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Rapid Particle Agglutination Test for Human Immunodeficiency Virus: Hospital-Based Evaluation

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The performance of a rapid particle agglutination test for human immunodeficiency virus (HIV) (Capillus HIV type 1 [HIV-1]/HIV-2) on hospital samples is compared with enzyme-linked immunosorbent assays. The test had a sensitivity and specificity of 99 and 98.9%, respectively. In addition, the test was reactive on plasma samples from all individuals infected with HIV-1 subtype C. This test can safely be used for voluntary counseling and testing in India.

The human immunodeficiency virus (HIV) epidemic is now well into its second decade. While in the West the epidemic is mainly among homosexual individuals, in most of the developing countries of Asia and Africa it is primarily among heterosexual individuals (6). There is hence an added risk of children being infected. Since the population at risk in these countries is larger than in the West, there is a significant need for simple tests for use in voluntary counseling and testing for HIV prevention measures.

During the initial phase of the HIV epidemic, enzyme-linked immunosorbent assay (ELISA) tests were most widely used for detection of infected individuals. These tests are sensitive but require the necessary infrastructure, trained personnel, and batch testing. In India, ELISA tests are available in the cities, but in smaller towns and rural areas, facilities for ELISA are unavailable. With the availability of commercial rapid tests, it has become possible to cost-effectively screen smaller numbers of samples without a huge initial input for the laboratory. A large variety of rapid devices are currently in the Indian market. Field testing of only two of these devices has been reported from India to date (3). As most of these devices are imported, the reliability of these devices on samples infected by HIV type 1 (HIV-1) genotype C, the prevalent genotype in India, is largely unknown. There is a report from the U.S. Centers for Disease Control and Prevention that one such device (Capillus HIV-1/HIV-2) missed two (25%) of eight subtype C samples tested (7). The authors suggested it would be prudent to evaluate a rapid test for sensitivity and specificity with the local population where it is used. In addition, in a study on 11 HIV-1 (subtype A) recent seroconverters from the Ivory Coast, Capillus HIV-1/HIV-2 was the second-best of four rapid tests, with a sensitivity of only 73% (4). This test has been supplied to the approved testing laboratories by the national AIDS control organization of India since 1997 and has been available regularly in the Indian market since 1999. We present an analysis of the data generated with this device to assess its performance characteristics with hospital samples. Additionally, we also undertook to test samples from individuals whose HIV-1 subtype was known.

Samples sent to the Department of Clinical Virology for rapid HIV testing between September 1997 and June 2001 and which were tested by the Capillus HIV-1/HIV-2 particle agglutination test (Cambridge Diagnostics Ireland Ltd., Galway, Ireland) were included in the analysis. Samples for rapid HIV screening were sent as part of presurgical screening, from antenatal women and before emergency procedures. In our hospital, general consent is obtained for all investigations, including blood tests. The HIV antibody testing was done with the sole purpose of better patient care. The required medical or surgical treatment was never withheld from any patient. The hospital policy is to refer HIV-positive individuals to the infectious disease clinic, where counseling services are offered.

The algorithm followed was a modification of the method of Kannangai et al. (3). All samples that came for rapid HIV testing were tested by the Capillus test, and the preliminary report was sent. All these samples were then tested by the in-use ELISA (ELISA-1) (UNAIDS and World Health Organization [WHO] approved) irrespective of their rapid test status. If both the rapid result and ELISA-1 result were negative, results were declared negative. If the rapid test was negative and ELISA-1 was reactive, the sample was tested by another ELISA (ELISA-2) and an immunoblot. The immunoblot result was final. If the rapid test was reactive (weak or strong as graded by the technician), the sample was tested by two other ELISA tests. If a sample was reactive by both ELISAs, the sample was declared reactive. If the rapid test was weakly reactive and both ELISA tests were negative, then the sample was declared negative. If there was a discrepancy between ELISA-1 and ELISA-2, the sample was tested by an immunoblot and this result was taken as final.

Plasma samples of 57 individuals infected with a known subtype of HIV-1 were also tested by Capillus HIV-1/HIV-2 to identify whether this test missed samples from individuals infected by subtype C. HIV-1 subtype was determined by heteroduplex mobility analysis (1).

Six thousand six hundred fifty-five samples were tested by

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Capillus HIV–1/HIV-2 between September 1997 and June 2001. Of these samples, one HIV-1-reactive sample was negative by the rapid test. There was concordance between the rapid test and both ELISA tests for 104 HIV-positive samples and 6,475 HIV-negative samples. Nine samples declared indeterminate by the immunoblot were excluded from the analysis. Seventy-five HIV-negative samples were reactive by the rapid test. The Capillus HIV-1/HIV-2 test had a sensitivity of 99% (confidence interval [CI], 94.0 to 100.0%) and a specificity of 98.9% (CI, 98.6 to 99.1%) with a high negative predictive value of 100% (CI, 99.9 to 100%) and a positive predictive value of 58.1% (CI, 50.5 to 65.4%).

There were 63 samples that were weakly reactive (rough reaction) by Capillus HIV-1/HIV-2. None of these results was confirmed by the ELISA tests. To calculate the performance characteristics of the test, these samples were considered positive by Capillus HIV-1/HIV-2, and it was the large number of weakly reactive samples that were responsible for the low positive predictive value.

In the evaluation with a panel of sera from individuals with known HIV-1 subtype, Capillus HIV-1/HIV-2 identified all the 57 samples tested. There were samples from 53 individuals infected with subtype C and 3 individuals with subtype A and one from an individual infected by a non-A, -B, or -C strain.

There is a possibility that if the two ELISA tests that followed the Capillus HIV-1/HIV-2 test used the same antigen, there could be a false-positive report among the samples that were reactive by the Capillus HIV-1/HIV-2 test and both ELISA tests. As per the information provided by the manufacturer, the Capillus HIV-1/HIV-2 test uses recombinant polypeptides from the envelope regions of HIV-1 and HIV-2. Most antibody detection tests for HIV use peptides from the envelope region of HIV-1 and HIV-2, while some also include peptides from the core region. However, the exact peptide used by a company is not revealed in the kit insert, and hence it is difficult to get this information. It is highly unlikely that the same peptide is used by another company too. In addition, the ELISA Recombigen HIV-1/HIV-2 EIA manufactured by the manufacturers of the Capillus HIV-1/HIV-2 test (Cambridge Diagnostics Ireland Ltd.) uses a different cocktail of antigens that includes the envelope and core regions. Hence, it is unlikely that a sample gives a false-positive reaction in all three tests due to the similarity of the antigens used. Using two ELISA tests after a rapid test is also in keeping with the WHO/UNAIDS HIV testing strategy 3 (for diagnosis), which has been recommended as a strategy to save on cost and at the same time maximize accuracy of results (5).

The Capillus HIV-1/HIV-2 test has proven to be a reliable test that was easy to use. At the present market rate of $1.60 per device, this test is cheaper than most of the commercial rapid tests. Since it is a particle agglutination test, it has the ability to identify both immunoglobulin M and immunoglobulin G antibody and hence to pick up seroconverters earlier. Anecdotally, over the past 3 years, this has proven to be the case from our experience with two samples from HIV-1 seroconverters who were positive by the Capillus HIV-1/HIV-2 test. One sample was negative by another rapid test (HIV Tridot; J. Mitra & Co. Ltd., New Delhi, India) and weakly reactive by two ELISA tests, Recombigen HIV1/HIV2 EIA (Cambridge Diagnostics Ireland Ltd.) and HIV-1/HIV-2 3rd generation plus EIA (Abbott Laboratories, North Chicago Ill.). The second sample was negative by one ELISA (Detect HIV; Biochem Immunosystems Inc., Quebec, Canada), reactive by another ELISA (Genedia HIV1/2 ELISA 3.0; Korea Green Cross Corporation, Yongin-shi, Kyonggi-do, South Korea) and also reactive by another rapid test (HIV Tridot; J. Mitra & Co. Ltd.). Both individuals were subsequently confirmed positive by the immunoblot. As these samples were not initially screened by Capillus HIV-1/HIV-2 and were tested as part of a protocol to identify seroconverters, they have not been included for estimation of accuracy indices.

Our finding contradicts that of the Centers for Disease Control and Prevention, for which Capillus HIV-1/HIV-2 missed two out of eight subtype C samples (sensitivity, 75%). This may be a problem with the small sample size of subtype C samples used. It could also represent the varied responses of infected individuals to strains of subtype C from different regions. It has been reported earlier that false-negative results were obtained when samples of individuals infected with HIV-1 subtype D were tested by some rapid test devices (2). These strains had a single amino acid substitution in the envelope region, which probably affected the response of the infected person in relation to the capacity of the test to detect a particular set of antibodies.

With the test performing well with a panel of 53 sera from individuals infected with HIV-1, subtype C from India, and with its acceptable overall sensitivity and specificity, we conclude that it can safely be used as a test in India, where the majority of infections are with subtype C. This we believe is a suitable test for voluntary counseling and testing centers in India, which may not have access to a moderate level of laboratory facilities.

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