Research Article

# Serological evidence of rickettsial infections in and around Davangere

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**Abstract**

**Background:** Fever of unknown origin (FUO) is one of the main causes of rickettsial infections. They are underestimated public health problems because of the difficulties with the clinical diagnosis and lack of laboratory methods in many geographical areas. The treatment is simple with doxycycline being the drug of choice.

**Objective:** To know the serological evidence of rickettsial infections in and around Davangere.

**Materials and Methods:** A prospective study was carried out for a period of 6 months in a tertiary-care centre, Karnataka, India. The serum samples from 60 FUO cases were analyzed for rickettsial antibodies by Weil–Felix test.

**Result:** Rickettsial antibodies were detected in 14 (23.33%) samples, of which 7 (50%) were positive for scrub typhus, 1 (7.14%) each for spotted fever group and typhus fever group, and 5 (35.71%) for more than one rickettsial illnesses. Seropositivity was higher among male subjects (57.14%) when compared with female subjects (42.86%). The maximum positivity (38.46%) was in the 46–60 years age group. The cases were more from August to October.

**Conclusion:** Rickettsial infections, particularly, scrub typhus, should be included in the differential diagnosis of FUO in and around Davangere region. This is, especially, after rainy season and during early cooler months.

**KEYWORDS:** Fever of unknown origin, Weil–Felix test, rickettsial infections, Davangere

## Introduction

The rickettsiae are cocco-bacilli and obligate intracellular parasites characterized by features such as being small, nonflagellate, gram-negative, and pleomorphic and transmitted by arthropod vectors. They are primary parasites of arthropods like lice, fleas, ticks and mites in which they are found in the alimentary canal. The vascular endothelium and reticuloendothelial cells in vertebrates, including humans, are infected by them.[1] The spotted fever, typhus, and scrub typhus groups, which are a group of antigenically related microorganisms, are categorized under the species of the genus *Rickettsia*.[2] Rickettsial fever is often marked as one of the main reasons for nonviral illnesses that present with a fever and rash, which are responsive to antimicrobial treatment; however, when untreated they can lead to significant morbidity and mortality.[3] Difficulty in diagnosis of these infections arise owing to conditions such as a reduced level of suspicion, nonspecific signs and symptoms, and the absence of widely available sensitive and specific diagnostic tests. Rickettsial infections prevail worldwide, except Antarctica. Several states in India such as Maharashtra, Tamil Nadu, Karnataka, Kerala, Jammu and Kashmir, Uttaranchal, Himachal Pradesh, Rajasthan, Assam, and West Bengal exhibited the prevalence of these infections.[4] To the best of our knowledge, information is scarce on the burden of these infections in Davangere region.[5] Therefore, this study was undertaken to determine the serological evidence of rickettsial infections in and around Davangere through the detection of their antibodies.

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## Materials and Methods

This is a prospective study, carried out for a period of 6 months from July to December 2014 in the Department of Microbiology, SS Institute of Medical Sciences and Research Centre, (SSIMS & RC), Davangere, Karnataka, India. SSIMS & RC is a tertiary-care centre situated in the central Karnataka committed to provide multispeciality medical services. A total of 60 patients in the age group from birth to 75 years attending the medicine and pediatric departments diagnosed with fever of unknown origin (FUO) in whom common illnesses including enteric fever, dengue, malaria, and brucellosis were ruled out were included.[6] Blood samples were collected from these patients to test for rickettsial antibodies by commercially obtained Weil–Felix test (PROGEN, Tulip Diagnostics (P) Ltd., Verna, Goa, India). The Weil–Felix test was performed according to the manufacturer's instructions. Serum samples positive in the slide test were confirmed with the tube test. Titers of more than 1:80 for OX2 and OX19 and more than 1:160 for OXK were considered diagnostically significant. This study was conducted after approval by Institutional ethics committee of SSIMS & RC, Davangere.

The Weil–Felix test is based on the principle that some strains of *Proteus* share common somatic constituents with certain species of *Rickettsia*. Sera from patients infected with *Rickettsia* will, therefore, produce agglutination with *Proteus* antigen suspensions. Antigen suspension of *Proteus* OX19 antigen reacts strongly with the sera of patients with typhus group rickettsiae and rocky mountain spotted fever, *Proteus* OX2 with the sera of patients with spotted fever infections, while the *Proteus* OXK with the sera of patients infected with scrub typhus.

## Result

A total 60 sera samples from FUO cases were tested by Weil–Felix test, of whom 14 (23.33%) were positive. Of these 14 positives, 7 (50%) were positive for OXK suggestive of scrub typhus and 1 (7.14%) each was positive for OX2 and OX19 suggestive of spotted fever group and typhus group, respectively. Remaining five were positive for more than one antigen namely, two (14.29%) were positive for OXK and OX19, one (7.14%) each was positive for OXK and OX2, and OX2 and OX19, and one (7.14%) was positive for OXK, OX2, and OX19 [Table 1].

Among these 14 positive sera samples, 8 (57.14%) were from male and 6 (42.86%) from female patients, and the sex ratio of male:female subjects was 1:33 [Table 2]. The mean age of the seropositive patients was 38.14 years, and the peak incidence of positivity was observed in the age group between 46 and 60 years (38.46%) [Table 3]. The maximum number of patients with seropositivity was observed between the months of August and October [Table 1].

**Table 2:** Sex-wise distribution of Weil–Felix test results in fever of unknown origin cases in and around Davangere (July to December 2014)

| Sex | Positives | % |
|---|---|---|
| Male subjects | 8 | 57.14 |
| Female subjects | 6 | 42.86 |
| Total | 14 | 100 |

**Table 3:** Age-wise distribution of Weil–Felix test results in fever of unknown origin cases in and around Davangere (July to December 2014)

| Age group (years) | Weil–Felix test | | Total |
|---|---|---|---|
| | Positive | Negative | |
| 0–15 | 1 | 10 | 11 |
| 16–30 | 5 | 12 | 17 |
| 31–45 | 3 | 12 | 15 |
| 46–60 | 5 | 8 | 13 |
| 61–75 | 0 | 4 | 4 |
| Total, *n* (%) | 14 (23.33) | 46 (76.67) | 60 (100) |

**Table 1:** Weil–Felix test results in fever of unknown origin cases in and around Davangere (July 2014 to December 2014)

| Month | Sample tested | No. of positive samples, (%) | Antigen | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | OX2 | OX19 | OXK | OX2 and OX19 | OX19 and OXK | OX2 and OXK | OX2, OX19 and OXK |
| July | 10 | 1 (10) | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| August | 9 | 3 (33.3) | 0 | 1 | 1 | 0 | 1 | 0 | 0 |
| September | 5 | 4 (80) | 1 | 0 | 1 | 0 | 1 | 1 | 0 |
| October | 11 | 3 (27.27) | 0 | 0 | 2 | 0 | 0 | 0 | 1 |
| November | 17 | 2 (11.76) | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| December | 8 | 1 (12.5) | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Total | 60 | 14 (23.33) | 1 | 1 | 7 | 1 | 2 | 1 | 1 |

" Significant titre :1:160 for OXK ;1:80 for OX2 and OX19

## Discussion

Although rickettsiae can be isolated from or detected in clinical specimens, serological tests still remain an indispensable tool in the diagnosis.[7] Many immunological tests that are accurate and sensitive are available for the diagnosis of rickettsial diseases. Among these specific tests, microimmunoflourescence test is considered the best approach, followed by latex agglutination (LA), indirect hemagglutination (IHA), immunoperoxidase assay (IPA), and enzyme-linked immunosorbent assay (ELISA). These specific immunological tests are not easily available in developing countries such as India. Moreover, 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.[6,8]

In this study, seroprevalence of rickettsial infections was reported to be 23.33%. Rickettsial infections detected were scrub typhus (50%), followed by spotted fevers (7.14%) and typhus fevers (7.14%). Corresponding figures in similar studies reported by other investigators vary significantly.[5,3,9,10] Mittal et al., in Delhi, tested 87 sera samples from suspected cases of rickettsial infections in whom 29 (33.3%) were positive for rickettsial antibodies. Of these 29 positives, 14 (48.2%) were positive for scrub typhus, 8 (27.5%) for spotted fever group, and 2 (6.8%) for typhus group, while remaining 5 (17.24%) were positive for two rickettsial illnesses.[11] Raoult et al.,[12] in Burundi during a field study, reported epidemic typhus in 75% of clinically suspected cases in refugee camps. Such a wide variation in the results could be because rickettsial diseases have a diversity of epidemiologic characteristics reflective of the variety of ecologic situations in which the bacteria are transmitted to humans.[13] Another explanation might be the criterion set for a positive result.[8,11,14]

Seropositivity for rickettsial infections are more common in male subjects (57.14%) when compared with female subjects (42.86%) in our study .This is in agreement with some earlier studies.[4,8,10] In contrast, few investigators reported rickettsial infections more predominantly with female subjects.[6,11] Chanyasanha et al.,[15] from Thailand in their study on seroprevalence of scrub typhus, observed no difference between the two sexes in relation with the rickettsial infections. Rickettsial infections with male preponderance in our study could be because of their occupational (farming) or recreational activities, which expose them to the risk of contracting the infection. Analysis of age-wise distribution of positivity for rickettsial infections revealed that it was predominant in older age group. This is in line with some other investigators.[8,10,15,16]

Seropositivity during this study clustered from August to October. This is because mites are active during or at the end of rainy season, which coincides with the months of August to September in India. Risk of exposure to *Orientia tsutsugamushi* is the greatest during the monsoon season.[8,17] Earlier studies from India reported a similar period of disease occurrence.[6,10,18] This is also the reason for scrub typhus to be the most common among rickettsial illnesses in our study.

Our study has the limitation in that the sample size was small (not more than 60 cases), which made it difficult to obtain a detailed information on the epidemiology of rickettsial infections prevalent locally.

## Conclusion

Rickettsial infections are prevalent in and around Davangere and need to be considered among the differential diagnosis in patients with FUO. This is, particularly, important after the rainy season and early cooler months (i.e., between August and October). General health education and public awareness about the disease, including the methods of transmission, is necessary for their prevention and control. As this study had small sample size, large-scale studies are needed to understand the magnitude of rickettsial infections in this region and other parts of India.

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