Reliability of HIV rapid tests is user dependent

Dhayendre Moodley, Pravi Moodley, Themba Ndabandaba, Tonya Esterhuizen

To the Editor: Rapid tests have been developed predominantly for the purposes of quick, easy-to-use, reliable on-site antibody testing for HIV by non-laboratory trained health professionals.[1] The introduction of rapid tests to resource-limited countries has resolved many logistical issues including limited access to laboratories, delayed results turnaround time, limited laboratory expertise, and exorbitant costs of enzyme-linked immunosorbent assay (ELISA) technology.[2,3]

Four HIV rapid tests used by nurses/counsellors versus skilled laboratory staff were evaluated for their performance characteristics against ELISA. Sensitivity and specificity of rapid tests when performed by nurses/counsellors were 92.5 - 97.3% and 97.6 - 98.2%, respectively, and 100% when performed by laboratory technicians. The suboptimal characteristics of rapid HIV tests when used by non-laboratory staff highlight the need for ongoing training, supervision and quality control in HIV testing programmes. Increased access to advanced technology such as rapid HIV tests is of limited value if users are not supervised and results not regularly monitored. The potential for false diagnoses could undermine public confidence in HIV testing and therefore negatively impact on all HIV prevention, treatment and support programmes.

Expanding voluntary counselling and testing (VCT) and prevention of mother-to-child transmission (PMTCT) programmes must include a reliable HIV testing algorithm and a strong supportive counselling programme. Countries are guided by the World Health Organization (WHO) recommendations that HIV rapid tests require laboratory evaluations to demonstrate sensitivity and specificity exceeding 99%.[4] Current commercialised rapid tests meet the required international performance specifications; however, field evaluations of rapid tests demonstrate inter-study and manufacturer variations in sensitivity and specificity.[5,6]

Women's Health and HIV Research Unit, Department of Obstetrics and Gynaecology, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban
Dhayendre Moodley, BSc, BSc Hons, MMedSci, PhD

Department of Virology, Nelson R Mandela School of Medicine
Pravi Moodley, MB ChB

Department of Health, KwaZulu-Natal, Durban
Themba Ndabandaba, STD, HRP

Medical Bioethics Unit, Nelson R Mandela School of Medicine
Tonya Esterhuizen, MSc

Corresponding author: *D Moodley (moodleyd1@ukzn.ac.za)*

Patients and methods

We conducted field and laboratory evaluations of four widely used HIV rapid tests to determine whether field performance and accuracy meet WHO requirements when the tests are used by nurses/counsellors.

Twelve primary health care facilities in KwaZulu-Natal that routinely provide PMTCT services were selected for field evaluation of HIV rapid tests performed on 961 antenatal attendees. Approval was obtained from the Research Ethics Committee of the Nelson R Mandela School of Medicine, and the KwaZulu-Natal Department of Health.

On-site field evaluation of rapid tests

The four HIV rapid tests (First Response HIV Card Test 1-2.0 (PMC Medical, India Pvt Ltd), Pareekshak HIV Triline (UCB Pharma), Abbott-Determine™ HIV-1/2 (Abbott Diagnostics, Illinois) and Sensa (Seyama Solutions, SA)) evaluated in this study were immunochromatogenic lateral flow rapid tests for the detection of HIV antibodies in whole blood. Approximately 3 ml of whole blood was obtained in EDTA tubes from the antenatal attendees following a written informed consent for participation.

Laboratory evaluations of rapid tests

Remaining whole-blood specimens were sent to the virology laboratory for independent rapid HIV testing by laboratory staff and confirmation with ELISA (Abbott Laboratories, Wiesbaden, Germany).

User survey

A qualitative self-reported assessment of the use of rapid tests in the form of a structured questionnaire was conducted among nurses and counsellors at the health facilities.

Statistical analysis

The sensitivity, specificity, positive and negative predictive values and their 95% confidence intervals (CIs) were calculated using the EpiCalc-2000 (version 1.02). The ranges of the 95% CIs of the reliability indicators were compared to determine whether tests differed from each other.

Results

ELISA

A total of 961 specimens were tested with the ELISA; 553 were HIV negative and 408 (42%) positive. Between 98% and 100% of the samples had HIV rapid test results that could be compared with their corresponding ELISA results.

Field evaluation of rapid HIV tests

Screening HIV tests were performed by lay counsellors in 11 of the 12 facilities, while a positive HIV result was confirmed independently by a nurse in 8 facilities. The sensitivity and specificity of the rapid tests performed by nurses/counsellors compared with the laboratory-based ELISA (gold standard) were 92.5 - 97.3% and 97.6 - 98.2%, respectively (Table I). The Abbott-Determine demonstrated the highest sensitivity (97.3%; 95% CI 95.1 - 98.6), while the Pareekshak demonstrated the highest specificity (98.2%; 95% CI 96.5 - 99.1) ($p<0.005$). There was a significant difference at the 95% level of confidence between the sensitivity estimates for the Abbott-Determine and Pareekshak rapid tests. There were no significant differences between the specificity estimates of the tests.

Accordingly the Abbott-Determine had the highest negative predictive value (NPV) (98%; 95% CI 96.3 - 98.9) while the Pareekshak demonstrated the highest positive predictive value (PPV) (97.6%; 95% CI 95.4 - 98.8).

Laboratory evaluation of rapid HIV tests

For the 88 confirmed HIV-positive samples and 103 confirmed negative specimens, all four rapid tests performed by laboratory technicians provided concordant results, with a sensitivity of 100% (95% CI 95.9 - 100) and specificity of 100% (95% CI 96.5 - 100), respectively.

User survey on performance characteristics

The following responses on performance characteristics were obtained from the nurses/counsellors performing rapid tests:

Time taken to perform tests. Average time was 8.5 minutes (range 3 - 15 minutes).

Time taken to interpret results. Average time was 5.3 minutes (range 2 - 10 minutes).

Ease of performance and interpretation. All users reported that the tests involved a simple and quick procedure. Eight (67%) facilities reported difficulties in labelling the rapid tests with clients' details.

Discussion

Documentation from manufacturer studies for each of the four tests satisfy international standards that the tests have sensitivity of at least 99% and specificity of at least 98% for detection of HIV-1 in whole blood and plasma. The laboratory evaluation in our study further confirms manufacturer claims of high sensitivity and specificity when tests are performed by skilled laboratory technicians. However, the field testing by nurses/counsellors demonstrated lower sensitivity, specificity and relative predictive values. The discrepancy in test performance between site and laboratory was probably due to user error. Furthermore, the lack of on-site supervision, non-adherence to manufacturer instructions and absence of quality control management are all potentially responsible for the sub-optimal quality of the rapid testing process.

All four rapid tests in this study fully satisfy international standards; however, in regions with a high birth rate, under-resourced health settings and high HIV seroprevalence even the use of tests with the highest PPV (97.6%) and NPV (98%) could result in large numbers of incorrect diagnoses. Exploring a worst-case scenario, in a country with a 30% HIV seroprevalence and an estimated 500 000 of the 1 200 000 pregnant women testing for HIV annually, an estimated 3 600 women (2.4%) could be falsely diagnosed as HIV positive and an additional 7 000 (2%) falsely diagnosed as HIV negative.

Our results suggest that although rapid tests perform well in laboratories, it is prudent to ensure adequate preparation of staff and intensive quality assurance in clinical settings that use internationally recommended rapid tests. The implications of unreliable testing are deleterious and tragic. Reports indicate personal emotional distress, severe physical trauma from partners, abandonment and suicides, and some pregnant women have even been advised on and exposed to interventions to reduce mother-to-child transmission.[7-9] Increased public awareness of false HIV diagnoses with rapid tests could undermine public confidence in these tests and negatively affect the uptake of HIV testing.

While rapid tests have increased the clients' confidence because the tests are performed in their presence and the chance of errors with incorrectly labelled specimens is minimal, an inappropriate testing algorithm and inadequate user training resulting in a large number of discordant results would unfortunately negatively impact uptake of VCT as demonstrated in clients' responses to discordant results in our study. Two-thirds of the facilities reported that clients did not return for their ELISA results following discordant results with rapid tests.

Table I. Sensitivity and specificity of rapid tests when used by nurses/counsellors

	True positives by ELISA		True negatives by ELISA	
Rapid tests	*N*=408	Sensitivity (95% CI)	*N*=553	Specificity (95% CI)
Abbott-Determine	397	97.3 (95.1 - 98.6)	540	97.6 (95.9 - 98.7)
First Response	384/396	96.9 (94.6 - 98.4)	530/541	97.9 (96.3 - 98.9)
Sensa	391	95.8 (93.3 - 97.5)	540/552	97.8 (96.1 - 98.8)
Pareekshak	368/398	92.5 (89.3 - 94.8)	531/540	98.3 (96.5 - 99.1)

Recommendations

This report emphasises the need for assuring accuracy and reliability of HIV rapid testing by applying a quality system approach that addresses continued supervision, development of standard operating procedures, prioritises ongoing training and ensures monitoring and improving of the testing process.

We express our gratitude to the following for assisting with the implementation of the study: District Co-ordinators Z Dladla (Uthukela district), O T Mhlongo (Umgungundlovu district), N Hlongwane (Uthungulu district), P Dladla (Ethekwini district), Z Ncama (Ugu district), B Ngubane (Umzinyathi district) for project co-ordination, and counsellors and nurses at the health facilities for participation in the study.

Views expressed here are personal opinions of the authors and have not been endorsed by manufacturers or any other party cited in this article.

References

1. Kanal K, Chou TL, Sovann L, Morikawa Y, Kakimoto YK. Evaluation of the proficiency of trained non-laboratory and laboratory technicians using a rapid and simple HIV test. *AIDS Res Ther* 2005; 2: 5.
2. Matambo JA, Moodley D, Moodley J. HIV seroprevalence and rapid testing in unbooked pregnant African women. *Int J Gynecol Obstet* 1999; 66: 289-290.
3. McKenna SL, Muyinda GK, Roth D, *et al*. Rapid HIV testing and counselling for voluntary testing centres in Africa. *AIDS* 1997; 11(1): S103-110.
4. World Health Organization. *Rapid HIV Tests. Guidelines for Use in HIV Testing and Counselling in Resource Constrained Settings*. Geneva: WHO, 2004.
5. World Health Organization and Centers for Disease Control and Prevention. *Guidelines for Appropriate Evaluations of HIV Testing Technologies in Africa*. 2002. http://www.who.int/diagnostics_laboratory/publications/EN_HIVEval_Guide.pdf (accessed 5 May 2008).
6. Delaney KP, Branson B, Fridlund C. Ability of untrained users to perform rapid HIV antibody screening tests. Centers for Disease Control and Prevention. National Center for HIV, STD and TB Prevention. Division of HIV/AIDS Prevention. American Public Health Association Annual Meeting. October 2002. http://www.cdc.gov/hiv/topics/testing/resources/abstracts/pdf/rt-screening.pdf (accessed 5 May 2008).
7. Guthrie J. Man led to believe he is HIV positive for 8 years. *The Chronicle* 2004; 28 August.
8. Leonard AS. Big award for false HIV results. *Gay City News* 2003; 2(23). http://204.2.109.187/gcn223/bigaward.html (accessed 5 May 2008).
9. Zacharias NM, Athanassaki ID, Sangi-Haghpeykar H, Gardner MO. High false-positive rate of human immunodeficiency virus serum screening in a predominantly Hispanic prenatal population. *J Perinatol* 2004; 24(12): 743-747.

Accepted 27 March 2008.