



## RICKETTSIAL FEVER A FORGOTTEN CLINICAL DOGMA !!

### Paediatrics

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### ABSTRACT

**Background:** The clinical presentation of Rickettsial infections is notoriously non-specific and varies from mild to severe and often mimics benign viral illness. The incidence of Rickettsial infection had seen a significant decline in the nineties secondary to the widespread use of insecticides. But the past decade has again witnessed a resurgence in the incidence of Rickettsial infection. **Objective:** To study the incidence, clinical profile, hematological parameters, efficiency of the serological test (WFT), complications, and outcome of Rickettsial fever in children. **Methods:** A prospective clinical study was done on 50 patients who were suspected clinically and supported by the lab. investigations of Rickettsial Fever in VIMS Ballari during the period of November 2021 to April 2022 were included in this study. All cases of acute febrile illness and positive Weil Felix test with a titer of 1:80 diagnosed as Rickettsial disease were analyzed using relevant statistical methods **Results:** 50 Children of < 14yrs diagnosed to have Rickettsial fever of which the majority were from rural (72%). Clinical features included fever (100%), rash (70%), constitutional symptoms (92%), edema (64%), pain abdomen (42%), and 28% of cases were having CNS symptoms. 54% of cases developed complications like encephalitis (28%), Pneumonia (20%), Hepatitis (16%), DIC (6%), AKI (4%), Sepsis (4%), Purpura fulminans (4%). 94% of cases have shown a good response to doxycycline and were discharged and only 6% of cases died during the study period. **Conclusion:** There is a re-emergence of Rickettsial disease in this part of north Karnataka which might have been overlooked earlier due to a low index of suspicion. In view of this, it is imperative that if intervened at an appropriate stage Rickettsial infection has an excellent prognosis. Weil-Felix test serves as a useful economic tool for laboratory diagnosis of Rickettsial disease in resource-poor settings.

### KEYWORDS

Rural, Pneumonia, Encephalitis, Purpura fulminans, Weil-Felix serology, Doxycycline.

### INTRODUCTION

Rickettsial diseases have been reported in various parts of India. The clinical presentation of these infections is notoriously non-specific and varies from mild to severe and often mimics benign viral illness<sup>1</sup>. The incidence of rickettsial infection had seen a significant decline in the nineties secondary to the widespread use of insecticides. But the past decade has again witnessed a resurgence in the incidence of rickettsial infection.

Though varieties of rickettsial infections are described in the literature the main agent that we come across is rickettsial typhus caused by *Orientia tsutsugamushi*. It is often underdiagnosed or misdiagnosed because of a low index of suspicion or lack of sensitive and specific diagnostic tools.<sup>2</sup>

Today rickettsial infection can be accurately diagnosed by immunofluorescence and ELISA. But these tests are very expensive and are not easily available. As a result, the main diagnostic tool in the clinician's hand is still the Weil Felix test. Even though the Weil Felix agglutination test is not very sensitive, when positive, it is a rather specific test.<sup>3,4</sup> has been proven to be quite acceptable.

In view of this, the wide and varied clinical presentations of rickettsial infections must be studied in detail because if intervened at an appropriate stage rickettsial infection has an excellent prognosis.

### MATERIALS AND METHODS

#### Study Design:

Hospital-based Prospective Study.

#### Source Of Data

All patients were suspected clinically and supported by the lab. investigations of Rickettsial Fever in VIMS Ballari during the period of November 2021 to April 2022 were included in this study.

#### Inclusion Criteria:

- The patients of both sexes aged < 14 years.
- Weil Felix positivity in dilutions greater than 1 in 160 or the rise of four-fold or more in titers on repeat testing starting from 1:80
- Typical clinical presentations with eschar

#### Exclusion Criteria:

- Subjects who do not consent to the study.

- Subjects more than 14 years of age
- Cases with other established causes of infection

#### Sample Size Estimation

50 cases based on the incidence of Rickettsial fever in the Paediatric age group in our hospital statistics during previous years

#### Statistical Analysis

##### Statistical Methods

Chi-square analysis: It is a method of testing the significance of the difference between two proportions. It has the advantage that it can be used when more than two groups are to be compared.

Descriptive statistics in the form of percentages and number of cases were considered in the study.

#### Statistical Software:

The statistical operations were done through SPSS (Statistical Presentation System Software) for Windows, version 17. Significance was taken at 5% level

### RESULTS

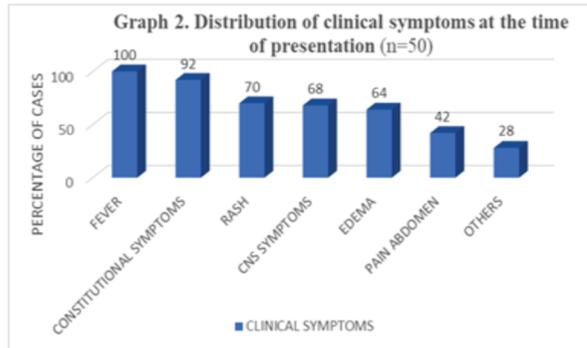
Rickettsial infections commonly were observed between 6 to 10yrs of age group (42%). The second most common age group affected is between 1 to 5yrs (34%).

Out of 50 cases, 27 cases (54%) were females and 23 cases (46%) were male. OUT OF 50 CASES, 36 CASES(72%) were from rural areas and the rest cases (28%) were from urban areas.

Clinically, out of 50 cases fever was the most common symptom which was seen in 100% of cases, followed by constitutional symptoms like facial puffiness, headache, vomiting, Myalgia, redness of eyes, etc., in 92% of cases. The rash is seen in 70% of cases, CNS symptoms in the form of convulsions and altered sensorium in 68% of cases, edema in 64% of cases, and pain abdomen in 42% of cases. Other symptoms like cough, melena, haematuria, hurried breathing, etc., is seen in 28% of cases.

All 50 cases in the study had (100%) fever and the duration of fever was 4-7 days in 23 cases (46%), less than 4 days in 20 cases (40%), 8-10 days in 6 cases (12%) and only 1 case and fever for more than 10 days. The mean duration of fever was 5 days and a standard deviation

of 2.3. Out of 50 cases, 35 cases (70%) had a rash that developed on 3<sup>rd</sup> day of illness in 46% of cases, on 4<sup>th</sup> day in 22% of cases, and on 5<sup>th</sup> day in 2% of cases. 24 cases (48%) had rashes involving the whole body and 11 cases (22%) showed the centripetal distribution of rash.



Clinically 43 cases (86%) were hemodynamically stable at the time of presentation and 7 cases (14%) were hemodynamically unstable. Rashes are seen in the form of Petechiae (58%) and Purpura (12%). CNS involvement is seen in 38% of cases and RS involvement in 20% of cases in the form of Encephalitis and Pneumonia respectively. There was hepatomegaly in 70% of cases and splenomegaly in 20% of cases. 12% of cases were found to have icterus, 10% of cases had lymphadenopathy and 4% of cases had Eschar.

Laboratory investigations showed anemia in 50% of cases, leukopenia in 16%, lymphocytic leucocytosis in 56%, thrombocytopenia in 78%, hyponatremia in 72%, and elevated C-Reactive Protein (CRP) in 88% of cases. Elevated liver enzymes were seen in 18% of cases and altered coagulation profile in 12% of cases. Weil Felix test is used for screening based on antibody titers. It showed rising antibody titers against OXK antigen in 52% of cases and OX19+OX2 in 38% of cases, OX19 alone in 8% of cases and 2% against all 3 antigens.

Chest x-ray was normal in 72% of cases, 16% of cases had lobar pneumonia, 4% of cases had bronchopneumonia and 1 patient had cardiomegaly with a CT ratio of 0.64.

Out of 19 patients who had CNS involvement, 11 cases showed an aseptic meningitis picture in CSF analysis. The majority of cases were having normal sugar levels with mainly lymphocytes in CSF. Only 21% of cases showed a raise in proteins, 10% showed decreased glucose levels and 58% of cases showed a rise in cell count.

Rickettsial infections have a good prognosis if treated early. Out of 50 cases, 47 were discharged (94%) and only 6% of cases have died and 54% of cases had developed complications.

Complications due to rickettsial infections were seen in 54% of cases. Out of which Rickettsial Encephalitis (52.2%) is the most common complication, followed by Pneumonia (43.5%), Hepatitis (34.8%), shock (17.4%), and DIC (13%). Other complications were meningoencephalitis, sepsis, AKI, and purpura fulminans in 8.7% of cases each.

## DISCUSSION

While rickettsial diseases are reported from various parts of India, including Karnataka, this study describes their existence in central Karnataka.<sup>5,6,7,8,9</sup> However, the reported cases underestimate the burden of rickettsial diseases in India due to the lack of both community-based studies and the availability of specific laboratory tests.<sup>10</sup>

Rickettsial infections are emerging tropical infectious diseases caused by obligate intracellular pleomorphic gram-negative coccobacilli.<sup>11</sup> Infection is acquired by transmission through arthropod vectors or by direct exposure to the reservoir animal. Common arthropod vectors that transmit the disease to humans include ticks, fleas, mites, and lice. Reservoir host animals harboring rickettsial organisms are rodents, dogs, cattle, and mice.<sup>12</sup> Deaths due to scrub typhus were observed during the World War II era.<sup>13,14</sup> Several reports of outbreaks of rickettsial diseases are described in India.<sup>15</sup> It is increasingly realized that rickettsial diseases are under-diagnosed in India and they significantly contribute to mortality and morbidity of tropical febrile illness. Rickettsial diseases most common being scrub typhus is

increasingly reported in the last 2 decades from all over India including Karnataka, Maharashtra, Tamil Nadu, Kerala, Himachal Pradesh, Delhi Haryana and Northeastern states.<sup>15,16,17,1</sup>

Most of the outbreaks are reported between June to December suggesting predilection for cooler months of the year.

Vasculitis is the basic mechanism for the pathophysiology of rickettsial illness including skin rash, edema, tissue hypoxia, formation of microthrombi, and end-organ damage.

The rash was observed in 18.5% of our cases while the occurrence of rash in various studies ranges from 15-91% of cases.

Eschar when present is a valuable sign for the diagnosis of rickettsial fever, especially scrub typhus. In the present study, eschar was observed in only 4% of the cases but they were all patients with scrub typhus. Similarly, other Indian studies have reported a higher occurrence of eschar in scrub typhus.<sup>16,17</sup> We found combined hepatosplenomegaly in the majority of cases (70%) while isolated hepatomegaly and splenomegaly were present in 70% and 20% of children respectively. In our study, vomiting, hepatosplenomegaly, anemia, myalgia, skin rash, lymphadenopathy, and elevated CRP is seen in patients with spotted fever as compared to scrub typhus. Clinical evidence of fluid accumulation in the form of edema was observed in 34% of cases indicating dengue fever as the main differential diagnosis.

Most of the complications of rickettsial fever are usually seen during the second week of illness. Common complications described in the literature include severe thrombocytopenia with bleeding diathesis, meningoencephalitis, pneumonia, ARDS, DIC, AKI, myocarditis, and purpura fulminans. Platelet count of <50,000/mm<sup>3</sup> was found in 26% of our cases. Except for anicteric hepatitis found in 18% of children, other common complications observed were meningitis, ARDS, pneumonia, AKI, and shock. The incidence of AKI was only 5% in this study, while other studies have reported an incidence ranging from 12-23% of the subjects.<sup>18</sup>

Laboratory parameters that are characteristically observed in children with rickettsial fever include anemia, leukocytosis, thrombocytopenia, and elevated CRP.<sup>18</sup> Anemia was found in 50% of subjects while leukocytosis was observed in 82% of children. Thus anemia and leukocytosis are commonly seen in rickettsial fever in contrast to dengue fever where hemoconcentration and leukopenia are common. Elevated CRP was found in 88% of cases and in all patients with spotted fever. Raised CRP was observed in 100% of patients in a study done in Taiwan.

We found hypoalbuminemia in a significant number of subjects (53.2%) with rickettsial fever. Hypoalbuminemia is a known finding in scrub typhus and is significantly associated with an increased number of complications and mortality as reported in a study conducted in the Republic of Korea. Endothelial damage with subsequent increased vascular permeability and extravascular protein loss is the basis of hypoalbuminemia. We found hyponatremia in 28% of children with rickettsial fever. Serological evidence is the mainstay for the diagnosis of rickettsial infections. The various serological tests available include Weil Felix Test, 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. The gold standard serological test for diagnosis is the IFA test.

## CONCLUSION

Fever for a duration of 5 days or more in a child hailing from an endemic area for rickettsial fever and a history of exposure to reservoir animals may give a possible clue in suspecting rickettsial fever by history.

The presence of maculopapular blotchy rash involving palms and soles, edema and hepatosplenomegaly are the characteristic features in clinical examination.

In view of this, it is imperative that the wide and varied clinical presentations of rickettsial infections be studied in detail because if intervened at an appropriate stage rickettsial infection has an excellent prognosis

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