Conventional versus reverse testing algorithm for syphilis in high-risk population: A diagnostic dilemma

Sir,

The archaic disease of syphilis has been elaborately studied for decades. The underlying immunological response to *Treponema pallidum* and related species forms the basis of the serological tests used in present-day diagnosis of syphilis. The estimated global burden of 17.7 million cases and 5.6 million new syphilis infections per year merely underscores the magnitude of the disease.[1] Syphilis incidence rates ranging from 5.4 per 100 persons each year in sexually transmitted infection (STI) clinics to a prevalence of 21.9% in long-distance truck drivers have been documented by several authors.[2,3] Concentionally, the diagnosis of syphilis employs a nontreponemal test such as rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) test, followed by specific treponemal tests such as *Treponnema pallidum* hemagglutination assay (TPHA) and fluorescent treponemal antibody absorption to establish the diagnosis of syphilis. However, alternative testing schemes are available that involve a preliminary treponemal assay, followed by reflex quantitative nontreponemal testing.[4] Both these diagnostic algorithms carry their unique merits and

constraints and there is no universally recognized testing sequence for diagnosing syphilis.[5] The scenario is further complicated by the rising trend of co-infections such as HIV and syphilis, among STIs. With over two decades of acquaintance with syphilis-HIV co-infection, the immune interference of syphilis with other STIs is poorly understood.[6] The seldom encountered prozone phenomenon while testing for syphilis in HIV/AIDS patients, often challenges the competency of traditional syphilis testing algorithms in screening these high-risk populations.[7] In the present study, we attempt to compare the adequacy of conventional and reverse algorithms to optimally diagnose syphilis in high-risk population.

Serum samples from 80 consecutive symptomatic STI and antiretroviral therapy (ART) clinic attendees were evaluated over a period of 3 months to assess the performance of the conventional and reverse algorithms. Two separate microbiologists, blinded to each other's findings, independently assessed both the algorithms. The conventional algorithm used RPR (RPR Card Test/ Carbogen Antigen for syphilis testing [Tulip Diagnostics Goa, India]) followed by *T. pallidum* hemagglutination assay (IMMUTREP TPHA kit of Omega Diagnostics Ltd., Scotland, United Kingdom), while reverse algorithm employed an immunochromatographic format (Medsource Ozone Biochemicals Pvt Ltd., India) for IgG and IgM against *T. pallidum,* followed by RPR for diagnosis. Statistical agreement analysis was done using SPSS software.

The conventional algorithm detected syphilis in 5 (6.2%) cases, while the reverse algorithm diagnosed one additional patient apart from the above 5, thus resulting yielding a positivity of 6 (7.5%) cases in the same group of patients. The percentage agreement between the two algorithms was 98.75% and the Cohen's κ coefficient was 0.906. The high concordance among the findings of the conventional and reverse algorithms offers an appealing alternative for detecting syphilis in high-risk population. The unusual immune response to syphilis in immunocompromised patients has always eluded many clinicians. A multitude of plausible interpretations of the specific treponemal and nontreponemal tests add to the perplexity in diagnosis. The relative lag in humoral immune response, especially in patients suffering from HIV/AIDS, daunts the diagnosis in very early and latent stages of syphilis.[8] As reflected in the higher detection rates of syphilis using a reverse algorithm in high-risk population, the reverse algorithm not only provides an appealing diagnostic strategy in terms of diagnosis of early/latent infection, relative ease, low false negativity, and the potential for automation, but its utility in optimally diagnosing missed cases of syphilis among targeted high-risk population solicits further deliberation.

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Conflicts of interest
There are no conflicts of interest.

Bineeta Kashyap, Rituparna Saha, Vikas Saini, Narendra Pal Singh
Department of Microbiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India

Address for correspondence:
Dr. Bineeta Kashyap,
Department of Microbiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India.
E-mail: dr_bineetakashyap@yahoo.co.in

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