

## Scrub typhus: Clinical spectrum and outcome

Sir,

We read with great interest the article “Scrub typhus: Clinical spectrum and outcome” in the April 2015 issue of Indian Journal of Critical Care Medicine.<sup>[1]</sup> The article definitely enlightens about the clinical presentations, complications, and management of scrub typhus patients in Southern India. We agree with the authors that high cost, nonavailability, and the requirement of technical expertise for conducting confirmatory investigations such as indirect immunofluorescence assay (gold standard), indirect immunoperoxidase test or polymerase chain reaction-based tests are the major hurdles in making an accurate diagnosis of scrub typhus in India. Weil-Felix test serves as a useful and affordable tool for laboratory diagnosis of rickettsial diseases in resource-poor countries. Recently, immunochromatographic tests (ICT) to detect antibodies against *Orientia tsutsugamushi* are commercially available and is used by many hospitals. However, there is no large-scale evaluation of these assays in our country so far. As the scrub typhus cases in the present study were diagnosed by ICT as well as Weil-Felix test, there are certain aspects of these tests, which need to be discussed in a little depth.

First, it will be informative if the authors can shed more light on the results of Weil-Felix test according to OX-2, OX-19, and OX-K titers. Second, it would be

helpful if the manufacturers' details of the ICT can be provided such as sensitivity, specificity, positive and negative predictive values, and the types of antibodies (IgM/total) detected.

Diagnosis by Weil-Felix test based on a single acute serum sample requires using a cut-off antibody titer.<sup>[2]</sup> Cut-offs ranging from 1:10 to 1:400 are quoted, often with little corroborating evidence and without establishing titers in the healthy local population (necessary to distinguish background immunity from acute infection); that cut off is then used for all patients, irrespective of whether or not they come from a scrub-typhus-endemic environment.<sup>[2]</sup> There is variation in the single Weil-Felix test cut-off titers used for the diagnosis of scrub typhus in different published studies across India.<sup>[3,4]</sup> With a single serum sample available, the test is suggestive of infection only at a high cut-off titer (>1:320) at which the positive predictive value and the specificity is reliable,<sup>[3]</sup> majority of Indian studies have used a cut-off titer >1:80.<sup>[4]</sup> Although agreement exists that a  $\geq$  four-fold increase in antibody titer between two consecutive samples is diagnostic, such a diagnosis is retrospective and cannot guide initial treatment.<sup>[2]</sup>

In the current study, the authors have mentioned about 70.5% (24/34) scrub typhus patients without acute respiratory distress syndrome (ARDS) belonged to endemic areas. Of these 34 patients, only four patients had high Weil-Felix titer of 1:320, three patients had 1:160 and 20 patients had 1:80. Low titer (1:80) in these 20 patients can probably be explained by the fact that, about 50% of scrub typhus patients have a positive test result only during the 2<sup>nd</sup> week of illness,<sup>[5]</sup> while in the current study, tests were performed in the 1<sup>st</sup> week of illness, ( $5.264 \pm 0.431$  days). Testing of paired sera sample might have yielded more relevant information in this group. Similarly in the other group, (scrub typhus patients with ARDS), 83.3% were from endemic areas. Of these 24 patients, 10 patients had Weil-Felix titer 1:320, six patients had 1:160 and eight patients had 1:80. Thus, higher percentage of patients having high titer in the ARDS group could either be due to more number of patients from endemic areas in this group or due to the tests performed in the 2<sup>nd</sup> week of illness ( $11.333 \pm 0.570$  days). However, positive ICT in all these cases raises a very important issue. Should all positive ICT cases be considered as diagnostic of scrub typhus? Should single Weil-Felix titers as low as 1:20 or 1:40 raise an alarm to the clinicians in suspected cases of typhus? The present study in a tertiary care

hospital has addressed one of the important neglected zoonoses of public health importance. A prospective evaluation of several commercial antibody-based rapid tests in Thailand had yielded the following sensitivities and specificities (the Panbio IgM ICT), 46% and 95%, respectively; the Standard Diagnostics IgM ICT, 68% and 73%, respectively; the AccessBio IgM ICT, 56% and 90%, respectively; and the AccessBio total antibody ABT ICT, 61% and 68%, respectively, during the acute phase of scrub typhus infection.<sup>[6]</sup>

More studies in India should evaluate the rapid, point of care diagnostic assays as well as enzyme-linked immunosorbent assays (which includes Indian *O. tsutsugamushi* genotypes of scrub typhus) for optimal patient benefit.

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