INTRODUCTION

Nigeria is the most populous country in Africa and ranks second after South Africa in the number of people living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS).\[1\] Her high HIV burden has continued to be a source of concern to the global community and is among the United Nations few HIV-priority countries (including Chad, Democratic Republic of the Congo) where <20% of pregnant women living with HIV were identified in 2010.\[2\] In these countries, antiretroviral (ARV) coverage for pregnant women living with HIV was only 9%, which is markedly below the 80% target set for the Millennium Development Goals by the United Nations General Assembly Special Session.\[2\]

To achieve universal access (80%) by 2015\[3\] and mitigate the impact of vertical transmission (VT), the Nigerian government with support from international partners, is rapidly scaling up prevention of mother-to-child transmission (PMTCT) services to secondary and primary health care centers.\[4,5\] Antenatal HIV testing and counseling (AHTC) is the entry point for PMTCT of HIV services.\[6-8\]

ABSTRACT

Objective: The objective of the study is to determine whether retesting for human immunodeficiency virus (HIV) in labor is important in Nigeria. Subjects and Methods: A prospective cohort study involving 400 antenatal women who tested HIV-negative at booking in an obstetric unit of a university college hospital in Nigeria were retested in labor at least 12 weeks from initial tests. Seropositive mothers and exposed infants had antiretroviral prophylaxis and were followed-up. Main outcome measures were rate of acceptance to rescreen, incidences of seroconversion, mother-to-child transmission and associated factors. Results: Majority 96.4% (400/415) accepted whereas 3.6% (15/400 N) declined retesting on the grounds of a previous negative result. The seroconversion rate was 0.25%. Maternal age ≥25 years (OR = 5.0), secondary and post-secondary education (OR = 622.4) and parity ≥1 (OR = 17.2) were significant factors for acceptance to rescreen whereas occupation (P = 0.25) and marital status (P = 0.23) were not. The only HIV-exposed infant from the seroconverted mother was not breastfed and tested negative at 6 and 12 weeks using deoxyribonucleic acid polymerase chain reaction. Conclusion: The rate of seroconversion was low, but perinatal HIV infection was averted. Supposedly low-risk women could seroconvert and cause vertical transmission (VT). Retesting may still be important in resource-constrained settings to identify women with recent infection, institute appropriate interventions to avert VT thereby achieving the international goal of “no new HIV infection by 2015”. Although a large multicenter study to evaluate our findings is ongoing, studies to determine the cost-benefits of such interventions are justified.

Key words: Averting perinatal human immunodeficiency virus, intrapartum screening, seroconversion
The recent antenatal seroprevalence survey of HIV in Nigeria showed persistent wide geographical variations. The South-south and North-central zones had the highest prevalence of 8.2% each. This was twice the national average of 4.1%.\[^{9}\] and this high prevalence could impact negatively on the rate of VT of HIV.\[^{10}\] In 2009, early infant diagnosis (EID) using polymerase chain reaction (PCR) for HIV deoxyribonucleic acid (DNA) test in Nigeria showed that 13.1% of infants born to HIV-infected mothers were themselves infected,\[^{10}\] which is unacceptably high. Without preventive interventions, HIV VT rates range from 15% to 45% especially when breastfeeding is continued for more than 18 months.\[^{8,11}\] More than 95% of MTCT of HIV occurs during the intrapartum period.\[^{12}\] The VT rate can be reduced to <2% when women receive triple ARV preventive therapy and do not breastfeed.\[^{3}\] Culturally, however, most Nigerian women breastfeed their infants.

Accessing HIV counseling and testing (HCT) at an opportune time during pregnancy is often limited by socio-cultural and economic factors.\[^{13}\] When AHTC is combined with intrapartum HIV testing and counseling (IHTC), the yield is expected to improve.\[^{14-16}\] In pregnancy, HIV poses additional physical, immunological and psychological stress and increases maternal and perinatal morbidity and mortality.\[^{17}\] High maternal viral load (VL) and low CD4 count are risk factors for VT. Maternal acute HIV infection during pregnancy is associated with higher VL.\[^{8}\]

In the last 2 decades, the availability of facilities for diagnosis and antiretroviral therapy (ART) has revolutionized HIV management including PMTCT.\[^{16-22}\] In pregnancy, the principle of management of HIV infection is aimed at reducing VT by reducing VL and improving maternal immunity through appropriate use of ARVS , nutritional supplementation, infant ARV prophylaxis and optimum infant feeding practices.\[^{18,23,24}\] EID and initiation of ART or prophylaxis is the mainstay of management.\[^{18,21,24}\] Effective utilization of triple ARVs (highly active ART or HAART) in pregnant women who qualify for it is beneficial for the women’s own health and best prophylaxis against MTCT.\[^{8,18,22}\] This standard of care in developed countries has dramatically reduced MTCT rates to <2% in those settings.\[^{3,18,22}\]

To benefit from these interventions, HIV diagnosis through HCT must first be done to enable initiation of ART or prophylaxis. In resource-constrained settings such as in Nigeria, HIV diagnosis is often based on rapid test; a method that cannot diagnose the infection in the “window period.”\[^{8,25}\] The use of PCR test to pick up the viral particles in patients’ blood or serum is confirmatory but not feasible as routine in antenatal settings.\[^{8}\] Consequently, when initial opportunity is missed, another window of opportunity is provided at 34–36 weeks gestation or in labor for repeat testing for HIV to detect women who may be acutely infected or seroconvert during the pregnancy.\[^{16}\] This provides benefit for ARV prophylaxis, modified obstetric interventions and infant feeding practices.\[^{8}\] This intervention targets women without access to AHTC; unbooked women or women with unknown HIV status. Others are women whose testing is more than 3 months previously. These women could benefit from early IHTC, peripartum ARV prophylaxis and other PMTCT interventions.\[^{8}\]

Repeat HIV testing in labor and delivery has been recommended as a standard of care as it increases ARV provision for women who seroconvert during pregnancy.\[^{26}\] Though recommended, this intervention is yet to be made routine in most hospitals in Nigeria. Reports from Uganda\[^{15,27}\] and South Africa\[^{16,28}\] where the HIV epidemics are considered to be generalized have shown that retesting for HIV is important. Nigeria’s status was recently changed from generalized to “mixed epidemic” by the United Nations Program on HIV/AIDS.\[^{29,30}\] The goal of this study, therefore, is to determine whether retesting is also important in Nigeria.

**SUBJECTS AND METHODS**

This prospective study was a pilot study to determine the feasibility and value of introducing routine repeat screening for women in labor. The study involved booked consecutive pregnant women confidentially enrolled at delivery at the University of Benin Teaching Hospital, Nigeria from July 1 through September 30, 2009. To qualify for enrolment into the study, each volunteer had to give informed consent after counseling and should have had a previous negative HIV test result not <12 weeks previously. Women with previous unknown HIV status, though are routinely screened for HIV and managed accordingly in this unit, were excluded from the study. Confidentiality
was maintained for all patients by coding of results known only to the care givers.

The hospital’s Ethics and Research Committee gave approval for the study.

**HIV screening and management protocol**

Each volunteer had a volume of 5 ml of blood taken from the ante-cubital vein and sent to the laboratory in a potassium ethylene diamine tetraacetic acid-anticoagulant containing specimen bottle for serological test. The specimens were centrifuged and the plasma separated and analyzed for HIV 1 and 2 antibodies using Capillus HIV-1/HIV-2 (Trinity Biotech PLC, Jamestown, New York, USA) and then Genie1 HIV-1/HIV-2 (Bio-Rad, Marnes La Coquette-France) rapid test kits. Determine HIV-1/2 (Abbott Laboratories, Illinois, USA) was used as a “tie-breaker” when there is serodiscordance in accordance with the WHO double/triple Algorithm.[25] Mothers had post-test counseling by regular hospital counselors of the PMTCT program as soon as it was convenient. Women newly diagnosed as HIV positive in labor received a single dose Nevirapine (sdNVP) tablet 200 mg orally followed by lamivudine (3TC) 150 mg 12 hourly and zidovudine (ZDV) 300 mg 12 hourly for 1 week (to prevent Nevirapine (NVP) resistance pending the outcome of the CD4 count result), in accordance with the Nigerian National Guideline on PMTCT of HIV.[8] The women also received psychological and social support from trained counselors throughout the duration of labor. When the diagnosis of HIV is made in early labor with intact fetal membrane, the women in addition to ARV prophylaxis were counseled for cesarean section (c/s) and those who accepted were so delivered.[31] Women that declined having c/s were offered appropriate labor management,[8] including delay in artificial rupture of the fetal membrane and vaginal cleansing with chlorhexidine hydrochloride if the membranes were ruptured. All HIV positive women were given infant feeding counseling.[8]

At the time of study, during the postpartum period, if the CD4 was ≤250 cells/ml, the woman was placed on HAART under the management of a trained physician in the adult ARV clinic. If the CD4 count >250 cells/ml she was followed-up at the adult clinic while ARVs were delayed until the CD4 count was ≤250 as recommended by the National Guideline on PMTCT of HIV/AIDS[8] (The current National Guideline has changed recommending HAART for pregnant women with CD4 count ≥350 cells/ml for prophylaxis irrespective of clinical stage of the HIV disease[32]).

The cost of ART/prophylaxis, hospitalization, delivery including cesarean sections and postnatal care were free to the patient under the Government of Nigerian (GON) free obstetric care program for HIV-positive women. This program was funded by the GON in collaboration with the United States Government through the President’s Emergency Plan for AIDS Relief (PEPFAR).[4,5]

**Data analysis**

The study was designed to have a sample size 400 at 95% level of confidence, α of 0.05, error margin of 2.5% and allowing for 25% rate of decline to test with a national antenatal HIV seroprevalence 4.6% (approximately 5%) in the 2008 serosentinel survey.[31] All analysis were intention-to-treat. The data were analyzed using the GraphPad Instat™ Software statistical package version 3.06 (GraphPad Software Inc., El Cammino Real, San Diego, USA). Subgroups were compared using Fisher’s Exact Test and descriptive statistics for proportions where appropriate. The two-sided \( P < 0.05 \) was considered to be significant.

**RESULTS**

Of the 415 women qualified for enrolment during the period of the study, 400 (96.4%) accepted while 15 (3.6%) declined. Those that declined cited their previous negative HIV test results. Furthermore, that there had been no changes in their social behavior and that of their spouses since the last test. The demographic characteristics of the study population are shown in the Table 1.

The mean age was 29.4 ± 3.6 (range 18-43) years, parity 2.0 ± 1.4 and gestational age 37.3 ± 8.6 weeks. Four out of 30 (13.3%) women who were ≤24 years declined the test compared with 11 out of 370 (3.0%) who were 25 years or older \( (P < 0.02); OR: 5.02 \). Women with no-formal and primary education 17.6% (13/17) compared with those that had secondary and tertiary education 0.5% (2/383) were more likely to decline the test \( (P < 0.0001; OR: 622.38) \). Nulliparous women 8.2% (12/146) compared with primiparous and multiparous 1.2% (3/254) were more likely to decline the test \( (P < 0.0001; OR: 17.15) \). There was no statistical
difference between those who accepted or declined the test in terms of occupation and marital status.

The HIV incidence was 0.25% (1/400) while 99.75% were seronegative. One seroconverter was a 27-year-old woman who booked and tested HIV-seronegative at gestational age of 15 weeks, had an uneventful antenatal care and presented in labor at 38 weeks. She received sdNVP 200 mg + 3TC 150 mg + ZDV 300 mg orally as soon as diagnosis was made in labor. Postpartum she had ZDV + 3TC for 7 days. Her CD4+ T-lymphocyte count was 386 cells/ml. For logistic reasons, we could not assess the woman's VL levels. She was counseled for and accepted cesarean delivery. She was delivered of a 3.1 kg male neonate.

The baby received sdNVP 6 mg (2 mg/kg) immediately after birth plus ZDV 12 mg 12 hourly (4 mg/kg/dose 12 hourly) for 6 weeks (This was the practice as at the time of study using the 2007 National PMTCT Guideline of the Federal Ministry of Health). The mother opted for breast milk substitute for her infant’s nutrition. She was referred to the adult and the baby to the pediatric ARV clinics respectively for follow-up management. Using PCR DNA for EID, the baby tested HIV negative at 6 and 12 weeks of age. The child’s growth parameters were normal. She later notified the spouse who accepted screening and he tested negative at 4 and 12 weeks from the time of diagnosis of HIV in the spouse.

**DISCUSSION**

Infants infected with HIV suffer ill-health and mortality especially in the absence of diagnosis and ART. Therefore, preventing maternal transmission through effective PMTCT interventions is an acceptable way of ensuring HIV-free infant survival. This study has provided one of such opportunity through repeat intrapartum screening.

In this study, the rate of acceptance to retest in labor of 96.4% is high and encouraging. Data for intrapartum testing of cohort of women antenatally seronegative for HIV is scarce in this environment making comparison difficult. However, the acceptance rate is comparable with the 86% for Ugandan women[27] and 95.3% for HIV negative Kenyan women who retested 6 weeks postpartum at immunization clinic.[32] The few studies from Northern[33] and South-west Nigeria,[34] and Cameroon[35] included women with unknown status. Thus, to the best of our knowledge, this is the only study from Nigeria that has a cohort of women who were all HIV-seronegative during the antenatal period and retested in labor.

The high rate of acceptance to rescreen may be attributable to knowledge acquired by the women from initial antenatal health education and counseling by the public health nurses/midwives and counselors of the PMTCT program respectively. Furthermore, the patients’ initial negative test results may have acted as further “stimulus” to rescreen. Maternal age more than 25 years, secondary and post-secondary education and parity ≥1 were all statistical significant factors associated with acceptance to rescreen. However, occupation and marital status were non-significant factors. Similar findings had been reported for Cameroonian women.[35] The low mean parity of women in this study was due to the high preponderance of nulliparous women (31.0%).

The incidence of HIV in this study, 0.25%, is much lower than the 2.3-12% reported for Ugandan women,[15,27] the 2.6%, 2.9%, 3.0% and 4.4% for women in Kenya,[32] Botswana,[36] South Africa[16] and

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**Table 1: Demographic characteristics of the study population**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Frequency (N=400)</th>
<th>Percentage (100)</th>
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<tbody>
<tr>
<td>Age in years</td>
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<tr>
<td>&lt;20</td>
<td>3</td>
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<td>20-25</td>
<td>37</td>
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<tr>
<td>41-45</td>
<td>14</td>
<td>3.5</td>
</tr>
<tr>
<td>Marital status</td>
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<td>1.5</td>
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<tr>
<td>Married</td>
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<td>Level of education</td>
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<td>Occupation</td>
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<tr>
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<tr>
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<tr>
<td>≥5</td>
<td>12</td>
<td>3.0</td>
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Swaziland[36] respectively. A recent study from South Africa showed an estimated point HIV incidence of 11.2% per year.[28] In a disaggregated data from a northern Nigerian study,[39] 2.1% seroconversion rate was reported. This is over eight-fold the incidence of HIV found in this study. In these other studies, the time interval from early pregnancy to repeat peripartum HIV testing ranged from 12 to 60 weeks. In this study, the minimum time interval was 12 weeks.

Early commencement of HAART and continuing during labor, delivery and immediate postpartum period plus neonatal ARV prophylaxis is the mainstay of reducing VT especially when the infant is not breastfed.[8,32] Such intervention is associated with VT ≤2% [1,3-8] even though WHO recently recommended breastfeeding with ARV prophylaxis.[18]

Without retesting, one woman in this study would not have received appropriate intrapartum and postpartum HIV interventions. This study highlights the benefit of this strategy especially when the risk of seroconversion or new infection cannot be convincingly excluded. In Botswana, it has been estimated that maternal transmission secondary to HIV seroconversion during pregnancy could account for more than 40%, [36,37] The outcome for the one HIV-exposed infant was good (HIV negative), which was the main objective of PMTCT interventions. The physical and psychological benefit to the couple, family members and friends, care-givers and the society of preventing perinatal HIV/AIDS compared with the high infant mortality and expensive cost of lifetime medical care of an infected child[38,39] cannot be quantified in monetary terms.

One limitation of this study is the relatively small sample size. In spite of this, one case of seroconversion (acute or new infection) was detected and a new infant infection averted. Thus, any measures that will avert perinatal HIV and reduce heterosexual HIV infections through HCT for spouse and safer sex practices are, obviously, well-directed interventions and intrapartum rescreening is one of them.

CONCLUSION

The study has attempts to highlight the benefit of repeat intrapartum screening of supposedly low-risk women whose status of HIV seroconversion (acute or new infection) was uncertain. Though the rate of seroconversion was low, a perinatal HIV infection was averted thus contributing to the realization of the international goal of “no new HIV infection by 2015”. Although a large multicenter study to evaluate our findings are ongoing, studies to determine the cost-benefits of such interventions are necessary.

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Announcement

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