimicrobials.

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