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Indeterminate rapid HIV-1 test results among antenatal and postnatal mothers

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Summary

The sensitivity and specificity of rapid HIV-1 tests may be altered during pregnancy and postpartum. We conducted a study to determine the prevalence and correlates of false-positive Abbott Determine™ and false-negative Uni-Gold™ rapid HIV-1 test results among antenatal and postnatal mothers attending a primary care clinic in Nairobi, Kenya. Mothers were tested for HIV-1 using Abbott Determine™ and non-reactive results were considered HIV-1 antibody negative. Reactive samples by Determine were re-tested by Uni-Gold™. Vironostika HIV-1 and Uni-FORM II Enzyme-linked immunosorbent assays were used to confirm samples that had positive Abbott Determine™ and negative Uni-Gold™. Among 2311 women who accepted HIV-1 testing, 1238 (54%) were tested antenatally and 1073 (46%) were tested postnatally. Of tested women, 274 (12%) women were reactive by Abbott Determine™ and on retesting with Uni-Gold™ 30 (11%) had indeterminate results. The prevalence of indeterminate results was significantly higher in antenatal women than in postnatal women (2% versus 1%, $P = 0.03$). In conclusion, indeterminate rapid HIV-1 test results are more common in the antenatal period and appropriate safeguards to confirm HIV-1 infection status should be implemented in antenatal programmes.

Keywords

indeterminate; HIV; rapid; ELISA; test

INTRODUCTION

Worldwide, almost half of the 42 million people with AIDS are women of child-bearing age. In Kenya, between 1999 and 2001, the ratio of infected women to men increased from 1.2:1 to 1.5:1 while among 15 to 19-year-old girls, HIV prevalence is seven times higher than among teenage boys.[1] HIV-1 testing, which is an essential component of HIV-1 prevention and care, is often offered to women during pregnancy and after delivery in prevention of mother-to-child HIV-1 transmission (PMTCT) programmes.[2–4] The need for counselling and testing of mothers has increased with studies demonstrating feasibility of low-cost interventions to reduce mother-to-child transmission of HIV (MTCT) using short courses of antiretroviral regimens.[5]

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Rapid on-site HIV-1 tests are preferred in PMTCT programmes as they are relatively easier to administer and interpret compared with enzyme-linked immunosorbent assay (ELISA). With the use of rapid HIV tests, patients can get results soon after testing and there is no possibility of some failing to return for results as it happens with the use of ELISA. Conventional ELISA-based HIV testing has been problematic as it is designed for batch testing, is time-intensive, and expensive. ELISA-based HIV testing also requires sophisticated equipment, a reliable power supply and skilled technicians, conditions that are often lacking in the field.[6]

HIV-1 tests are, however, to some extent, unreliable as target antibodies can cross-react with other proteins in human blood. False-positive results can be caused by allo-antibodies resulting from pregnancy, transfusion, transplantation or autoimmune disorders.[7] There is also potential for false-positive results related to other diseases, such as malaria.[8] False-negative results can be due to the low levels of antibody as in early sero-conversion, infection with variants of the virus that are less detectable by the assay configuration, antibodies that do not react with specific antigens utilized in the assay configuration and improper specimen handling resulting in loss of HIV antibody multivalency.[9,10] This study was conducted to determine the prevalence and correlates of false-positive Abbott Determine™ (Abbott Labs, Abbott Park, IL, USA) rapid HIV test results and false-negative Uni-Gold™ (Trinity Biotech Plc, Bray, Co. Wicklow, Ireland) rapid HIV test results among antenatal and postnatal mothers.

METHODS

Rapid HIV test results from three studies conducted at Mathare North City council clinic were analysed. Two studies (the Couple Counseling and Testing and HIV-1 Incidence studies) enrolled pregnant women at their first antenatal visit irrespective of gestation and one study (Interventions to Reduce HIV-1 Incidence After Delivery Study) enrolled mothers bringing children for measles vaccination at nine months after delivery.[11–13]

All patients were tested using Abbott Determine™ HIV-1/2 rapid test kit and non-reactive results by this test were considered HIV negative and reactive samples were retested using, Uni-Gold™. Samples reactive by both tests were considered positive. Samples that gave a reactive result using Abbott Determine™ and non-reactive results using Uni-Gold™ were retested by an ELISA assay using Vironostika HIV Uni-FORM II Ag/Ab and if reactive were confirmed by Enzygnost HIV Integral. The ELISA results were considered the true results and based on these we classified indeterminate results into false-positive Abbott Determine™ results or false-negative Uni-Gold™ results.

The Abbott Determine assay is an immunochromatographic rapid technique with HIV-1 and -2 recombinant antigens as well as peptides of HIV-1 and -2 envelope antigens. To run the test, 50 μl of plasma was pipetted on the sample pad of a well-labelled test device and results were read after 15–60 minutes. The Uni-Gold™ assay is an immunochromatographic rapid technique with recombinant proteins representing the immunodominant region of the envelope protein of HIV-I and 2, glycoprotein gp41and gp120 of HIV-1 and gp130 of HIV-2 are immobilized at the test region of the nitrocellulose strip. To run the test approximately, 60 μl of plasma was carefully placed in the sample port, followed by the addition of 60 μl of wash detergent (buffer). Results were read after 10 minutes.

Data were entered into a password-secured Microsoft Office Access 2003 Data Base and analysed using the Statistical Package for Social Scientists (SPSS® Inc) Version 13.0. In univariate analysis, we used the χ^2 test to compare categorical variables and the *t*-test for independent samples for continuous variables and multivariate logistic regression was used

to determine independent correlates of indeterminate false-positive and false-negative results.

RESULTS

Two thousand three hundred and eleven women were tested. The majority of women were married (89%), not formally employed (74%), had had a previous pregnancy (90%) and 67% of the women had sexual debut at an age of 16 years or later (Table 1). Of the women tested, 1238 (54%) were tested antenatally and 1073 (46%) after delivery. Overall, 2037 (88%) women tested negative, 244 (11%) tested positive and 30 (1%) had indeterminate results. Of the 30 indeterminate results, 21 (73%) were false-positive Abbott Determine™ results and 9 (27%) were false-negative Uni-Gold™ results (Table 1). Frequency of indeterminate results did not differ by women's sociodemographic, sexual or obstetric characteristics. However, indeterminate results were more common among women tested antenatally than those tested postnatally ($P = 0.03$; Table 2).

DISCUSSION

The use of rapid HIV-1 tests in antenatal and postnatal clinics has led to increased numbers of mothers who are tested and receive test results.[6] Thus, rapid HIV-1 testing may contribute to ensure that HIV-1-infected mothers and their infants can receive interventions to prevent mother-to-child HIV-1 transmission, be referred for HIV-1 care, receive prophylaxis against opportunistic infections and be counselled on positive living. However, false-positive HIV-1 results can cause psychological distress to HIV-1-negative mothers while false-negative results may cause HIV-1-positive mothers and their infants not to receive appropriate interventions and care.

In our study, we found that the rate of indeterminate results was low, and comparable to what was observed in a previous study that used Determine and Capillus.[14] However, the frequency of indeterminate results among pregnant women in our study was higher (2%) than that reported in Ivory Coast studies (0.7%), and (1.1%) in which Abbott Determine and Genie II assays were used.[15,16] Similar results were produced in a Rio de Janeiro pilot study, which employed Determine and Double Check Orgenics rapid tests (1%).[17]

Our study confirms findings from an earlier study that indeterminate results are more common among pregnant than among non-pregnant women.[18] Therefore, counselling and testing programmes targeting pregnant women will require more support to deal with indeterminate tests. In our study, we found that the majority of women with indeterminate results were actually negative. Rio de Janeiro pilot study demonstrated similar findings.[17] This should be taken into account when counselling women who have indeterminate results to ensure that they return for ELISA results that are not usually readily available.

A limitation of this study is that Uni-Gold™ was only used to confirm tests that were positive on Abbott Determine™; therefore, we are not able to report on false-positive rates for the Uni-Gold™ tests or false-negative rates of the Abbott Determine tests. In addition, false-negative Uni-Gold prevalence was assessed only in Abbott Determine reactive women. However, our findings on false-positive HIV-1 test results using Determine and false-negative Uni-Gold™ results among patients testing positive with Determine are important for guiding counselling of women who have indeterminate results.

Our findings that although rare indeterminate results are more common during pregnancy and that the majority of women with indeterminate results are negative should be taken into consideration when deciding on whether to use parallel or serial testing algorithms, in counselling women with indeterminate results and deciding whether women with

indeterminate results should receive intervention to prevent mother-to-child transmission of HIV as they await ELISA results.

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Table 1

Study population characteristics (N = 2311)

Characteristic	Number (%)
Age (years)	
<24	1421 (61)
>24	890 (39)
Marital status	
Not married	256 (11)
Married	2051 (89)
Employment	
Unemployed	1709 (74)
Employed	592 (26)
Monthly rent (KSh)	
<1600	1190 (54)
>1600	1027 (46)
Parity	
Primigravida	236 (10)
Multigravida	2035 (90)
Sexual debut (years)	
<16	742 (33)
>16	1516 (67)
Time of testing	
Antenatal	1238 (54)
Postnatal	1073 (46)
HIV test result	
Negative	2037 (88)
Positive	244 (11)
Indeterminate	30 (1)
Type of indeterminate result, *n* = 30	
Determine false-positive	21 (73)
Unigold false-negative	9 (27)

Table 2

Correlates of indeterminate results

Correlate	Concordant (*N* = 2281)	Indeterminate (*N* = 30)	*P* value
Age (years)			
<24	1402 (99%)	19 (1%)	0.8
>24	879 (89%)	11 (11%)	
Level of education			
Less than secondary	1632 (99%)	24 (1%)	0.3
Secondary and above	647 (99%)	6 (1%)	
Mean monthly rent (KSh)			
<1600	1170 (98%)	20 (1%)	0.1
>1600	1018 (99%)	9 (2%)	
Parity			
Primigravida	232 (98%)	4 (2%)	0.5
Multigravida	2009 (99%)	26 (1%)	
Age of first sex (years)			
<16	729 (98%)	13 (2%)	0.2
>16	1499 (99%)	17 (1%)	
Marital status			
Not married	252 (98%)	4 (2%)	0.6
Married	2025 (99%)	26 (1%)	
Employment			
Unemployed	1689 (99%)	20 (1%)	0.3
Employed	582 (99%)	10 (2%)	
Time of testing			
Antenatal	1216 (98%)	22 (2%)	0.03
Postnatal	1065 (99%)	8 (1%)	
Lifetime sexual partners			
1 partner	733 (99%)	9 (1%)	0.8
>1 partners	1534 (99%)	21 (1%)	