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Original Research Article

Clinicopathological profile of rickettsial fever in tertiary healthcare centre: a prospective case study

Mallesh K., Sarala Sabapathy*, Rashmi Patil, Niharika Shetty

Department of Paediatrics, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Sarala Sabapathy,
E-mail: sarala.s@hotmail.com

ABSTRACT

Background: Rickettsia are obligate intracellular proteobacteria spread by eukaryotic vectors like ticks, mites, fleas and lice. Rickettsial infections are generally incapacitating and difficult to diagnose; Case fatality rates up to 45 percent is seen in cases with multiple organ dysfunction. The disease continues to be under diagnosed and treated. Objective of this study was to study the clinicopathological profile and outcome of children admitted with rickettsial fever. To study the correlation between Rathi-Goodman-Aghai score and Weil-Felix test. To study the response of rickettsial fever to Doxycycline.
Methods: This study is a prospective observational study conducted from December 2017 to April 2019 at a tertiary health care center in South India, involving patients admitted between 2 months to 18 years of age with a diagnosis of Rickettsial fever. Clinical data and investigations were collected and analysed. The response to doxycycline was recorded.
Results: Total of 49 patients were enrolled in the study. Most common age group affected was between 1 to 5 years accounting for 32.7% of the cases. 78% of the patients hailed from rural background. Most common presentation being fever, present in 100% of the cases. 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.
Conclusions: Rickettsial infection is re-emerging with propensity for life threatening complications. There is no statistical significant correlation between Rickettsial score and Weil Felix test. Early treatment has better outcome.

Keywords: Rathi-Goodman-Aghai score, Response to doxycycline, Rickettsial fever, Weil- Felix test

INTRODUCTION

Rickettsial diseases, caused by a variety of obligate intracellular, Gram-negative bacteria from the genus Rickettsia, belonging to the Alphaproteobacteria, are considered some of the most covert emerging and re-emerging diseases and are being increasingly recognized.[1,2] The infection has established itself as an endemic disease in Southeast Asia including Thailand, China, and Taiwan.[3-5] Rickettsial disease has been reported from various parts of India, such as Tamil Nadu, Karnataka, Kerala, Maharashtra, and some parts of northern India.[1,2]

Among the major groups of rickettsioses, commonly reported diseases in India are scrub typhus, murine flea-borne typhus, Indian tick typhus and Q fever.[1,2,6] Rickettsial infections are generally incapacitating and difficult to diagnose; untreated cases have case fatality rates as high as 30-45 per cent.[1,2,7]

Despite multiple studies being published on rickettsial fever, the disease entity continues to be under diagnosed and hence is the need for the study.

METHODS

This study is a prospective observational study conducted from December 2017 to April 2019 at a tertiary health care center in South India, involving patients admitted between 2 months to 18 years of age with a diagnosis of Rickettsial fever. Clinical data and investigations were collected and analysed. The response to doxycycline was recorded in terms of clinical improvement within 2 days.

Inclusion criteria

- Eligible patients 2 months to18yrs of age who had undifferentiated fever >5days
- Compatible clinical scenario[8]
- Suggestive epidemiological features.

Exclusion criteria

- Cause of fever known at the time of admission.
- Patients diagnosed with other causes of fever, during course in the hospital.
- Children treated elsewhere prior to admission.
- Patient treated on outpatient basis or details not available.

Methodology of this study was the patients with rickettsial fever, admitted to the department of pediatrics were enrolled in the study. Demographic data, presenting symptoms, rickettsial score, investigations which included complete blood count, serum electrolytes, liver function test, Weil-Felix test of the patients were collected.[9] Probable rickettsial fever cases were treated with Doxycycline (4.4mg/kg day in two divided doses) for 3 days after subsidence of fever or total of 7 days in uncomplicated cases and up to 10 days in severe or complicated cases. Doxycycline was administered through intravenous route or nasogastric tube or per orally according to their clinical status.[8] The response to treatment was recorded in terms of defervescence within 48 of starting therapy.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

The total number of rickettsial cases admitted during the study period were forty-nine (Figure 1). Most common age group observed was 1-5 years accounting to 32%. The youngest affected patient was 2-month-old. Males (61%) were most commonly affected group in our study. 78% of the patients hailed from rural background (Table 1).

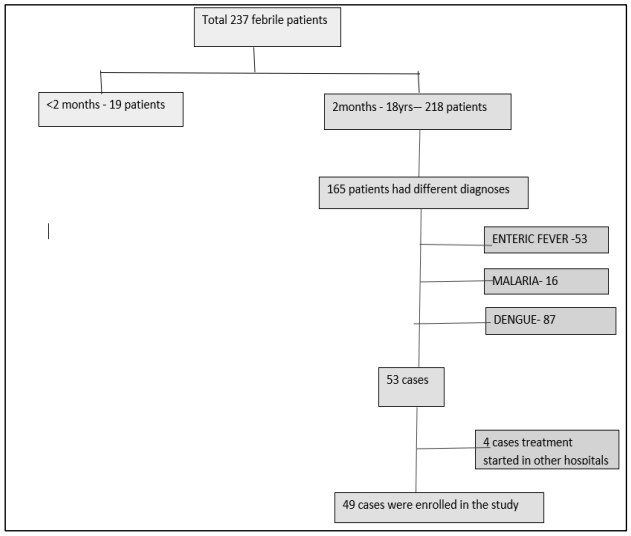

Figure 1: Enrollment of cases in the study.

Table 1: Demographic details of the study population.

Parameter	Frequency	Percentage
Age		
<1 year	3	7%
1-5 years	16	32%
6-10 years	15	31%
>10 years	15	30%
Gender		
Male	30	61%
Female	19	39%
Geographical location		
Rural	38	78%
Urban	11	22%

Fever was the most common symptom present in all the cases enrolled in the study followed by rash in 28(57%) cases. Eschar though a characteristic feature of rickettsial infection was found in only 5(10%) of the cases. Clinical examination revealed hepatomegaly in 45(91.8%) cases, followed by lymphadenopathy in 14(28.6%) cases and splenomegaly in 11(22.4%) of cases (Table 2).

Investigations done in our study subjects showed that out of the 49 cases, 45(91.8%) had thrombocytopenia. Hypoalbuminemia was seen 44(89.8%) cases and hyponatremia was seen in 43(87.7%). Anemia was seen in 25(51.1%) of the cases (Table 3).

Table 2: Symptoms and clinical findings in study population.

Parameter	Frequency	Percentage
Symptoms		
Fever	49	100%
Maculopapular rash	28	57.1%
Headache	17	34.7%
Altered sensorium	16	32.7%
Convulsions	13	26.5%
Difficulty in breathing	13	26.5%
Abdominal distension	12	24.5%
Eschar	5	10.2%
Gangrene	3	6.1%
Clinical examination		
Hepatomegaly	46	91.8%
Edema	25	51%
Lymphadenopathy	14	28.6%
Splenomegaly	11	22.4%

Table 3: Laboratory findings.

Laboratory derangements	Frequency	Percentage
Thrombocytopenia	46	91.8%
Hypoalbuminemia	45	89.8%
Hyponatremia	44	87.7%
Anemia	26	51.1%
Leucocytosis	17	34.6%
Weil-Felix test		
Scrub typhus (OX-K)	33	67%
Spotted fever (OX-19, OX-2)	10	21%
Other typhus	6	12%

Out of the 49 cases, 39(80%) cases had rickettsial score more than 14. In our study Rickettsial score had a sensitivity of 97.17% and positive predictive value of 100%. Weil- Felix test was positive in 48(98%) of the patients. In Weil-Felix test OX-K was positive in 33(67%) of the patients suggestive of scrub typhus, followed by spotted fever in 10(21%) and typhus in 6(12%) of the cases (Table 3). There was no statistical significant correlation between Rickettsial score and Weil-Felix test according to our study (Table 4).

All children with probable rickettsial fever cases defined according to IAP guidelines were treated with Doxycycline (4.4 mg/kg in two divide doses) through intravenous route or nasogastric tube or per orally according to their clinical status.[8]

Authors studied the response to Doxycycline which showed 39(78%) cases improved within 48 hours of start of treatment. Out of the remaining 10 cases, 5 cases showed delayed response and the remaining 5 cases showed no response due to late presentation and for whom treatment was started after 2 weeks of illness.

Complications were seen in 29(59%) of the cases, of which meningoencephalitis was the most common seen in 9(18%) of the cases, followed by pneumonia and hepatitis in 4 (8.2%) cases each. 13(26.5%) cases required respiratory support in the form of non-invasive ventilation or endotracheal intubation. 1(2%) patient required hemodialysis (Table 5).

Table 4: Correlation of rickettsial score with Weil Felix test.

Rickettsial score	Weil-Felix		Total	p value
	Positive	Negative		
<14	10	0	10	0.736
>14	38	1	39	
Total	48	1	49	

Table 5: Morbidity and mortality.

Parameter	Frequency	Percentage
Meningoencephalitis	9	18%
Pneumonia	4	8.2%
Hepatitis	4	8.2%
Vasculitis	3	6%
Pleural effusion	2	4.1%
Acute kidney injury	1	2%
Hepatic encephalopathy	1	2%
Bronchitis	1	2%
MODS	1	2%
Myocarditis	1	2%
Death	1	2%

Outcome was measured in terms of improvement or death. 5(11%) cases admitted with Rickettsial fever succumbed due to complications. Non survivors had duration of hospital stay ranging from 3-14 days.

DISCUSSION

Rickettsial infections have a global distribution and are reported from almost all parts of India. Rickettsial diseases vary in severity from self-limited mild illnesses to fulminating life threatening infections.[1,2,10] In the scenario of over-whelming bacterial and viral infections and parasitic infestations, Rickettsial diseases continue to be under-diagnosed.[1,2,6,10]

Authors studied the clinical profile of patients presenting to a tertiary hospital with rickettsial fever over a period of one year and four months. A total of 49 cases were enrolled in the study. This study showed most common age group being affected was between 1-5 years (32%) followed by 6-10 years (31%). Males (61%) were most commonly affected which was in concurrence with other studies. [6,11,12] Of the study population,78% hailed from rural background. Most common presentation of this patients was fever (100%), followed by maculopapular rash in 57% cases consistent with study conducted by Thomas et al unlike the findings observed in studies

conducted by Kumar et al, (20%) and Murali et al, (100%).[6,11,12] Though a characteristic feature eschar was found only in 10% of the patients presenting with rickettsial fever, which was the same in other studies.[6,13] Hepatomegaly was seen in 91.8% cases which was consistent with other studies.[6,12,13] Lymphadenopathy was found in 28.6% of the cases and splenomegaly was found in 22.4% of the cases which was less common as compared to study conducted by Reddy et al.[13]

Haematological investigation done in this study showed leukocytosis in 34.6% cases which was less as compared to study conducted by Hullatti et al.[14] On the other hand thrombocytopenia was found in 91.8% cases in this study and 42% of the cases had thrombocytopenia in study conducted by Hullatti et al. Hyponatremia was observed in 87.7% patients which was similar.[14]

Rickettsial score of more than 14 was considered significant (Rathi score). 80% cases had significant rickettsial score. According to this study sensitivity of rickettsial score was 97.1% and positive predictive value was 100%.

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.[1,8] Weil-Felix was positive in 98% of this study population. OX-K was positive in 67% of the patients suggestive of scrub typhus.

Authors studied the correlation between Rickettsial score and Weil-Felix test and found no statistical significance (p value=0.736).

Response to doxycycline was measured in terms of time for defervescence. 78% of the patients responded to doxycycline within 48 hours of starting the treatment. 10.2% of the cases showed delayed response. No response was seen in patients who presented late, for whom treatment was started after 2 weeks of illness.

Complications were seen in patients presenting after 1 week of illness and was present in 59% of the cases. Most commonly seen was meningoencephalitis in 18% cases which was comparable to studies.[6,11] Supportive treatment in the form of ventilatory support was required in 26% cases and 2% required peritoneal dialysis. 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.[6,11,12]

Limitation of this study was to Diagnosis of rickettsia was made clinically for enrolling in the study and confirmatory test was not conducted.

CONCLUSION

Any child with undifferentiated fever >5 days, hailing from rural background; strong suspicion of rickettsial fever to be made.

Rathi-Goldman-Aghai score and Weil-Felix test combined together aid in early diagnosis.

Early initiation of treatment prevents complications and results in rapid recovery of the patient, hence reducing morbidity and mortality.

Outcome isn't satisfactory in patients for whom delayed initiation of treatment is done.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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