Seroprevalence of Rickettsial Diseases in a Tertiary Care Hospital

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A B S T R A C T

Rickettsial diseases are still prevalent in most of the countries including India and are also classified under the causes of pyrexia of unknown origin (PUO). Early signs and symptoms of these infections are nonspecific making diagnosis more difficult. If untreated mortality may be as high as 30-35%. Though Weil Felix test is less sensitive but still it serves as a useful and cheapest available screening tool for the laboratory diagnosis of rickettsial diseases. A prospective study was carried out for a period of 6 months from November 2015 to April 2016 in a tertiary-care hospital, Shimoga, Karnataka, India. The serum samples from 277 PUO cases which included patients of all age group and from both Out Patient Department (OPD) and In Patient Department (IPD), were subjected to Weil–Felix test (PROGEN, Tulip Diagnostics (P) Ltd., Verna, Goa, India). The 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 1:160 for OX-K and more than 1:80 for OX-2 and OX-19 were considered significant. Of 277 samples, rickettsial diseases were detected in 73(26.35%) samples. Seropositivity was higher among male subjects 52(71.23%) when compared with female subjects 21(28.77%). All positive cases were in 1-18 age group. Prevalence of rickettsial diseases 73(26.35%) is significantly high, especially in children’s and hence should be included in the differential diagnosis of PUO.

Keywords
Rickettsial diseases, PUO, Weil–Felix test.

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Introduction

Rickettsiae comprise of group of small non-motile gram negative coccobacilli and are obligate intracellular, transmitted by arthropod vector like lice, fleas, ticks (Raghu Kumar et al., 2015). Species of Rickettsia can be categorized into spotted fever, typhus, and scrub typhus groups based on clinical manifestations (Tay et al., 2003). Rickettsial infections are one of the important causes of pyrexia of unknown origin (PUO) and this needs to be differentiated from other common febrile illnesses like enteric fever, malaria, dengue etc (Veena Mittal et al., 2012). They have a global distribution and are reported from almost all parts of India like Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Rajasthan, Assam, West Bengal, Maharashtra, Kerala and Tamil Nadu (Anuradha Sood et al., 2013).
Rickettsial diseases widely vary in severity from self-limited mild illnesses to fulminating life-threatening infections. These diseases usually manifest as fever, rashes and vasculitis (Suchitra Shenoy et al., 2015). Although clinical manifestations of rickettsial infections are well documented, recent studies in Asian countries have reported complications such as gastrointestinal manifestations, tinnitus, and hepatitis syndromes (Tanveer Nawab et al., 2015). Mortality due to these infections is reported to occur in 1% to 30% of untreated cases (Narendra rathi et al., 2010; Prabhakaran et al., 2010).

As no single laboratory finding is specific for early diagnosis, treatment needs to be started empirically on clinical and epidemiological suspicion. The greatest challenge to the clinician is the diagnostic dilemma posed by these infections early in their clinical course when antibiotic therapy is most effective. Micro-immunofluorescence, latex agglutination, indirect hemagglutination, immunoperoxidase assay, and enzyme-linked immunosorbent assay are various serological tests available. Immunofluorescence assay (IFA) is the “gold standard” technique (Mahajan et al., 2006). Even though the sensitivity and specificity of Weil Felix test is low, in most of small laboratories, this method is the only one available. This study was conducted to know the prevalence of rickettsial diseases.

**Materials and Methods**

Prospective study of 6 months from November 2015 to April 2016 was done in a tertiary-care hospital, Shimoga, Karnataka, India. Rickettsial diseases were diagnosed by Weil–Felix test (PROGEN, Tulip Diagnostics (P) Ltd., Verna, Goa, India). Total of 277 serum samples from PUO cases were subjected to Weil–Felix test. 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. 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.

**Result and Discussion**

Of 277 samples, rickettsial diseases were detected in 73(26.35%) samples. Seropositivity was higher among male subjects 52(71.23%) when compared with female subjects 21(28.77%). All positive cases were in 1-18 age group. 13 samples were reactive to OX 2 only, 5 to OX K only but none to OX 19 individually. When reactivity was seen towards two or more antigens in the same serum sample, combination of antigens demonstrated it are OX 19 + OX 2, OX 19 + OX K, OX 2 + OX K and OX 19 + OX 2 + OX K. Maximum (27) reactivity was in combination OX 19 + OX 2 + OX K.

Rickettsial disease is an acute infectious disease transmitted to humans by ticks, mites or lice. They are underdiagnosed because of their varied presentation and lack of availability of reliable, specific laboratory tests. Rickettsial fever can be present with conjunctivitis, generalized oedema, meningoencephalitis and pupura fulminance.
In the present study, rickettsial diseases were detected in 73 (26.35%) samples with male predominance 52 (71.23%) which is similar to studies done by Raghu Kumar KG et al., (2015) and Anuradha Sood et al., (2013). Maximum (27) reactivity was in combination OX 19 + OX 2 + OX K which is consistent with study done by Ganavalli Subramanya Ajantha et al., (2013). Rickettsial disease is a very less known cause of fever of unknown origin. They are re-emerging with increased reports from different parts of the world (Ponugoti et al., 2015). The Rickettsial diseases are endemic in Southeast Asia, Northern Australia and pacific islands. Amongst Rickettsiosis scrub typhus is most common and is endemic in the tropical and subtropical regions of the Asian continent. The presence of rickettsial diseases in India have been documented in subhimalayan region of the country (Anuradha et al., 2005).

| Table.1 Total PUO cases with their reactivity |
|---------------------------------------------|
| Positive samples No. (%) | Negative samples No. (%) | Total No. (%) |
| 73 (26.35) | 204 (73.65) | 277 |

| Table.2 Sex -wise distribution of total cases |
|---------------------------------------------|
| Sex | Positive samples No. (%) | Negative samples No. (%) | Total No. (%) |
| Male | 52 (71.23) | 116 (56.87) | 168 (60.65) |
| Female | 21 (28.77) | 088 (43.13) | 109 (39.35) |
| Total | 73 (100) | 204 (100) | 277 (100) |

| Table.3 Weil–Felix test results |
|--------------------------------|
| Antigen | No. of positive samples |
| Only OX 19 | - |
| Only OX 2 | 13 |
| Only OX K | 05 |
| OX 19 + OX 2 | 09 |
| OX 19 + OX K | 05 |
| OX 2 + OX K | 14 |
| OX 19 + OX 2 + OX K | 27 |

Although rickettsiae can be isolated from or detected in clinical specimens, serological tests, especially Weil–Felix test, still remain an indispensable tool in diagnosis. In recent years the micro immunofluorescence assay (IFA) has become the reference test. The procedure appears to be the most sensitive and specific method for the diagnosis of rickettsial infections. Hechemy et al., demonstrated 70% agreement between WF test and micro IF results especially with a rise in WF titre (Deepali et al., 2015). Greater clinical awareness, a higher index of suspicion, better use of available diagnostic tools would increase the frequency with which rickettsial diseases are diagnosed (Sanjay et al., 2012). A delay in diagnosis and therapy is a significant factor associated
with death or severe illness and irreversible damage to important organs (Rajesh et al., 2009). Empirical treatment with chloramphenicol, doxycycline should be considered to reduce the high mortality and morbidity (Nigwekar et al., 2013).

In conclusion, prevalence of rickettsial diseases 73(26.35%) is significantly high, especially in children’s and hence should be included in the differential diagnosis of PUO. Simple serological test (Weil-Felix test) is helpful in diagnosis. Though it is not a very sensitive test but is rather specific test and has to be interpreted in the correct clinical context.

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