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SEROLOGICAL EVIDENCE OF RICKETTSIAL INFECTIONS IN A TERTIARY CARE CENTER IN PUNJAB

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ABSTRACT

Rickettsial infections, being one of the causes of FUO (Fever of Unknown Origin), are being under diagnosed with high mortality in untreated cases. Due to paucity of confirmatory tests, early and accurate diagnosis is a challenge in India. Even though widespread infection is suspected in India, only a few reports are available which provide an incomplete picture. This study was conducted to determine the seroprevalence of Rickettsial infections in Punjab. Retrospective study done for a period of 3 years from 2012 to 2015; Weil-Felix test was done using standard protocols in patients with FUO. Of the total 457 samples evaluated, 78 (17%) were positive for scrub typhus, 31(6.8%) were positive for spotted fever and 1 sample was positive for tick typhus. Even though Weil Felix test has many drawbacks, it still serves as an economical and simple tool for initial investigation of Rickettsial infections. Active surveillance is required to know the exact magnitude of the disease.

Keywords: Rickettsioses, Weil-Felix Test, Heterophile Agglutination Test, Scrub Typhus

INTRODUCTION

The *Rickettsiae* are a heterogeneous group of small, obligately intra cellular, gram-negative coccobacilli and short bacilli, most of which are transmitted by a tick, mite, flea, or louse vector (Fauci, 2015). Rickettsial infections are one of the important causes of fever of unknown origin (FUO) and this needs to be differentiated from other febrile illnesses (Mittal, 2012). Based on antigenic and genetic data, pathogenic *Rickettsiae* are traditionally divided into three groups—the spotted fever group, the typhus group, and the scrub typhus group. The spotted fever group accounts for most tick borne rickettsioses. The typhus group comprises two human pathogens transmitted by insects. Epidemic typhus is caused by *Rickettsia prowazekii* and is transmitted by the body louse. Murine typhus is caused by *Rickettsia typhi* and is transmitted by rat and cat fleas. The scrub typhus group is composed of *Orientia tsutsugamushi* only and is transmitted by “chiggers” (Mandell, 2010).

Rickettsioses is an under diagnosed group of diseases presenting as acute febrile illness, with high mortality in untreated cases; the reported sero positivity in clinically suspected infections is up to 33%. Many cases have been reported from Maharashtra, Karnataka, Tamil Nadu, Kerala, Jammu and Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, West Bengal, and Assam (Mittal, 2012; Rathi, 2010; Mahajan, 2006; Ajantha, 2013). Widespread existence of the infection is suspected; however, only a few reports are available that provide an incomplete picture. As rickettsioses have nonspecific presentation and there is paucity of confirmatory diagnostic tests, accurate and early diagnosis remains a challenge in India. There is a need to undertake studies wherever possible to understand the Indian scenario in a better perspective.

MATERIALS AND METHODS

A retrospective study was conducted in the department of Microbiology, Christian Medical College and Hospital, Ludhiana from 1st September 2012 to 31st August 2015 for a period of 3 years to detect the sero prevalence of rickettsial infections amongst the population. After ruling out Dengue and Malaria in patients with fever, Weil Felix test was done by agglutination. Antigens *Proteus vulgaris* OX2, *P. vulgaris* OX19 and *P. mirabilis* OXK were obtained from Central Research Institute (CRI), Kasauli, India. Weil Felix test was done using standard protocol with doubling dilution of 1:40 to 1:640.

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RESULTS AND DISCUSSION

Results

The cut-off titre was taken as 1:160 for the population and the results were interpreted accordingly. Of the total 457 samples evaluated, 78 (17%) were positive for scrub typhus, 31(6.8%) were positive for spotted fever and 1 sample was positive for tick typhus. Our study shows that scrub typhus is the most prevalent among the rickettsial infections in Punjab (Table 1, Figure 1).

Table 1: Distribution of Rickettsioses in Punjab

Rickettsial Disease	Number
Spotted Fever	6.8% (31)
Tick Typhus	0.2% (1)
Scrub Typhus	17% (78)

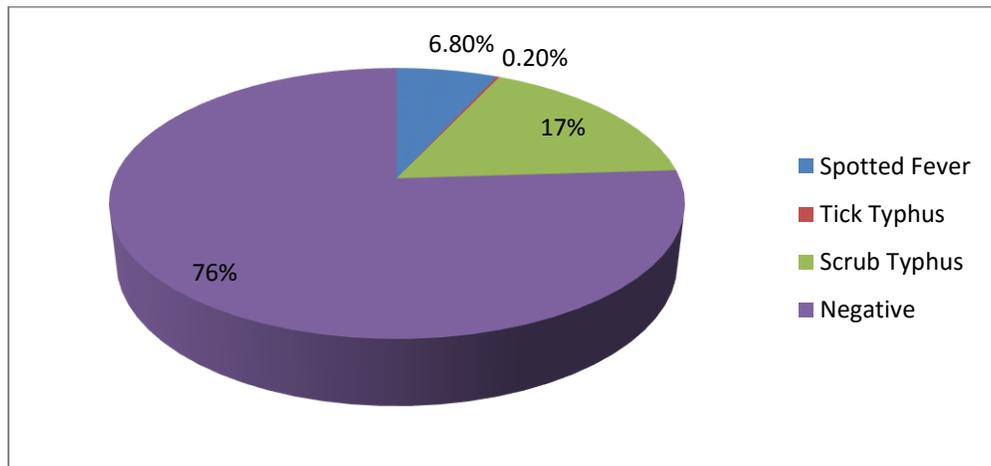


Figure 1: Distribution of Rickettsial Diseases in Punjab

It was also found that out of the total cases, 13 (11.8%) were pediatric cases (upto 18 years of age), and 97 (88.2%) were adults. Gender-wise distribution is depicted in Figure 2. More cases of Rickettsiosis were found during the months of July to December, in the cooler months following the rainy season (Figure 3). This may be due to the fact that during this period, the transitional vegetation is more, and it provides a suitable environment for the multiplication of vectors.

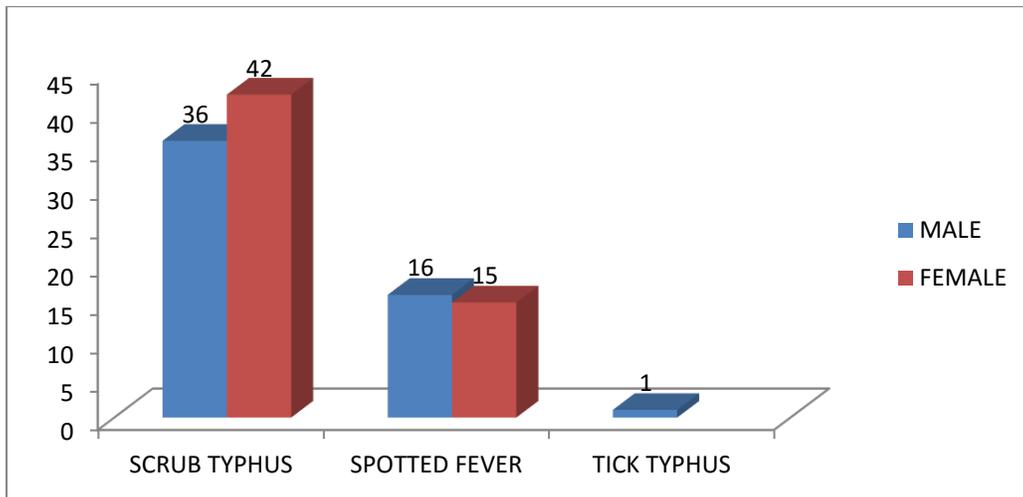


Figure 2: Gender-Wise Distribution of Rickettsioses

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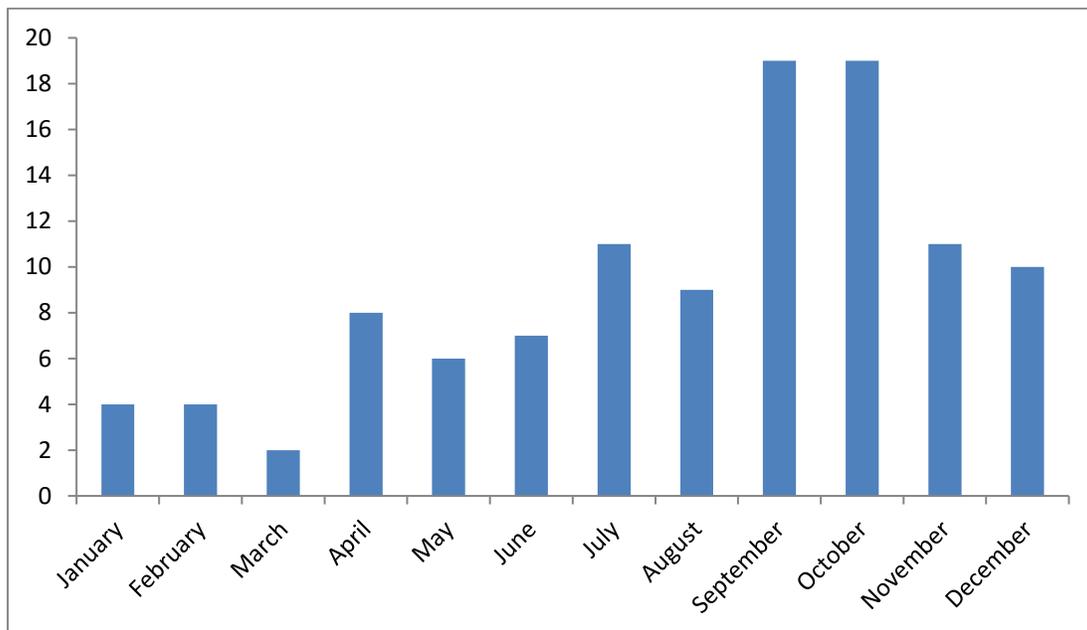


Figure 3: Month-Wise Distribution of Rickettsioses

Discussion

Organisms belonging to family Rickettsiaceae are obligate intracellular parasites, and they do not grow on cell free media and need tissue cultures and laboratory animals for their isolation. Weil Felix test is the oldest assay based on detection of antibody to various Proteus antigens that cross-react with rickettsiae. This can be used as a screening test, which detects more cases than misdiagnosed ones and when positive, is reasonably specific (Rathi, 2010). In developing countries like India, where there is lack of availability of definitive tests, Weil-Felix test may be used as first diagnostic step in diagnosis of rickettsial diseases when interpreted in the correct clinical context (Isaac, 2004; Mahajan, 2006). In Weil Felix test, which is based on heterophile agglutination, cross-reactivity often exists among antigens of pathogen within the same genus and occasionally in different genera which is one of the major limitations (Parola, 2001).

Weil Felix test detects IgM antibody detectable 5-10 days following the onset of symptoms. Whole cells of *P. vulgaris* OX2 react strongly with serum from person infected with spotted fever group (SFG) rickettsiae with the exception of those with Rocky mountain spotted fever (RMSF); and whole cells of *P. vulgaris* OX19 react with serum from person infected with typhus group rickettsial as well as with RMSF. Also, OXK strain of *P. mirabilis* agglutinates with serum from scrub typhus patients (Amano, 1992a; Amano, 1992b).

Various studies done in different parts of India show that there is a wide distribution of rickettsial diseases (Isaac, 2004; Ajantha, 2013; Sharma, 2005). But more studies are required to know the exact magnitude of the disease in India. A study done in Puduchery also shows that Rickettsial infections are more during the cooler months of the year which is similar to our study (Stephen, 2015). Serological studies done in Singapore (Sekhar, 2000) and Spain (Lledo, 2014) also suggests that rickettsial infections are prevalent among the population and this should be one of the differential diagnosis when evaluating F.U.O.

The major limitation of our study was that four-fold rise in antibody titre with paired serum samples could not be demonstrated.

In developing countries like India where epidemiology and burden of rickettsial disease is largely undiscovered, high cost of conducting investigations like immunofluorescence, Western blot or PCR based tests is additional hindrance in making accurate diagnosis of rickettsial diseases. However, Weil Felix test which is simple and economical can serve as initial investigation and can guide a clinician in

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instituting appropriate treatment (Mittal, 2012). The most useful drug in children and in adults is doxycycline. It can be prescribed in short courses (Mandell, 2010).

Conclusion

Rickettsial infections are one of the important causes of fever of unknown origin. Active surveillance of rickettsial diseases is required to know exact magnitude and distribution of the disease. In spite of all its drawbacks, Weil-Felix test still serves as a useful and cheap diagnostic tool, but not the sole method for laboratory diagnosis of rickettsial diseases.

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