Short Communication

Access this article online

Quick Response Code:

Website: www.jacmjournal.org

DOI: 10.4103/jacm.jacm_10_17

Limitations of the 2016 National AIDS Control Organization guidelines regarding Human Immunodeficiency Virus testing in India

Sanjay Bhattacharya, Kasturi Sengupta, Gaurav Goel

Abstract:

The current article discusses certain limitations of the 2016 National AIDS Control Organization guidelines regarding human immunodeficiency virus (HIV) testing in India. Incorporation of fourth-generation HIV antigen plus antibody tests in the screening test along with the need of immunoblot techniques (such as the western blot) for HIV confirmation would make the guidelines more robust.

Keywords:

4th generation immunoassay, human immunodeficiency virus, India, serological diagnosis, window period

Introduction

Accurate diagnosis of human immunodeficiency virus (HIV) infection is essential in the field of HIV/AIDS diagnosis, transfusion medicine, management of clinical scenarios such as needlestick injuries and putting in place appropriate prevention and infection control strategies.[1] The National AIDS Control Organization (NACO) guidelines on HIV testing (December 2016) provides detail algorithm with regard to the interpretation of HIV test results in different settings.[2] For example, with regard to transfusion and transplantation safety, surveillance, diagnosis of individuals with AIDS indicator disease symptoms and finally to detect HIV infection in asymptomatic individuals. These guidelines have helped India in adopting a systematic strategy in diagnosing HIV infection and help reduce its prevalence. However, there are exceptional situations and outliers which the current guideline does not cover. Adopting the same algorithm (meant for certain testing centres) in all situations may lead to diagnostic errors and missed infections.

In low-risk settings, where HIV testing is done pre-intervention (such as before a major intervention such as surgery or chemotherapy or transplantation), algorithms II and III are used which is the practice in Integrated Counselling and Testing Centres. Algorithm II is used for HIV infection surveillance [Figure 1]. In these algorithms, if the initial screening test is reactive, the second/third tests are carried out using other methods, and if these results come as non-reactive, the report is given as negative or indeterminate.[2] We highlight a number of situations where this interpretation is potentially erroneous.

First, if the screening test is a combined antigen + antibody test (4th generation assay) for HIV and the reactivity is in the antigen component, and the second and third tests

Department of Microbiology, Tata Medical Center, Kolkata, West Bengal, India

Address for correspondence:
Dr. Sanjay Bhattacharya, Department of Microbiology, Tata Medical Center, 14 Major Arterial Road (EW), Newtown, Kolkata - 700 156, West Bengal, India.
E-mail: drsanjay1970@hotmail.com

How to cite this article: Bhattacharya S, Sengupta K, Goel G. Limitations of the 2016 National AIDS Control Organization guidelines regarding human immunodeficiency virus testing in India. J Acad Clin Microbiol 2018;20:57-9.

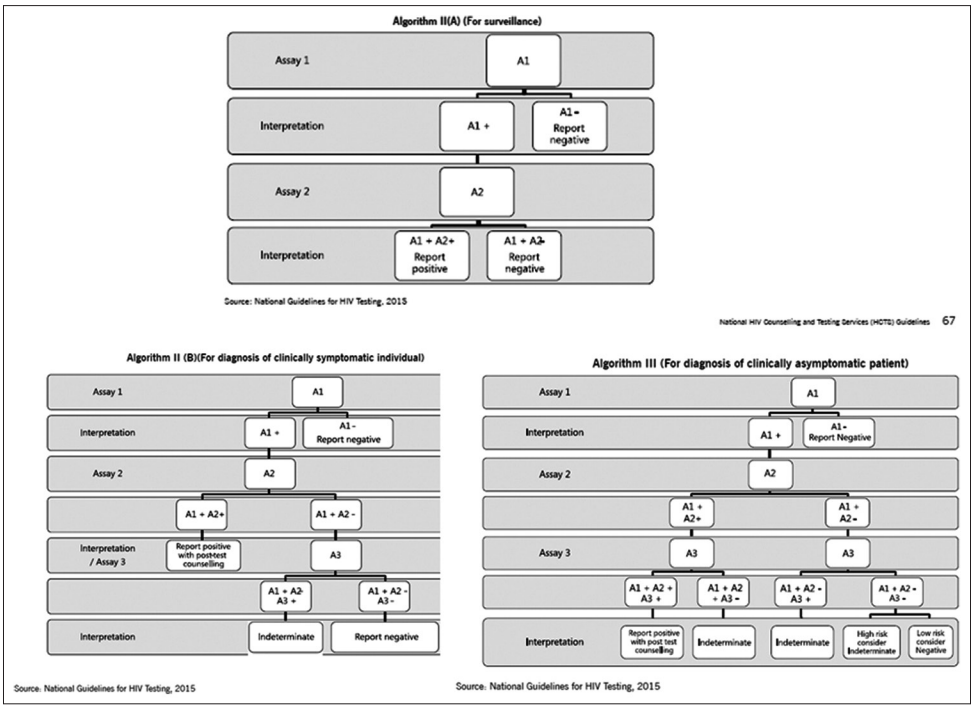

Figure 1: Algorithms for the surveillance and diagnosis of human immunodeficiency virus infection in India. (Based on the National Guidelines for human immunodeficiency virus testing, 2015, India)

detect antibody only there is a possibility of missing an early HIV infection by following the NACO algorithm.[1]

Second, immunodeficient patients, who fail to generate antibody responses (e.g., those with agammaglobulinaemia, hypogammaglobulinaemia and common variable immunodeficiency), may never be antibody reactive and would be missed again by following the NACO algorithm.[3]

Third, certain patients may be falsely classified as being HIV infected, if the NACO algorithm is followed without exercising clinical and technical judgement with regard to HIV testing interpretation. An example is a situation where all three tests may be reactive but the patient, not HIV infected due to immunological cross reactivity. This can happen when the three tests employed show a non-specific reactivity and western blot has not been done to detect HIV type-specific antibody responses. It has been reported before that patients participating in HIV vaccine trials and those with leprosy may have multiple HIV tests reactive, which sometimes even includes the western blot tests.[4,5] It was reported by the National JALMA Institute for Leprosy, and Other Mycobacterial Diseases (Indian Council of Medical Research), that serum samples of certain patients with leprosy showed high reactivity with HIV-related p18, Gp41 and p55 antibodies and lower reactivity with other HIV proteins.[4]

False-positive HIV tests can be caused by influenza vaccination, and viral infections, autoimmune disease, renal failure, multiple pregnancies, blood transfusions, liver diseases, parenteral substance abuse, haemodialysis or vaccinations against hepatitis B and rabies. All these may contribute to seroreactivity against one or more HIV antigens.[6]

We suggest a modification of the NACO algorithm which incorporates fourth-generation assays for HIV testing (dual antigen + antibody testing) and requires an HIV type-specific assay such as the western blot as essential for concluding HIV reactivity.

HIV viral load cannot be used for confirmation of HIV status due to the possibility of false positives and false negatives (especially those with low copy numbers and due to non-optimised polymerase chain reaction (PCR), failed RNA extraction, degradation of the RNA due to suboptimal transport or storage and negative PCR results in long-term non-progressor and those on antiretroviral therapy). Therefore, performance of a specific and comprehensive serological assay which gives a detailed understanding of the antibody reaction becomes essential for the diagnosis of HIV. In case of exclusive antigen reactivity, it is essential that the p24 antigen neutralisation test be done before designating the HIV status. Elaborate testing for confirmation of HIV is essential in view of the long-term medical, social, psychological and financial implications of a positive HIV diagnosis.

The NACO algorithm has immensely helped resource-constrained settings in India, where the

4th generation assays, western blot and HIV viral load or HIV proviral DNA assays are not readily available. However where these constraints are not present and for referral laboratories, and tertiary care centres, additional tests (such as p24 antigen neutralisation assay, viral load, western blot and proviral DNA assay) should be made mandatory. It has been previously reported in India that the difference in price of the 3rd and 4th generation immunoassay for HIV diagnosis was minuscule (Rs. 18 and Rs. 38), respectively, whereas the differences in sensitivity for the diagnosis of acute HIV infection were huge as follows: 42.2% versus 89.1%, respectively.[7,8] The Center for Disease Control and Prevention (CDC) reported in 2012 that rapid test sensitivities for early HIV infection ranged from 22% to 33%, 55% to 57% for the 3rd generation assay and 76% to 88% for the 4th generation tests.[9] In 2013, the CDC reported that in 99 cases, though the initial immunoassays were reactive, the supplemental tests were negative/indeterminate (by Multispot test) and of these, 55.6% actually had acute HIV infection (as detected by the presence of HIV-1 RNA).[10]

In a recent publication, it was reported that the sensitivity of the HIV 3rd generation assays is about 99.5%, whereas the sensitivity of the HIV 4th generation assays is about 99.8%. This translates to the detection of three additional cases of HIV per 1000 samples screened if the 4th generation rather than the 3rd generation tests are used.[11]

In another study from Chandigarh, it was reported in the blood donor screening context that the 3rd generation enzyme-linked immunosorbent assay missed four donors reactive by the 4th generation assay (n = 1075).[12] The price of the 4th generation HIV assay and a western blot test in a private sector service provider was found to be Rs. 500 and Rs. 3050, respectively.[13] However, this increased investment in HIV screening by the 4th generation tests and confirmation by the western blot may be justified when we compare it with the long-term investment required in the care of HIV-positive patients. A recent report from the NACO and the WHO has estimated the cost for anti-retroviral services in India as US$ 133.89 (Rs. 8032) per patient per year, of which 66% is for antiretroviral drugs and 34% is for non-ART recurrent expenditure.[14]

Modification of the NACO algorithms to take care of the above situations described in this article would enable a better understanding of the epidemiology of HIV in India, a country with a large population and HIV prevalence (0.26% of 1.3 billion).

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Cohen MS, Gay CL, Busch MP, Hecht FM. The detection of acute HIV infection. J Infect Dis 2010;202 Suppl 2:S270-7.
2. National HIV Counselling and Testing Services (HCTS) Guidelines. GOI/NACO/BSD (ICTC)/OGL/01122016. Government of India. National AIDS Control Organization; December, 2016. Available from: http://www.indiahivinfo.naco.gov.in/naco/resource/national-hiv-counselling-and-testing-services-hcts-guidelines-2016. [Last accessed on 2016 Dec 22].
3. Padeh YC, Rubinstein A, Shliozberg J. Common variable immunodeficiency and testing for HIV-1. N Engl J Med 2005;353:1074-5.
4. Hussain T, Sinha S, Katoch K, Yadav VS, Kulshreshtha KK, Singh I, *et al.* Serum samples from patients with mycobacterial infections cross-react with HIV structural proteins gp41, p55 and p18. Lepr Rev 2007;78:137-47.
5. VISR Working Group of Global HIV Vaccine Enterprise; Voronin Y, Zinszner H, Karg C, Brooks K, Coombs R, *et al.* HIV vaccine-induced sero-reactivity: A challenge for trial participants, researchers, and physicians. Vaccine 2015;33:1243-9.
6. Mahajan VS, Pace CA, Jarolim P. Interpretation of HIV serologic testing results. Clin Chem 2010;56:1523-6.
7. Roy P, Sahni AK, Jindamwar P. An urgent need for introduction of fourth-generation Ag-Ab based EIA for detection of HIV infection. Med J Armed Forces India 2014;70:89-90.
8. Pandori MW, Hackett J Jr., Louie B, Vallari A, Dowling T, Liska S, *et al.* Assessment of the ability of a fourth-generation immunoassay for human immunodeficiency virus (HIV) antibody and p24 antigen to detect both acute and recent HIV infections in a high-risk setting. J Clin Microbiol 2009;47:2639-42.
9. Patel P, Bennett B, Sullivan T, Parker MM, Heffelfinger JD, Sullivan PS, *et al.* Rapid HIV screening: Missed opportunities for HIV diagnosis and prevention. J Clin Virol 2012;54:42-7.
10. Centers for Disease Control and Prevention (CDC). Detection of acute HIV infection in two evaluations of a new HIV diagnostic testing algorithm – United States, 2011-2013. MMWR Morb Mortal Wkly Rep 2013;62:489-94.
11. Alexander TS. Human immunodeficiency virus diagnostic testing: 30 years of evolution. Clin Vaccine Immunol 2016;23:249-53.
12. Kaur R, Basu S, Kaur G, Singh D. Fourth-generation enzyme immunoassays for screening of HIV in blood donors: Need of the hour. Indian J Pathol Microbiol 2011;54:433-4.
13. Test for AIDS; Labs LP. Available from: https://www.lalpathlabs.com/test-for-aids. [Last accessed on 2018 Apr 02].
14. Agarwal R, Rewari BB, Shastri S, Nagaraja SB, Rathore AS. Delivery of antiretroviral treatment services in India: Estimated costs incurred under the national AIDS control programme. WHO South East Asia J Public Health 2017;6:94-8.