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Original Research Article

Study to Find Out Various Clinical Manifestations and Laboratory Diagnosis of Rickettsial Disease in Pediatric Age Group

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Abstract

Aim: The aim of the present study was to find out various clinical manifestations and laboratory diagnosis of Rickettsial disease in pediatric age group.

Material & Methods: A prospective observational study was conducted at Department of Pediatrics for the duration of 24 months, involving patients admitted between 2 months to 18 years of age with a diagnosis of Rickettsial fever. A total of 50 cases who were admitted with complaints of fever and presence of one or more of the following clinical features: Rash, edema, eschar, hepatosplenomegaly, lymphadenopathy, History of contact with pets and history of tick bite.

Results: Most common age group observed was 1-5 years accounting to 34%. The youngest affected patient was 2-month-old. Males (64%) were most commonly affected group in our study. 80% of the patients hailed from rural background. Fever was the most common symptom present in all the cases enrolled in the study followed by rash in 29 (58%) cases. Eschar though a characteristic feature of rickettsial infection was found in only 5 (10%) of the cases. Clinical examination revealed hepatomegaly in 45 (90%) cases, followed by lymphadenopathy in 15 (30%) cases and splenomegaly in 12 (24%) of cases. Investigations done in our study subjects showed that out of the 50 cases, 47 (94%) had thrombocytopenia. Hypoalbuminemia was seen 46 (92%) cases and hyponatremia was seen in 43 (86%). Anemia was seen in 27 (54%) of the cases. There was no statistical significant correlation between Rickettsial score and Weil-Felix test according to our study. Complications were seen in 28 (56%) of the cases, of which meningoencephalitis was the most common seen in 8 (16%) of the cases, followed by pneumonia and hepatitis in 4 (8%) cases each. 1(2%) patient required hemodialysis.

Conclusion: A proper history and careful physical examination help in the diagnosis of Rickettsial disease. Laboratory tests can be carried out to support the diagnosis. Weil-Felix test can be carried out for early detection of suspicious case in resource limited set up.

Keywords: Rickettsial infection, maculopapular rash, thrombocytopenia, Weil-Felix test.

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Introduction

Rickettsial diseases, caused by a a heterogenous group of small obligate intracellular, Gram-negative bacteria from the genus Rickettsia, belonging to the Alphaproteobacteria, are considered some of the most covert emerging and reemerging diseases and are being increasingly recognized and most of which are transmitted by a tick, mite, flea or louse vector. [1,2] Clinical infections with rickettsiae were earlier classified according to the taxonomy and diverse microbial characteristics of the agents, into six genera Rickettsia, Orientia, Ehrlichia, Anaplasma, Neorickettsia, and Coxiella. [3] The incidence of rickettsial infection had seen a significant decline in the nineties secondary to widespread use of insecticides. [4]

The clinical presentation of rickettsial infection is wide and varied. Severity varies from subclinical illness to severe illness with multiple organ system involvement, which can be serious enough to be fatal, unless diagnosed early and treated. [5] Untreated cases have case fatality rates as high as 30-45% with multiple organ dysfunction, if not promptly diagnosed and appropriately treated. Other major tropical fevers include dengue, malaria, leptospirosis and chikungunya which present as undifferentiated febrile illness. Rickettsial fever is difficult to diagnose early due to low index of suspicion and widely variable sensitive and specific serological tests.6

Common serological tests used to diagnose rickettsial fever are non-specific. The gold standard

serological tests like indirect immunofluorescent antibody assay are expensive and not easily available. [6,7] Most of the commonly available serological tests show significant positivity only after the first week of illness. Immunofluorescence Assay (IFA) is the gold standard test for serodiagnosis of rickettsial disease which detects IgG and IgM antibodies, but main drawbacks of IFA is that it is very expensive and not widely available. [8,9] WeilFelix (WF) test is classic serological test which is widely available but not widely acceptable because of its low sensitivity and specificity. But in developing countries where specific diagnostic tests are not widely available WF can be used as screening test. [10]

The test should be interpreted in conjugation with history and clinical presentation. Initial diagnosis and treatment should be based on a high index of suspicion and appropriate clinical features. 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. [7]

Hence the present study was conducted to know various clinical manifestations and laboratory diagnosis of Rickettsial disease in pediatric age group so that it can be diagnosed early with high index of suspicion and specific treatment is initiated to prevent mortality.

Material & Methods

A prospective observational study was conducted at Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India for the duration of 24 months (December 2016 to Jan November 2018), involving patients admitted between 2 months to 18 years of age with a diagnosis of Rickettsial fever. A total of 50 cases who were admitted with complaints of fever and presence of one or more of the following clinical features: Rash, edema, eschar, hepatosplenomegaly, lymphadenopathy, History of contact with pets and history of tick bite. Tick exposure was said to occur when ticks were seen on clothes of child or inside the house or history of playing in an area where ticks were seen.

Inclusion Criteria

- Children less than 18 yrs of age
- Hospitalized children with fever and presence of one or more of the following clinical features: Rash, edema, eschar, hepatosplenomegaly and lymphadenopathy.
- History of contact with pets or live stocks and history of tick bite.

Exclusion Criteria

- When cause of fever is established.
- Reliable informant not available.
- Refusal for admission

Methodology

Data was collected from patients and/or their reliable informants who were admitted in Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India. Questions were asked regarding symptoms and signs to patients and relevant investigations carried out based on Rathi Goodman Aghai (RGA) clinical scoring system for spotted fever group. [11]

Statistical Analysis:

Data collected was entered in Microsoft excel and analysed using EpiInfo 3.5.3 software. Descriptive statistics like proportion was calculated. Chi-square test was used as test of significance.

Results

Table 1: Demographic details of the study population

Parameter	Frequency	Percentage
Age		
<1 year	3	6
1-5 years	17	34
6-10 years	16	32
>10 years	14	28
Gender		
Male	32	64
Female	18	36
Geographical location		
Rural	40	80
Urban	10	20

Most common age group observed was 1-5 years accounting to 34%. The youngest affected patient was 2-month-old. Males (64%) were most commonly affected group in our study. 80% of the patients hailed from rural background.

Table 2: Symptoms and clinical findings in study population

Parameter	Frequency	Percentage
Symptoms		
Fever	50	100
Maculopapular rash	29	58
Headache	18	36
Altered sensorium	16	32
Convulsions	14	28
Difficulty in breathing	14	28
Abdominal distension	12	24
Eschar	5	10
Gangrene	4	8
Clinical examination		
Hepatomegaly	45	90
Edema	26	52
Lymphadenopathy	15	30
Splenomegaly	12	24

Fever was the most common symptom present in all the cases enrolled in the study followed by rash in 29 (58%) cases. Eschar though a characteristic feature of rickettsial infection was found in only 5 (10%) of the cases. Clinical examination revealed hepatomegaly in 45 (90%) cases, followed by lymphadenopathy in 15 (30%) cases and splenomegaly in 12 (24%) of cases.

Table 3: Laboratory findings

Laboratory derangements	Frequency	Percentage
Thrombocytopenia	47	94
Hypoalbuminemia	46	92
Hyponatremia	43	86
Anemia	27	54
Leucocytosis	18	36
Weil-Felix test		
Scrub typhus (OX-K)	34	68
Spotted fever (OX-19, OX-2)	11	22
Other typhus	7	14

Investigations done in our study subjects showed that out of the 50 cases, 47 (94%) had thrombocytopenia. Hypoalbuminemia was seen 46 (92%) cases and hyponatremia was seen in 43 (86%). Anemia was seen in 27 (54%) of the cases.

Table 4: Correlation of rickettsial score with Weil Felix test

Rickettsialscore	Weil-Felix		Total	p value
	Positive	Negative		
<14	12	0	12	0.740
>14	36	2	38	
Total	48	2	49	

There was no statistical significant correlation between Rickettsial score and Weil-Felix test according to our study.

Table 5: Morbidity and mortality

Parameter	Frequency	Percentage
Meningoencephalitis	8	16
Pneumonia	4	8
Hepatitis	4	8
Vasculitis	3	6
Pleural effusion	2	4
Acute kidney injury	2	4
Hepatic encephalopathy	1	2%
Bronchitis	1	2%
MODS	1	2%
Myocarditis	1	2%
Death	1	2%

Complications were seen in 28 (56%) of the cases, of which meningoencephalitis was the most common seen in 8 (16%) of the cases, followed by pneumonia and hepatitis in 4 (8%) cases each. 1(2%) patient required hemodialysis.

Discussion

Common serological tests used to diagnose rickettsial fever are non-specific. The gold standard serological tests like indirect immunofluorescent antibody assay are expensive and not easily available. [6,12] Most of the commonly available serological tests show significant positivity only after the first week of illness. 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. [12]

Most common age group observed was 1-5 years accounting to 34%. The youngest affected patient was 2-month-old. Males (64%) were most commonly affected group in our study which was in concurrence with other studies. [13,14] Rickettsial organisms predominantly infect the vascular endothelium and reticuloendothelial cells. Vasculitis is the basic mechanism for the pathophysiology of rickettsial illness including skin rash, edema, tissue hypoxia, formation of microthrombi and end organ damage. These organisms induce various subsets of chemokine genes in infected cells, some in response to transcription factor activator protein 1 which is mainly responsible for microvascular injury. [15] 80% of the patients hailed from rural background. Fever was the most common symptom present in all the cases enrolled in the study followed by rash in 29 (58%) cases. Eschar though a characteristic feature of rickettsial infection was found in only 5 (10%) of the cases which was the same in other studies. [13,16]

Clinical examination revealed hepatomegaly in 45 (90%) cases, followed by lymphadenopathy in 15 (30%) cases and splenomegaly in 12 (24%) of cases. Investigations done in our study subjects showed that out of the 50 cases, 47 (94%) had thrombocytopenia. Hypoalbuminemia was seen 46 (92%) cases and hyponatremia was seen in 43 (86%). Anemia was seen in 27 (54%) of the cases which was less as compared to study conducted by Hullatti et al. [17] There was no statistical significant correlation between Rickettsial score and Weil-Felix test according to our study. The diagnosis of rickettsial fever was made using serological testing. Though rickettsial DNA-PCR and immunofluorescence assay are the confirmatory tests due to their non-availability and expensiveness in a resource limited setting like this, Weil-Felix is a cheaper alternative. Hence, Weil-Felix test was used in this study. A titre of 1:80 was considered to be positive. [18] Complications were seen in 28 (56%) of the cases, of which meningoencephalitis was the most common seen in 8 (16%) of the cases, followed by pneumonia and hepatitis in 4 (8%) cases each. 1(2%) patient required hemodialysis. Unlike studies done by Thomas et al, Murali et al and Kumar et al authors observed a higher mortality rate of 10.2% due to late presentation and hence delay in starting appropriate therapy. [13,19,20]

Serological evidence is the mainstay for the diagnosis of rickettsial infections. The various serological tests available include Weil Felix Test, Enzyme Linked Immuno Sorbent Assay (ELISA), Indirect Haemagglutination Test (IHA) and Indirect Immunofluorescence Antibody Test (IFA). Weil-Felix test is a heterophile agglutination test widely available for the diagnosis of rickettsial diseases even in limited resource settings. [21] The gold standard serological test for the diagnosis is Indirect Immunofluorescence Antibody (IFA) test. Disadvantages of IFA are it is expensive and requires a fluorescence microscope which is not easily available in all centres. In view of the disadvantages of both IFA and Weil-Felix tests, an alternate serological test, ELISA is the most cost effective method.

Conclusion

A proper history and careful physical examination help in the diagnosis of Rickettsial disease. Laboratory tests can be carried out to support the diagnosis. Weil-Felix test can be carried out for early detection of suspicious case in resource limited set up.

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