Research Paper

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SEROPREVALENCE OF SCRUB TYPHUS IN PATIENTS WITH ACUTE FEBRILE ILLNESS AT A TERTIARY HEALTH CARE INSTITUTION IN JAIPUR, RAJASTHAN

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ABSTRACT **Objectives;** Scrub typhus is an important cause of acute febrile illness and need to be differentiated from other causes of febrile illness such as malaria, enteric fever, dengue etc. The present study reports a recent epidemic of scrub typhus amongst cases of PUO from different areas of Rajasthan, India. There was high mortality in undiagnosed cases of PUO which lead to the diagnosis of scrub typhus. Methods; Patients presenting with undiagnosed febrile illness between January 2013 to December 2015 were evaluated. Testing was done using a commercial ELISA kit for specific IgM antibodies against Orientia tsutsugamushi. **Results;** 793samples (23.81%) were positive for the presence of IGM antibodies against O tsutsugamushi. The number of adult male and female positive patients were 19.09%(368/1927) and 28.58% (425/1487) respectively. Serum samples of FUO cases were analysed for IgM antibodies to Orientia tsutsugamushi along with dengue, malaria, typhoid. The cases were seen mainly in the months between August to November. **Conclusion:** The present study emphasises the importance of scrub typhus among cases of PUO especially after rainy season and during early cooler months. The study also highlights the significance of ELISA method for rapid and early reporting and ruling out scrub typhus in PUO cases.

KEYWORDS

ELISA, Fever of unknown origin, Orientia tsutsugamushi, Scrub typhus

ARTICLE HISTORY

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Introduction

Rickettsial diseases are widely distributed throughout the world and many recent reports suggest to their continued presence in several part of the Indian subcontinent,particularly that of scrub typhus [1-6].Scrub typhus is an acute febrile illness caused by infection with Orientia tsutsugamushi. The organism is transmitted through the bite of larval form (chiggers) of trombiculid mites[7].

Scrub typhus is an important cause of acute febrile illness and need to be differentiated from other causes of febrile illness such as malaria, enteric fever, dengue etc[7].This disease is also significant as any undue delay in diagnosis and initiation in appropriate therapy can often result in severe complication such as acute respiratory distress syndrome, septic shock and multi system organ failure often culminating in death in morbid patients. Acute kidney failure associated with scrub typhus has also been reported in the tropic[8].

Scrub typhus is increasingly implicated as an important cause of acute undifferentiated febrile illness in several parts of India[9]. Observing the increase in the number of undifferentiated febrile illness in our hospital along with persistent clinicians demand, a serological test for the detection of scrub typhus antibodies was introduced in our laboratory. Here we present the scrub typhus scenario in our tertiary care hospital in 3 year study.

In India, epidemic of scrub typhus have been reported from north, east and south India[3-5,10-14]. Rickettsial diseases are generally notoriously difficult to diagnose, and untreated cases can have fatality rates as high as 30-35 per cent. Thus, the reported historical numbers of cases of infections with rickettsiae are probably not very accurate and are known to be severely underreported. When diagnosed properly, they are often easily treated but, lack of definitive diagnostic tools and the hazards of handling these microorganisms aggravate the difficulties of diagnosis and treatment. After ruling out complicated malaria, dengue and enteric fever, many of these cases remained undiagnosed. The present study was undertaken to assess the etiological agent in these fever cases.

There are not many community-based studies on rickettsial infections in Rajasthan. It is also true that the specific gold standard techniques like the immunofluorescence antibody test (IFA), the indirect imunoperoxidase (IP) test, are not easily available and the isolation of the organisms in animals or cell culture is limited by the lack of containment facility as well as the lack of expertise in handling these high risk group pathogens. To date, the diagnosis of a rickettsial illness has most often been confirmed by serologic testing. Serologic evidence of infection occurs no earlier than the second week of illness for any of the rickettsial diseases; thus, a specific diagnosis may not be available until after the patient has recovered or died.

In the present study, we used ELISA testing for IgM antibodies against O. tsutsugamushi for diagnosis. This test has shown good sensitivity and specificity 90% for detecting specific antibodies[5,15,16] and has been adequately validated[11]. It also has an advantage to provide positive results within 3-4 days after the onset of disease. Serum samples from suspected febrile patients were tested for the presence of IgM antibodies against O. Tsutsugamushi.

Material & Method

This study was conducted in department of Microbiology, Sawai Man Singh hospital & medical college, Jaipur .

All consecutive samples of patients received in lab presenting with febrile illness from January 2013 to December 2015 were evaluated. Other likely diagnosis such as malaria, dengue fever and enteric fever were ruled out by appropriate laboratory investigation. Samples were tested for specific IgM antibodies against O. tsutsugamushi using a commercial ELISA kit (InBiOS International Inc. USA). The kit uses O tsutsugamushi derived recombinant antigen mix. The test was performed as per manufacturer's instructions.

Results

A total 3330 consecutive sample with undiagnosed fever were included in the study. During the 3 year (2013-2015) study period, a total of 3330 serum samples were received in the department of microbiology for the detection of O. tsutsugamushi specific antibody Of these 793samples (23.81%) were positive for the presence of antibodies against O tsutsugamushi. Of the 793 positive samples,279 were positive in 2013,265 were positive in 2014 and 249 were positive in 2015. The number of adult male and female positive patients were

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19.09% (368/1927) and 28.58% (425/1487) respectively.

The age of patients ranged between 2 and 80 years. Among females with PUO, positivity for ST Ig M antibody was highest in 31-45 years (47.31%) followed by 16-30 years of age group (31.22%). In male highest positivity was seen in 31-45 years (25.07) as shown in table 1. The laboratory parameters, leukocytosis was considered when white cell count(WBC) was more than 10,000 cells/cumm and leucopenia was defined as WBC <4300 cells/cumm. Thrombocytopenia was considered when platelet count was< 140,000 cells /cumm The laboratory parameters thrombocytopenia were seen in 525 patients (66.20%). Total Leucocyte count was raised in 221 patients (27.86%) as shown in table 2.

Additional tests were carried out like Widal tube test, serological tests for dengue and peripheral blood film examination for malarial antigen detection in blood.

Maximum number of cases were seen after the rainy season and during early cooler months i.e. between September and October as shown in fig. 1.

Discussion

There have been reports of the outbreaks of scrub typhus from various parts of the country in the recent past with serological evidence of widespread prevalence of spotted fevers and scrub typhus in different states[2,3,5,10,12-14]. Thus, there was a strong possibility of presence of scrub disease in Rajasthan.

793samples (23.81%) were positive for the presence of antibodies against O tsutsugamushi. Of the 793 positive samples,279 were positive in 2013,265 were positive in 2014 and 249 were positive in 2015. The number of adult male and female positive patients were 19.09% (368/1927) and 28.58% (425/1487) respectively.

The study shows more positivity of ST in females particularly above 30 years of age. Vivekanandan M et al[12] and Bithu et[17] al also reported female preponderance in their study. This could be due active involvement of females as field and farm workers in Rajasthan.

The mainstay of diagnosis in scrub typhus is serology[15].The gold standard serological tests are immunoflorescence antibody test or indirect immunoperoxidase assay[15] but are out of reach in our country owing to high costs. The cheapest test currently available and used extensively in our country[2,3,5,11,12] is Weil-Felix test which is highly specific, but lacks sensitivity[18-19]. In the present study, we used ELISA testing for IgM antibodies against O. tsutsugamushi for diagnosis. This test has shown good sensitivity and specificity 90% for detecting specific antibodies[5,15,16] and has been adequately validated[11]. It also has an advantage to provide positive results within 3-4 days after the onset of disease.. A future study can be done comparing various diagnostic techniques and their feasibility for the diagnosis of scrub typhus.

In the present study most of the cases were seen during the months of August to November Such post monsoon surge is reported earlier also[3,10-13]. This is because, during the months of August to November, farmers are involved in the harvesting activity in the fields, where they are exposed to the bites of larval mites. Further,in the immediate post monsoon period (September to early months of the next year), there is growth of secondary scrub vegetation, which is the habitat for trombiculid mites[20].

In the laboratory parameters, Thrombocytopenia is an important feature of ST, dengue, malaria. the most important abnormality notice was thrombocytopenia (66.20%). Similar abnormalities have been observed by Vivekanandan M et al[12] and Bithu et al[17]. The central pathophysiological derangement of thrombocytopenia is because of wide spread vasculitis and perivasculitis of these organs. This is due to multiplication of the organism in the endothelial cells lining the small blood vessels and consumption of platelets in the process of intravascular microthrombosis[21].

Other laboratory finding noted were leukocytosis. Leukocytosis is thought to be associated with severe scrub typhus[22,23].In this study Leucocytosis was seen in 28 % patient.

Conclusion

Scrub typhus though prevalent is under-reported in our country. It should be considered as an important differential diagnosis in a febrile patient with thrombocytopenia. This is particularly important after the rainy season and early cooler months, i.e. between August and November months. Rapid and specific diagnostic methods using ELISA can be carried out timely for early diagnosis of scrub typhus in patients in developing countries like India. Early diagnosis and appropriate treatment is rewarding and prevents morbidity and mortality.

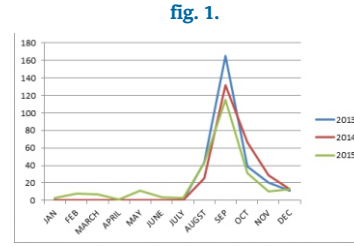
TABLE 1: Age and sex –wise distribution of fever of unknown origin cases

Age group (In years)	Male Total	pos(%)	neg (%)	Female Total	pos(%)	neg (%)
0-15	230	47(20.43)	183(79.56)	95	21(22.10)	74(77.89)
16-30	832	130(15.62)	702(84.37)	570	178(31.22)	392(68.77)
31-45	355	89(25.07)	266(74.92)	279	132(47.31)	147(52.68)
46-60	281	68(24.19)	213(75.81)	237	61(25.73)	176(73.41)
>60	229	34(14.84)	195(85.15)	222	33(14.86)	189(85.13)
Total	1927	368(19.09)	1511 (78.41)	1403	425(30.29)	978(69.56)

Table 2 : laboratory parameters of scrub typhus cases

Investigation	No.of patients	Percentage
Total leukocyte count	170	21.43
-Less than 4.3×103/mm3	402	50.69
-Between 4.3×103/mm3	221	27.86
-More than 10×103/mm3	525	66.20
Platelet count below 1.4 lacs /mm3		

fig. 1.



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