International Journal of Current Research in Chemistry and Pharmaceutical Sciences
www.ijcrcps.com Volume 1 Issue: 3 2014 Pages: 29-35
(p-ISSN: 2348-5213; e-ISSN: 2348-5221)

RESEARCH ARTICLE

OUTCOME OF MATERNAL-FOETAL HIV TRANSMISSION INTERVENTION IN UNIVERSITY OF UYO TEACHING HOSPITAL, UYO, NIGERIA

E.M.UMOFFIA[1*], J. EPOKE[2], S.J. UTSALO[2], J.E. EYOH[3] AND A.I.ETUK[3]

[1]Department of Medical Microbiology and Parasitology/Molecular Virology Unit. University of Uyo Teaching Hospital.
[2]Department of Medical Laboratory science, Medical Microbiology and Parasitology Unit, University of Calabar
[3]Department of Chemical Pathology/Molecular Virology Unit. University of Uyo Teaching Hospital
Department of Obstetrics and Gynaecology, University of Uyo Teaching Hospital, Uyo.
*Corresponding author e-mail: eddy_mike1@yahoo.com

Abstract

Prevention of mother-to-child transmission of HIV is a global intervention program that is aimed at preventing mother-to-child transmission of human immunodeficiency virus (HIV). Qualitative DNA-PCR assay is a preferred method for diagnosis of HIV in early infants. 418 HIV positive pregnant women who were on anti-retroviral therapy (ART) for long-term, (3 months and above) and 100 who were administered at labour (short-term) were monitored till delivery. Dried blood spots of babies who were administered nevirapine within 72 hours of birth and zidovudine (ZDV) for 6 weeks were taken for qualitative HIV-1 DNA PCR analysis using Amplicore method. Parameters of babies of long-term ART treated mothers were compared with those of short-term ART treated mothers. The results showed that out of 412 babies, 53(12.9%) were infected with HIV at birth, as against 359(87.1%) who were negative. Long-term ART treated pregnant women had less number of babies, 20(6.3%) who were HIV infected at birth compared with short-term treated 33(34.4%). The Maternal-foetal transmission intervention could be considered successful in University of Uyo Teaching Hospital.
.

Keywords: Maternal-foetal HIV transmission, long-term and short-term ARV treatment

Introduction

Prevention of mother-to-child transmission (PMTCT) of HIV is the intervention in the transmission of Human immunodeficiency virus (HIV) from a woman infected with HIV to her child during pregnancy, childbirth and breastfeeding (Newell, 2003; Filteau, 2003; Brahmbhatt et al., 2006; Eke, 2007). The mode of HIV transmission is also referred to as vertical transmission or perinatal transmission.

Intervention is an action or strategy to address a particular problem or issue to prevent it from resulting in a given outcome.

The global epidemic of HIV infection continues to spread, with about 4.3 million new infections occurring annually (Federal Ministry of Health, Nigeria, 2007). HIV-infected individuals annually. Over the years, the epidemic has shifted from one dominated by infected males to one with a preponderance of infected females, particularly in sub-Saharan Africa which carries 75% of the global HIV burden (8). As more women become HIV-infected, there is a growing HIV and AIDS epidemic among children, who acquire the infection through mother-to-child transmission (MTCT) (Federal Ministry of Health, Nigeria, 2007).

HIV transmission to children can occur by three main routes:

Mother-to-child transmission of HIV (MTCT) during pregnancy, labour and delivery and breastfeeding.
Exposure to contaminated blood or other body fluids, e.g through transfusions of infected blood products or through contact with needles or other instruments contaminated with infected blood or other body fluids.

Sexual exposure

Without interventions to prevent transmission, the risk of MTCT of HIV is about 15-30% if the mother does not breastfeed; the risk is as high as 30-45% if the mother breastfeeds her baby for a prolonged period of time (De Cock, *et al*, 2000).

The widespread availability and acceptance of interventions to prevent MTCT of HIV has dramatically reduced the number of children who become infected with HIV each year in industrialized countries. For example, the estimated incidence of HIV infection among children of HIV infected mothers in the United States had declined from an estimated peak of approximately 1,800 per year to less that 200 per year (8). This contrasts with the estimated 1,450 children who acquire HIV infection each day in sub-Saharan Africa mostly through MTCT (Federal Ministry of Health, Nigeria, 2007).

Mother-to-child transmission (MTCT) of HIV remains a major public health problem worldwide, especially in developing countries home to more than 95% of people living with HIV/AIDS (PLHA) globally.

Recent scientific developments have led to feasible and effective interventions to reduce the risk of MTCT in resource-poor settings. Because many prevention of mother-to-child transmission of HIV (PMTCT) programmes are only as good as the existing services into which they are integrated, these interventions rely heavily on functioning maternal and child health (MCH) clinics. HIV counselling and testing (HCT) rely on existing maternal and child health clinics and PMTCT services using as priorities in their national strategic framework. A few have moved from pilot to national programmes and are moving even closer to positioning PMTCT as a basic component of care for pregnant women. Many PMTCT programme planners now recognize that PMTCT should be part of comprehensive (HIV/AIDS prevention, care and support programme, both are at the national level and within centralized systems.

Materials and Methods

Sources and collection of samples

This study was carried out on 418 sero-positive pregnant women who were attending antenatal clinic and babies born of them at the University of Uyo Teaching Hospital, Uyo (UUTH).

Ethical approval was obtained from University of Uyo Teaching Hospital. Questionnaires and consent forms were filled by the pregnant women at the antenatal clinic.

Samples of blood were taken blood were taken from the pregnant women at the antenatal clinic and HIV screening tests were carried out.

Those who tested positive were recruited into the study and followed-up till their babies were delivered.

Obstetric history of each of the HIV positive pregnant women were taken. These include gestation period, parity, age, mode of delivery, time of diagnosis of HIV infection, mode of delivery of previous babies if any.

HIV negative pregnant women and their babies were used as controls.

The pregnant women whose HIV screening were carried out were of two groups, the long-term and short-term antiretroviral drugs treated pregnant women. The long-term group were those who had antiretroviral therapy from first trimester for three months and above (≥ 3 months). They were on routine ART, Lamivudine (3TC) and Zoduvudine. The short-term group are the pregnant women who were brought into the hospital during labour (emergency) and those who were on short-term prophylaxis as they were not eligible to be administered ART. Their blood samples were taken for HIV screening. If tested positive they were included in the study. The treatment of the short-term pregnant women started during labour. They were administered Nevirapine (NVP).Highly active antiretroviral therapy (HAART) (short-course prophylaxis).

After six weeks of delivery of babies of HIV positive mothers, blood samples from babies were taken for qualitative HIV-DNA Polymerase Chain Reaction (PCR) test,using Amplicor HIV-.These were administered with Nevirapine within 72 hours of birth and Zidovudine for one week after delivery. Their mothers were also administered with combined antiretroviral (ARV) or short course (ARV) prophylactic therapy. Blood Samples were taken in Dried Blood Spot.

Demographic data(age) of the HIV seropositive and seronegative pregnant women were taken.

Processing of samples

Serodiagnosis of HIV

HIV serodiagnosis of the pregnant women were done using serial algorithm2, (FMOH,2007). This is consistent with WHO recommended strategies for resource – poor setting countries.

The **first-line** test kit was Determine HIV-1/2(Abott Japan), if a positive result was obtained, it was repeated with a **second line**UniGold test kit (Trinity Biotech), where positive result was still obtained, the result was recorded as positive. Where there was a discordant result, both tests were repeated. If discordant result was still obtained, a third line test kit, Stat- Pak HIV-1/2 (Chembio) test kit was used **as a tie breaker**. If positive result was obtained, it was recorded as positive. But if negative, it was recorded as negative but following-up test was done in one month's time or Polymerase Chain Reaction test (PCR) recommended.

Quality Control

The use of control specimen to ensure proper device performance at least once daily was done. A built in procedural control on the test device indicates that the test was functioning correctly. A pink/red band should always appear at the control window.

Interpretation of the results

Negative: A line in the control region only indicates a negative test result.

Positive: A line of any intensity forming in the test region, plus a line forming in the control region indicates a positive result.

Inconclusive

No line appears in the control region. The test was repeated with a fresh device. Irrespective of a line developing in the test region.

Collection of dried blood spots (DBS) from infants for PCR Testing

1. Necessary collections were gathered: Gloves, Blood collection cards (filter paper), Lancet (2mm),70% spirit or alcohol ,Gauze or cotton wool, ,All necessary paperwork completed, Infant diagnosis registration form, Clinic register, Laboratory request/report form, DBS card.
2. The area to be pricked was chosen and the mother was asked to warm the area. Infants 6 weeks – 4 months: heel, Infants 4 months – 10 months: big toes, Infants > 10 months or > 10kg: finger, Hands were washed powder free gloves worn.
3. The baby was positioned with the foot or hand down then the spot to be pricked cleaned with spirit or alcohol, and allowed to dry for 30 seconds.
4. The area to be pricked was gently squeezed and released until ready to be bled, then the infant was pricked in the selected spot with the 2mm lancet.
5. The first spot of blood was wiped away, then a large drop of blood was allowed to collect.
6. The filter paper was touched gently against the large drop and allowed to completely fill the circle in the DBS card. At least 3 good drops were collected.
7. The area was cleaned, no bandage was needed.

Drying and packaging dried blood spot (DBS) Samples

DBS were left on a drying rack in clean, dry, protected area for at least 4 hours or overnight.

Qualitative HIV -1 DNA PCR from DBS using amplicor HIV-1

It is becoming increasingly important to diagnose HIV infection in the exposed infants as early as possible in order to initiate antiretroviral therapy. Serologic tests have been shown to have a limited role in paediatric HIV diagnosis, because passively

acquired maternal antibodies may persist for 18 months or more in infants.

The lack of interpretable results from serological testing has led to the development of Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA) assays for the presence of viral nucleic acid during early infection, with a qualitative DNA PCR assay as the preferred method for the diagnose of HIV-1 infection (Federal Ministry of Health, Nigeria, 2007).

Principles of the procedure

The AMPLICOR HIV-1 DNA Test, version 1.5 (V l.5 DNA in human whole blood. The test utilizes amplification of target DNA by the Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the detection of HIV-1 DNA in human whole blood.

The AMPLICOR HIV-1 DNA Test, Vl.5 is based on four major processes: sample preparation; PCR amplification of target DNA using HIV-1 specific complementary primers; hybridization of the amplified products to oligonucleotide probes specific to the target(s); and detection of the probe-bound amplified products by colorimetric determination.

Sample preparation

HIV-I DNA was isolated by washing the whole blood sample to extract the leucocytes, which were then lysed in a detergent solution containing protainase K.

PCR Amplification

The processes in PCR Amplification are Target selection, Target Amplification, Internal control Amplification, Selective Amplification, Hybridization Reaction and Detection Reaction.

Principles of the procedure

The AMPLICOR HIV-1 DNA Test, version 1, 5 (Vl.5) is a qualitative test for the detection of HIV-I DNA in human whole blood. The test utilizes amplification of target DNA by the Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the detection of HIV-I DNA in human whole blood.

The AMPLICOR HIV-1 DNA Test, version (V I.5) is based on four major processes; sample preparation, PCR amplification of target DNA using HIV-I specific complementary primers; hybridization of the amplified products to oligonucleotide probes specific to the target(s); and detection of the probe-bound amplified products by colorimetric determination.

The AMPLICOR HIV-1 DNA Test, permits simultaneous PCR amplification of HIV-I target and HIV-I Internal Control DNA. The Master Mix reagent contains a biotinylated primer pair specific for both HIV-I and HIV-I Internal Control DNA. The detection of amplified DNA is performed using target-specific oligonucleotide probes that permit the independent identification of HIV-I amplicon and HIV-I internal Control amplicon. The detection of amplified Internal Control DNA is performed at the user's option.

Data Analysis

The data generated in this study were analysed for level of significance using Chi-square test.

Results

Age distribution of HIV seropositive and seronegative pregnant women were shown on table 1.The age distribution of HIV Pregnant women were predominantly in the age of 21 – 25 years with 155 (37.1%) followed by the age group of 26- 30 years with 126 (30.1%) (Table.1).

The age distribution of HIV negative pregnant women were predominantly in the age group of 26 – 30 years (40.0%) followed by the age group 21- 25 years 29(29.0%) . There was no significant difference (P > 0.05) in age distribution of HIV positive and HIV negative pregnant women. (Table.1).

Discussion

The outcome of intervention of mother- to -child transmission of HIV in this study showed that out of the 418 HIV positive pregnant women,318 of long-term antiretroviral (ART) treated mothers and 100 of short term ART treated , 53 (12.9%) babies were infected with HIV at birth, while 359 (87.1%) were HIV negative out of the 412 surviving babies. This agrees with recent study of Henry of 2011, which showed that HIV treatment can reduce risk of

Table 1. Age distribution of HIV Sero-positive and HIV Sero-negative pregnant women

Age distribution **Age**	Number of subjects HIV positive (%)	HIV negative (%)
< 20	11(2-63)	8(8.0)
21-25	155(37.1)	29(29.0)
26-30	126(30.1)	40(40.0)
31-35	71(17.0)	10(10.0)
36-40	55(13.2)	8(8.0)
>40	0(0)	5(5.0)
Total	418	100
P value X^2 P > 0.05		

Table 2. Babies infected with HIV at birth in women who received long-term and short-term antiretroviral therapy (ART)

Treatment Duration	No. of babies (n=412)	No.(%) of babies and their HIV status Positive (n=53)	Negative (n=359)
Long -Term	316	20 (6.3)	296 (93.7)
Short- Term	96	33 (34.4)	63 (65.6)
P-value	<0.05	<0.05	

Table 3. Comparing mode of HIV treatment (Long-term and short-term) in mothers who had normal delivery and HIV status of their babies

Treatment Duration	No. of babies (n=234)	No.(%) of babies and their HIV status Positive (n=40)	Negative (n=194)
Long -Term	202	18 (9.0)	184 (91.0)
Short- Term	32	22 (68.8)	10 (31.0)
P- value		< 0.05	< 0.05

transmission by 96%. The long-term ART treated pregnant women were those who were placed on ART for 3months and above. The short-term ART treated pregnant women were those who were brought to the labour ward under emergency who had not previously had ART. They were administered with Nevirapine (NVP) during labour followed with Lamivudine (3TC), Zudovudine (AZT) and Nevirapine combination therapy at postpatum. Those who also fell under short-term were the non-eligible pregnant women who were not placed on highly active antiretroviral therapy (HAART). They did not meet the criteria for HAART, for example if their $CD4^+$ cell count were > 350 cell (Table.2).

Among the 53(12.9%) HIV positive babies, 20 (6.3%) were from the long -term ART treated mothers while 33(34.4%) babies were from short-term ART treated mothers. This is in accordance with the work of Conor *et al*, (1994) which showed the first major breakthrough in prevention of mother-to- child transmission of HIV clinical trial, that long-term course of antiretroviral prophylaxis given early in pregnancy and intravenously during delivery to the mother, as well as six weeks to the infant dramatically reduces the risk of vertical transmission from 25% to 8% (Table. 3).

It also agrees with the studies by Doranbaum *et al.*, (2002); Moodley (2003); Debis *et al.*, (2005) who have reported that if eligible HIV positive pregnant women are started on ART and those not eligible are given highly active antiretroviral therapy (HAART) prophylaxis including nucleoside reverse transcriptase inhibitors (NRTIS) such as zudovudine and lamivudine, and the non-nucleoside reverse transcriptase inhibitor such as nevirapine either alone or in combination of two or three drugs have been shown to reduce mother to child transmission (MTCT) of HIV to 2%.

Age

The age distribution of HIV positive pregnant women were predominant in age group of 21-25 years with 155 (37.1%), followed by the age group of 26-30 years with 26(30.1%). This is in accordance with the work of Henry, 2011 of the united nations coalition which showed that the black women between the ages of 22-30 years have the highest increase rate of HIV infection.

Among the HIV negative women, the highest percentage falls between the ages of 26-30 years with 40 (40.0%) followed by 21-25 years with 29 (29.0%) There was no clear cut difference in the age distribution between HIV positive and HIV negative thus HIV infection is independent of age.

When compared the HIV status of babies delivered by caesarean section (CS) and normal delivery of the long-term ART treated mothers and short-term ART treated mothers, it was found that more babies who were delivered by caesarean section (CS) in the long-term treated mothers had more HIV negative babies at birth 112(35.4%) than those who had normal delivery (ND) 18 (5.7%).In the short term ART treated mothers, who delivered by CS, there were more HIV negative babies 56(58.3%) as against those who were delivered by normal delivery 14 (14.6%). This is in line with Laura Jones, 2002 whose study showed that elective CS usually performed in 38 weeks of gestation prior to rupture of membrane reduces HIV transmission by preventing contact between the foetus and the mother's membrane fluids. One of the sources of perinatal transmission of HIV is believed to occur through labour and delivery. Infants born with HIV are infected in the birth canal (Federal Ministry of Health, Nigeria, 2007; Newell, 2003) in the randomised delivery trial in Europe, the result showed a significant and substantial effect of elective caesarean section (CS). The rate of transmission through (CS) was less than 2% compared to more than 10% vaginal delivery. Perez, 2004 data showed 50% reduction in vertical transmission. Moreover the effect of CS is similar to the risk of transmission for women with viral load above the median and below median (European Collaborative Study, 2003). It reduces the risk for women with RNA load of less than 1000 copies /ml around the time of delivery (Newell, 2003).

This study showed that the long -term ART treated mothers had more HIV negative babies 296(93.7%) at birth than short- term ART treated mothers 63(65.6%). Babies who were infected with HIV through the long-term ART were 20(6.3%) while those from the short-term ART were 33(34.4%). This could be for the fact that the long-term ART treated mothers had lower viral load and were not likely to infect their babies than the short-term treated mothers with high viral load count whereas babies were at risk to be infected. This is in agreement with Read et al, (2005); Dorenbaum (2000) who showed that the risk of mother-to-child transmission of HIV (MTCT) can be reduced to 2% by interventions that include ART prophylaxis given to women during pregnancy, labour and infant in the first week of life.

Summary and Conclusion

This work showed that the age distribution of HIV pregnant women fell between 21-25 years of age while the HIV negative women fell between 26-30 years of age; long-term antiretroviral therapy (ART) treated HIV positive pregnant women had less number of babies 20(6.3%)who were infected with HIV at birth as compared to the short-term ART treated 33 (34.4%) pregnant women; it was concluded that maternal-foetal HIV transmission intervention programme is successful in University of Uyo Teaching Hospital as greater numbers of babies 359(87.1%) were born not infected with HIV at birth. Total percentage of babies infected were 53 (12.9%).

References

Brahmbhatt, H., Kigozi, G, Wabwire-mangen, F, Serwadda, D., Lutalo, T., Halugola, F., Sewankambo, N, Kiduggavu, M, Wawer, M and Gray, R. 2006. Mortality in HIV-infected and uninfected children of HIV-infected and uninfected mothers in rural Uganda. J.Acquir. Immune. Deficien. Syndro. 41: 504-508.

Connor, E. M., *et al*, 1994. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 study Group. New England J. Medicine. 33118: 1173-1180.

De Cock, K. M., *et al*, 2000. Prevention to mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. J. American Medical Association. 2839: 1175-1182.

Dorenbaum, A., et al, 2002 Two-dose intrapartum/newbornnevirapine and standard antiretroviral therapy to reduce perinatal HIV transmission: a randomized trial. J. American Medical Association. 2882: 189-198.

Eke, C., 2007. HIV and Nutrition in Nigeria. The Challenges. Nigeria World Message Board. Availablefrom:http://nigeriaworld.com/board/viewtopic.php?P=25051&sid=34e384628dae7788da8062d6. Access 4th March, 2007.

European Collaborative Study. 2003. Exposure to antiretroviral therapy in utero or early life: the health of uninfected children born to HIV-infected women. J. Acquir. Immune. Deficien. Syndro. 324: 380-387.

Federal Ministry of Health, Nigeria 2007. Laboratory Based HIV rapid Test validation in Nigeria Phase 1. 8-18.

Federal Ministry of Health, Nigeria 2007. Prevention of mother-to-child Transmission of HIV. Nigeria Curriculum. Trainers Manual.

Filteau, S., 2003. Reducing childhood mortality in poor countries: infant-feeding strategies to prevent post-natal transmission. Trans. Royal Soc. Trop. Med. Hygiene. 97: 22-24.

Moodley, D., et al, 2003. A multi center randomized controlled trial of nevirapine versus as combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. J. Infect. Dis. 1875: 725-735.

Newell, M. L., 2003. Current issues in the prevention of mother-to-child transmission of HIV-1 infection. Trans R. Society Trop. Med. Hygiene. 100:1-5.

Perez, F., Orne-Gliemann, J, Miller, A. Mukotekwa, T. Glenshaw, M. Mahomva, A and Dabis, F 2004. Prevention of mother-to-child transmission of HIV: evaluation of a pilot programme in a district hospital in rural Zimbabwe. British. Med. J. 329:1147-1150.

Read, J., et al, 2005. A prospective cohort study of HIV-1-infected pregnant women and their infants in Latin America and the Caribbean: the NICHD International site Development initiative perinatal study; *12th* Conference on Retroviruses and Opportunistic Infections. Boston, MA, USA, 22-25 February Abstract 790.

Roche Molecular Systems. 2007. Qualitative HIV-1 DNA-PCR from DBS using Amplicor HIV-1 Test, *An* Amplicare Initiative inc. Branchburg, NJ, 08876 USA, A member of the Roche Group. 1-20.

.

