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Letter to Editor

Microbiology Section

Comment on "Serological Evidence of Scrub Typhus among Cases of PUO in the Kashmir Valley- A Hospital Based Study"

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Dear Editor,

We came across an interesting article titled Serological Evidence of Scrub Typhus among Cases of PUO in the Kashmir Valley- A Hospital Based Study by Farhana A et al., [1]. In their hospital-based cross-sectional study, authors have studied 162 serum samples of patients with Pyrexia of Unknown Origin (PUO) for scrub typhus by Weil-Felix Agglutination Test (WFT) and Enzyme Linked Immunosorbent Assay (ELISA).

However, following issues and concerns need to be addressed:

- There is no clarity on inclusion or exclusion of the patients. Rahi M et al., have formulated the guidelines for diagnosis and management of rickettsial diseases [2].
- Majority of the patients were reported based on WFT positive. However, its reliability is suspected due to its poor sensitivity and specificity. Fever duration or time of sample collection should be reported. Incubation period for rickettsial infection ranges from 6 to 20 days. The agglutinating antibodies are detectable after 5 to 10 days following the onset of symptoms. However, the WFT may be positive without the rise of IgM antibody titer.
- Only typhoid fever and brucellosis tests were done. It is important to rule out differential diagnoses such as dengue, measles, enteroviral diseases, mononucleosis, meningococcemia, typhoid, l eptospirosis, scarlet fever, malaria, Kawasaki disease, and adverse drug reactions [3].
- How did the author get the cut-off value for ELISA? Since this is the first report of scrub typhus from Kashmir Valley, the actual ELISA cut-off value may vary when compared to other regions of India. The cut-off value obtained from in and around New Delhi region was 0.87 whereas in South Indian states, it was >0.5 or >0.6 [2,4]. The cut-off value can be determined by using the mean absorbance +2 or 3 standard deviation value of control serum samples positive for a range of non-rickettsial infections (i.e. dengue, chikungunya, leptospirosis, malaria, enteric fever etc.) and non-infectious from normal healthy volunteers [2,4,5]. These values should be used for all patients, irrespective of whether they come from a scrub typhus endemic environment.
- In the present study, a lower positivity for scrub typhus IgM/IgG ELISA could be attributed to poor sample selection. Time of sample collection is crucial as IgM and IgG can be positive at the end of first and second weeks of infection, respectively [2]. In addition, presence of other typhus and spotted fever groups of rickettsiae cannot be ruled out.
- Clinical response was reported only in ELISA tested cases. There is no clarity about the clinical response among those who were not tested for the ELISA. Treatment should be started whenever rickettsial disease is suspected and an immediate response to the treatment indirectly indicates rickettsial infection.

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AUTHOR'S REPLY

Dear Editor,

Kindly find below the response to the comments and queries raised against our article entitled "Serological Evidence of Scrub Typhus among Cases of PUO in the Kashmir Valley-A Hospital Based Study".

1. We have in our study made the exclusion criteria very clear. The clinical presentation of scrub typhus is non-specific and varies from undifferentiated febrile illness to multiorgan faliure. The diagnosis actually requires a high index of clinical suspicion with favourable ecology and climate. The article publised by Dr. Manju Rahi, whose reference has been cited in the comments, has neither been endorsed by the Ministry of Health and Family Welfare nor circulated as official guideline for diagnosing the disease.

2. We have mentioned in our study that the sensitivity and specificity of Weil-Felix test are low in view of which the results should be confirmed with other substantial tests like ELISA etc. Nonetheless the sensitivity and specificity of WFT is 30-60% and 45-100% respectively and it can serve as a useful aid in diagnosing rickettsial

infections especailly in resource constraint settings as it is afordable, easily available, technically non-demanding with results available next day.

3. We took samples from patients who had been clinically worked up for and found negative for respiratory tract infections including tuberculosis, pneumonias etc., and urinary tract and gastrointestinal tract infections, malignancies and other associated illnesses. Such a workup included and was not limited to laboratory paramaters other than those that come under microbiology. Enteric fever and brucellosis are endemic in our valley and were thus rightfully excluded. It is uneconomical and a waste of time to exclude diseases that are rare or non-existent in the valley.

4. The cut off OD value was calculated as per the manufacturer's instructions on the kit and has been mentioned in the paper.

5. The samples were collected from patients with PUO of 7-20 days duration. We have in our study mentioned some of the limitations which are self explanatory. Indeed the serological response to disease including rickettsial infections is as explained in literature and hence there are limitations of serology in the early diagnosis of diseases but newer tests like IFA, PCR which can confirm the presence or absence of scrub typhus are not available everywhere.

6. Treatment was given to suspected cases and/or those diagnosed by serological tests.

Scrub typhus or for that matter any other rickettsial infection requires a high degree of clinical suspicion. In our study, we made an effort to find out whether or not scrub typhus is a valid entity in the differential diagnosis of PUO cases in our state. Since, it is the first study from Kashmir Valley, it was meant to draw attention to the possibility of any such illness in our population and serve as a road map for further more detailed research in this area.