



## Original Research Article

## Prevalence of Rickettsial infections in a tertiary care centre

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## ABSTRACT

**Introduction:** Rickettsial infections are the most covert re-emerging infections of the present times. They are considered one of the important causes of Pyrexia of Unknown origin (PUO). They are often under diagnosed due to low index of suspicion, nonspecific signs and symptoms and absence of widely available sensitive and specific diagnostic tests. These diseases have a high mortality, which can be averted if diagnosed and treated early. Weil- Felix test is the cheapest and widely used test for diagnosis in India.

**Aim:** The present study was undertaken with the objective of evaluating the patients with Febrile illness, for rickettsial infection using Weil- Felix test and study their demographic and clinical profile.

**Materials and Methods:** Weil-Felix test was done on serum samples of 120 patients with fever since 7-10 days, from October 2017 to October 2019 and evaluated for Rickettsial infection. Detailed history, signs, symptoms were recorded.

**Results:** Out the 120 patients, 25 showed a titre of >1:80 in OX2, OX19 and 5 cases showed titre of >1:160 in OX K. The disease was more common in children and in the cooler months. Fever, rash, headache, vomiting and pain abdomen were common symptoms. Most common signs were rash (27 cases) and conjunctival congestion (19 cases).

**Conclusion:** Though the sensitivity and specificity of Weil-Felix test is low, it is done even today as it is the most convenient and economical test available for the diagnosis of Rickettsial infections. Prevalence of Rickettsial diseases is significant in this region and greater clinical awareness in the differential diagnosis of fevers is required for early diagnosis and treatment.

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## 1. Introduction

Rickettsial infections are some of the most covert re-emerging zoonotic diseases. They are incapacitating and notoriously difficult to diagnose. Untreated cases may have fatality rate as high as 30-35% but when diagnosed properly can be easily treated.<sup>1</sup> Rickettsial diseases have been one of the great scourges of mankind, occurring in devastating epidemics during times of war and famine.<sup>2</sup>

Rickettsia are a group of small non-motile, obligate intracellular Gram negative coccobacilli which are transmitted by arthropod vectors like lice, fleas, ticks and mites.<sup>3</sup> Many Rickettsiae are transmitted transovarially in the arthropod,

which serves as both vector and reservoir.<sup>4</sup> Infection in man occurs by infected vector bite or exposure to reservoir host.

After entering the host they target the vascular endothelium and reticulo endothelial system explaining thereby the basic pathogenesis of vasculitis seen in these infections. Due to their obligate intracellular nature, these organisms cannot be cultivated in culture media and require tissue culture or laboratory animals for their isolation. These organisms are classified into four groups: Scrub typhus (*Orientia tsutsugamushi*), Spotted fever group (*Rickettsia rickettsii*, *Rickettsia conorii*, *Rickettsia akari*), Typhus group (*Rickettsia prowazekii*, *Rickettsia typhi*) and miscellaneous group like *Ehrlichia*, *Anaplasma* etc. Of these *R.conorii* and *O.tsutsugamushi* are the commonest organisms causing Rickettsial infections in India. Vasculitis is responsible for

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rash, tissue hypoperfusion, oedema and end organ ischemic injury. Formation of thrombi leads to infarction and haemorrhagic necrosis. Vascular leakage results in edema and complications like meningoencephalitis, respiratory distress, Acute Renal failure. Finally a clinical syndrome resembling DIC may occur.<sup>5</sup>

Incubation period is 2-21 days. High grade fever of abrupt onset, headache, myalgia, rash are the most common symptoms. Rash is centripetal, macular, papular or ecchymotic. Eschar is a painless necrotic area covered with crust and is usually seen at the site of attachment of vector. Nonspecific gastrointestinal, respiratory or neurological symptoms and signs may be seen. Edema over Periortibial region, dorsum of foot and hand or generalised edema may be seen. Leucopenia, thrombocytopenia, hyponatremia, elevated transaminases are observed.

Rickettsial infections are distributed throughout the world and are reemerging in the Indian subcontinent, especially among children.<sup>6</sup> Rickettsial infections have been reported in various states of India like Jammu and Kashmir, Himachal Pradesh, Haryana, Madhya Pradesh, West Bengal, Assam, Sikkim, Kerala and Tamil Nadu.<sup>7</sup> These reported cases are an under estimate due to low index of suspicion, nonspecific signs and symptoms and nonavailability of specific diagnostic test.

Microimmunofluorescence, Indirect haemagglutination test, immune peroxidase assay, latex agglutination, ELISA, PCR, dot-blot immunoassay, Weil-Felix test are various serological tests for diagnosis of Rickettsial infections. Microimmunofluorescence is considered as the gold standard test. ELISA techniques, particularly immunoglobulin M (IgM) capture assays are probably the most sensitive tests available. In cases of infection with *O. tsutsugamushi*, a significant IgM antibody titre is observed at the end of 1<sup>st</sup> week, whereas IgG antibodies appear at the end of 2<sup>nd</sup> week. Polymerase chain reaction is a specific test for diagnosis. The Real Time PCR is used to target the gene encoding the major 56 kDa and/or 47 kDa surface antigens.<sup>8</sup> These tests are positive only after 5-7 days and play no role in initiation of specific therapy. Moreover these specific immunological tests are not easily available in developing countries like India. They require highly trained personnel and production of antigens may vary among different laboratories leading to inconsistencies in the interpretation of results. Weil-Felix test serves as a useful and affordable tool for laboratory diagnosis of rickettsial diseases in resource-poor countries.<sup>9</sup> The test has low sensitivity and specificity, but it is cost effective and widely available.

The present study was undertaken in Vijaya Diagnostic Centre, Kurnool with the intention to present the scenario of Rickettsial infections and study their demographic and clinical profile.

## 2. Materials and Methods

The samples were collected from patients admitted in Government General Hospital, Kurnool with complaints of fever since 10 days or more. The study period was from October 2017 to October 2019. The samples were subjected to Weil-Felix test at Vijaya Diagnostic centre, Kurnool.

Weil-Felix test is a Heterophile Tube Agglutination test based on the principle that some strains of *Proteus* share common somatic antigens with certain species of *Rickettsia*. Sera of patients infected with *Rickettsia* will, therefore, produce agglutination with *Proteus* antigen suspensions. Antigen suspensions of *Proteus* OX 19 antigen reacts strongly with sera of patients with the Typhus group *Rickettsia* and Rocky Mountain spotted fever, *Proteus* OX 2 with the sera of patients with Spotted fever infections, while the *Proteus* OX K with the sera of patients infected with Scrub typhus. Titres of > 1:80 for OX 2, OX 19 and titres of >1:160 for OX K were considered diagnostically significant.

The blood samples were collected in a BD vacutainer under aseptic precautions and serum separated. Antigens were procured from Tulip Diagnostics Ltd. and the Weil Felix test was done using standard protocol with serial doubling dilutions from 1:20 to 1:640. The titres of more than 1:80 for OX2 and OX19 and more than 1:160 for OX K were considered to be highly suggestive of Rickettsial infection.

The results were correlated with clinical history and manifestations. Investigations like complete blood picture, Liver function test, serum creatinine were also observed.

## 3. Results

Out of total 120 cases tested, 30 were positive for Rickettsial infection. 25 were positive for OX 2 and OX 19 and 5 were positive for OX K.

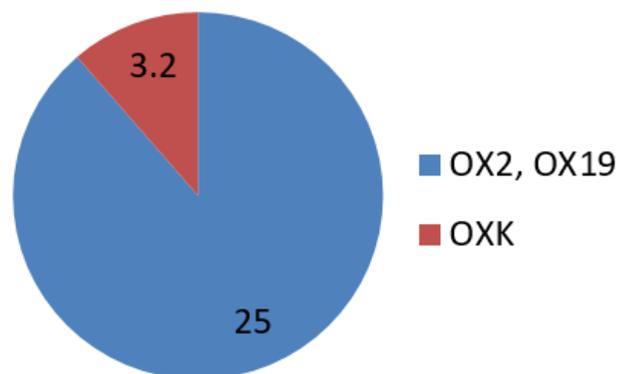


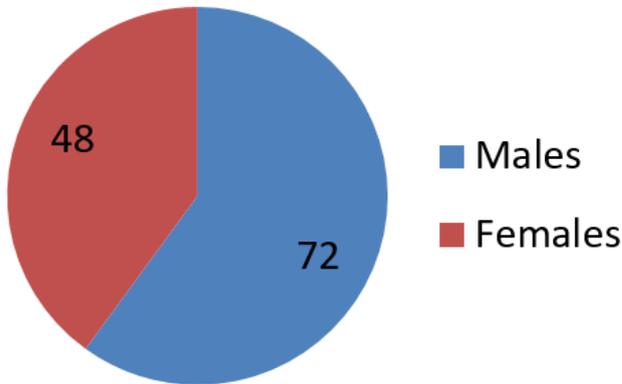
Fig. 1: Results of Weil Felix test

Most of the cases were in the age group of 0-10 years (38.33%) followed by 10-20 years (20%).

**Table 1:** Age wise distribution

Age (years)	No. of cases
0-10	46 (38.33%)
10-20	24 (20%)
20-30	14 (11.67%)
30-40	20 (16.67%)
40-50	16 (13.33%)

Males were 72 in number (60%) whereas females were 48 in number (40%).

**Fig. 2:** Sex wise distribution

Maximum no. of cases showed high titres of 1:640

**Table 2:** Titres obtained by Weil-Felix tube agglutination test

Titres	1:640	1:320	1:160	1:80
OX 2	18	5	2	-
OX 19	17	5	3	-
OX K	3	2	-	-

Most of the cases presented with clinical features of fever, rash, hepatomegaly, conjunctival congestion and headache.

**Table 3:** Clinical features in patients with positive Weil Felix Test (WFT)

Clinical features	No. of cases
Fever	30
Rash	27
Hepatomegaly	18
Conjunctival congestion	19
Headache and Myalgia	25
Pain abdomen and vomiting	16
Jaundice	11
Pedal edema	17
Altered sensorium	7
Eschar	2

Various laboratory abnormalities like mild anaemia, thrombocytopenia, leucopenia and hypoalbuminemia were observed.

**Table 4:** Investigations in patients with positive WFT

Investigations	No. of cases
Anaemia with Hb <10 g%	25
Thrombocytopenia	24
Hypoalbuminemia	17
Leucopenia	18
Leucocytosis	12
Hyponatremia	9
Elevated ALT levels	13

Out of 30 positive cases, 21 cases (70%) were seen during rainy season and 9 cases (30%) were seen winter.

All 30 patients diagnosed with Rickettsial infection were started on Doxycycline and 20 of them showed improvement without any sequelae, 10 did not come for follow up.

#### 4. Discussion

Rickettsial infections have been present in several states of India. They are difficult to diagnose and require consideration of clinical features, environmental factors, serological tests and response to antibiotics. In spite of all its drawbacks, Weil-Felix test still serves as an economical and useful diagnostic tool for laboratory diagnosis of rickettsial diseases provided the test is interpreted in the correct clinical context.<sup>3</sup>

Disease was more common among males (60%), similar to studies by Ramyashree et al., 2015, Sanap et al., 2017<sup>10,11</sup> Prevalence in paediatric population was 38.33%, correlated with study by Chunchanur et al.<sup>12</sup> Increased outdoor activity may be the reason for this gender and age bias. Majority of the cases were seen during rainy season (70%) followed by (30%) in winter, similar observation has been made in other studies as well.<sup>13</sup> This seasonality may be attributed to change in climate. After the rainfall, hatching of mite eggs into larvae (chiggers) responsible for the disease transmission may be favoured by increased humidity.<sup>14</sup> Awareness of seasonality is essential for taking up preventive measures.

Fever was the commonest clinical feature in our study followed by rash. A study by Udayan et al. showed 61.7% association<sup>15</sup> and a study by Mittal et al. showed 51.7% association of rashes with positive WFT a study by Mittal et al. showed 5.% association of rashes with positive WFT.<sup>16</sup> Our cases were from both urban and rural areas. Presence of disease in urban areas is reported in another study as well.<sup>13</sup> Eschar which is considered as pathognomic of Scrub typhus was seen only in 6.67%. Anaemia and thrombocytopenia was observed in many cases.

Weil-Felix test still remains an indispensable tool for diagnosis of rickettsial infections. In recent years Microimmunofluorescence assay (IFA) has become the reference test but the test is not widely available. Evaluations done by Prakash et al. showed that the Weil-

Felix test had a specificity of over 98% & and a sensitivity of about 43%.<sup>17</sup> Hechemy et al., demonstrated 70% agreement between Weil-Felix test and Microimmunofluorescence results especially with higher titres in Weil-Felix test.<sup>16</sup>

Greater clinical awareness, a high index of suspicion, better use of available diagnostic tools would increase the frequency with which rickettsial diseases are diagnosed which is necessary for their prevention and control.<sup>2</sup>

## 5. Conclusion

Rickettsial infections are re-emerging. They should be considered in the differential diagnosis of PUO, especially when associated with rash, gastrointestinal symptoms, seasonality etc. Delay in diagnosis and treatment may lead to complications and higher mortality. Early recognition and treatment with doxycycline can control the disease. Weil Felix test can be considered useful for initial diagnosis in resource poor settings, where specific tests are not available. Weil Felix test has low specificity/ sensitivity, so results should be interpreted in correlation with clinical features. Confirmatory tests such as Immunofluorescence assay or PCR should be performed whenever feasible for specific diagnosis.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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