



Anti retroviral drug prophylaxis in prevention of mother-to-child transmission of HIV infection in a treatment centre in Jos, Nigeria

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Abstract

Prevention of mother-to-child transmission through the use of antiretroviral (ARV) prophylaxis has been identified as one of the ways of reducing prevalence of HIV/AIDS in children and many centers are implementing it. A study to assess the use and effectiveness of antiretrovirals in the prevention of mother-to-child transmission (PMTCT) in a treatment center in Jos, Nigeria, was carried out. The prophylaxis given to HIV positive mothers and their babies were reviewed over a 20 months period (Jan 2009 to August 2011) and the outcome of the intervention was assessed. Of the 135 pregnant mothers' records reviewed, all of them were on triple ARV before delivery with 2 of them on second line regimen. The study revealed that 221 babies were given post exposure prophylaxis of single dose nevirapine at birth followed by 7 day course of zidovudine (AZT). Out of these babies 96.4% (213) returned negative Polymerase Chain Reaction (PCR) test results for HIV ($P < 0.01$). The breast feeding options showed that 35.5% were on mixed or exclusive breastfeeding; 21% were on infant formula. The antiretroviral prophylaxis to the mothers and infants was given in accordance with recommended guidelines and was effective in reducing the perinatal transmission of HIV to the babies.

Keywords: Peri-natal transmission; ARVs; PMTCT

INTRODUCTION

The scourge of HIV/AIDS has had its devastating effects in Sub-Saharan Africa in the past three decades. It has been identified as a common cause of death in the region and the fourth largest killer disease in the world (Lamprey *et al.*, 2002). The pandemic has not spared children who have had to contract the disease through infected mothers. It was established that 57% of adults living with HIV/AIDS in sub-Saharan Africa were women (UNAIDS, 2004a) and this has serious implications for the survival of

children in Africa. Of the estimated 700,000 annual new infections in children worldwide, mother-to-child transmission (MTCT) accounts for the majority (PEPFAR, 2010). In the year 2004, six hundred and forty thousand (640,000) children acquired the infection with about 90% of them through mother to child transmission (UNAIDS, 2004a). One third of children infected with HIV die in developing countries within their first year of life. It has been established that a HIV infected mother has a more than 50% overall risk of transmission to her child during

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pregnancy, delivery and breast feeding (PEPFAR, 2010). The danger to children becomes grimmer when it is realized that more than 1.25 million of the 18 million women who deliver annually are HIV positive. In a study carried out in Nigeria it was found that the rate of transmission in antiretroviral (ARV) naïve mothers was as high as 45% (Audu *et al.*, 2006).

In 1998 it was discovered in a HIVNET 012 trial in Uganda that a single dose of nevirapine given to the infected mother at the onset of labor and a single dose given to the baby at birth reduced the rate of infection by 47% (Guay *et al.*, 1999). Even though the use of nevirapine for prevention has been hampered by its induced drug resistance, this discovery gave rise to the Prevention of Mother-to-Child Transmission (PMTCT) initiative (UNAIDS, 2004b). Even though comprehensive PMTCT programs have nearly eliminated Mother- to- Child Transmission in the developed world, in resource limited countries like Nigeria, it is not the case as only 9% of all HIV positive mothers are benefiting from PMTCT services (PEPFAR 2010). Clinical trials have demonstrated that ARV prophylaxis can reduce risk of mother to child transmission by approximately 75% (De Cock *et al.*, 2000). Studies have shown that ARVs have helped in no small measure to reduce the rate of mother-to-child-transmission from 30% to 2% and below (Fowler *et al.*, 2007).

In order to reduce the rate of vertical infection of children by HIV positive mothers, the PMCT program, as advocated by the World Health Organization (WHO), has been instituted in many countries including Nigeria. The PMTCT program has gained wide acceptance as a way of controlling mother- to- child transmission of HIV. By way of operational research, it is necessary to find out from time to time if the program is giving the desired results. This has become necessary when one considers that there have

been reported cases of resistance to ARV drugs used in PMTCT prophylaxis (Arrive *et al.*, 2007). While there is abundant information about efficacy of intervention to reduce peri-natal transmission, our current understanding of effectiveness (field studies) is lacking (Stringer *et al.* 2008). This study therefore aims at finding out the effectiveness of ARV prophylaxis in the Prevention of Mother- to- Child Transmission of HIV at a major HIV/AIDS treatment center in Jos, Nigeria.

METHODS

Study setting. The study was carried out in the PMTCT unit of the Faith- Alive Foundation, Jos. It is located in the centre of the City of Jos. It is a Non- Governmental Organization that has been in operation since 1998 and offers free medical services especially to HIV/AIDS patients. Patients come from Plateau State and other neighboring states to receive treatment for HIV/AIDS. Jos is the capital of Plateau state which is one of the 36 states in Nigeria. Plateau state is located at latitude 8° N and longitude 8°E and 10°E and has an area of 30,193 sq kilometers and has a population of 3.178 million people.

Inclusion/ exclusion criteria. Children born to HIV positive mothers between January 2009 and August 2011, who had been on Highly Active Antiretroviral Therapy (HAART) or those who were given the necessary antiretroviral drugs before and during labor, as recommended in the PMTCT guidelines, were included. The children born the previous eighteen months were included in the study so as to capture all who may have had the PCR test. Children that were not tracked after delivery were excluded from the study.

Sample size estimation. The sample size was estimated using the Bennett's formula which

gave a minimum of 134 pairs of mother and infant.

Data collection and analysis. A retrospective study of HIV positive pregnant mothers and their infants enrolled into the PMTCT unit of Faith-Alive Foundation was conducted. The records of the pregnant women were reviewed and the relevant data entered into the already prepared data collection form that had been validated by a statistician and pretested at the Foundation. The data collected included the biodata of the mother, her medication record, the age of the pregnancy at delivery and the type of delivery. The children's records, which were kept in a notebook, were reviewed and entered into the data collection form. The kind of data collected for the baby included kind of ARV prophylaxis given, the feeding options used the type of HIV test used and the results. Since the record of the mother and infant were kept separately, effort was made to identify and pair mother to baby. The data gathered were then analyzed using the SPSS 16.0 software.

Ethical consideration. All the patient folders were handled in the most confidential manner possible in order to protect the mother and child's identity. In addition ethical clearance was obtained from the authorities of Faith-Alive before conducting the study.

RESULTS

Demographic data. A total of 135 HIV positive mother's folders were reviewed while 232 children's records were also reviewed. Out of the latter only 47 could be linked to the mothers' folders already reviewed. A majority of the mothers were between the ages of 25 – 40 years and 67.4% of them were literate. Most of the mothers were Christians and were mainly traders and/or house wives (See Table 1).

Post exposure prophylaxis. Records show that of the total children reviewed, 95.3% were given post exposure prophylaxis of a

single dose of nevirapine and a 7 days' course of zidovudine each while 3.4% were not given for unstated reasons (Figure 1).

Children's feeding practices. The result of the feeding practices of the babies showed that 83 (35.8%) were breast fed either exclusively or mixed with formula and 49 (21.1%) were not breastfed as at the time of the HIV test while there were no records for 100 (43.1%) of the babies whose records were reviewed.

Children's HIV test results. All the children were tested using the PCR method. The HIV test results indicated that out of the 232 tests carried out only 12(5.2%) were positive with the remaining 220 (94.8%) being negative (See figure 2). Of the 221 babies that had their post exposure prophylaxis, 8 (3.6%) of them tested HIV positive while the 8 babies that had no prophylaxis 3 (37.5%) tested positive for HIV (see Table 2). Of those that were breast fed 79 (95.2%) were HIV negative while those that were not breast fed at all had 45 (91.8%) of them returning HIV negative ($P > 0.05$).

Management of mothers during pregnancy and delivery. The reviewed medical records of each pregnant woman indicated that 109 (80.7%) of the women knew of their HIV status before they were pregnant while only 8 (5.9%) did not know. The CD4 count of the pregnant mothers at the time of delivery showed that 47 (34.8%) had their CD4 lower than 350cell/ml while 84 (62.2%) had CD4 count higher than 350 cells/ml. (Table 3). All the women were on HAART for their own infection during the period of pregnancy, delivery and after. The commonest first line HAART regimens were AZT + 3TC + NVP (33.3% and TDF + FTC + NVP (65.2%) while only 1.5 % was on second line regimen of TDF+FTC+LPV/r (1.2%). The frequency of the use of the available regimens is contained in Table 3. The 47 mothers and babies pairs studied the result showed no

measure of association for the cross-tabulation between the HIV test outcome of the babies and the mothers' ARV regimen,

CD4 count and knowledge of mother's status before pregnancy.

Table 1: Distribution of maternal demographic data

| Variable | Category | Frequency | Percentage |
|----------------------|---------------------|-----------|------------|
| Mother's age (years) | 15-20 | 3 | 2.2 |
| | 21-25 | 8 | 5.9 |
| | 25-30 | 48 | 35.6 |
| | 31-40 | 49 | 36.3 |
| | >40 | 5 | 3.7 |
| Literacy | Not indicated | 22 | 16.3 |
| | Literate | 91 | 67.4 |
| | Illiterate | 8 | 5.9 |
| Religion | Not indicated | 36 | 26.7 |
| | Christianity | 99 | 73.3 |
| | Islam | 7 | 5.2 |
| | Others | 1 | 0.7 |
| Occupation | Not indicated | 28 | 20.7 |
| | Farmer | 4 | 3.0 |
| | Civil servant | 15 | 11.1 |
| | Trader | 31 | 23.0 |
| | Full time housewife | 38 | 28.1 |
| | Others | 23 | 17.0 |
| | Not indicated | 24 | 17.8 |

Table 2: Effects of babies' post-exposure prophylaxis and HIV status

| Prophylaxis | N | HIV Negative n (%) | P-value |
|-------------|-----|--------------------|---------|
| Given | 221 | 213 (96.4%) | 0.004* |
| Not given | 8 | 5 (62.5%) | |

*P < 0.01

Table 3: Distribution of the mothers' medical and treatment record

| Variable | Category | Frequency | Percentage |
|--------------------------------------|-----------------------------------|-----------|------------|
| Knew HIV status before pregnancy | Yes | 109 | 80.7 |
| | No | 8 | 5.9 |
| | Not indicated | 18 | 13.3 |
| CD4 count | ≤ 350 cells/ml | 47 | 34.8 |
| | > 350 cells/ml | 84 | 62.2 |
| | Not indicated | 4 | 3.0 |
| Mother HAART eligible | Yes | 134 | 99.3 |
| | No | 1 | 0.7 |
| Mothers ARV regimen during pregnancy | AZT + 3TC + (NVP or EFV) | 45 | 33.3 |
| | TDF + (3TC or FTC) + (NVP or EFV) | 88 | 65.2 |
| | Second line regimen | 2 | 1.5 |

AZT = zidovudine; 3TC = Lamivudine; NVP = Nevirapine, TDF = Tenofovir; FTC = Emtricitabine; EFV = Efavirenz.

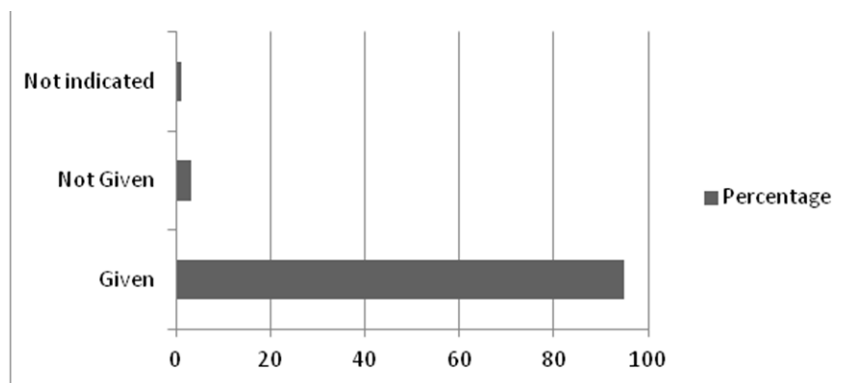


Figure 1: Post exposure prophylaxis status of children in the study.

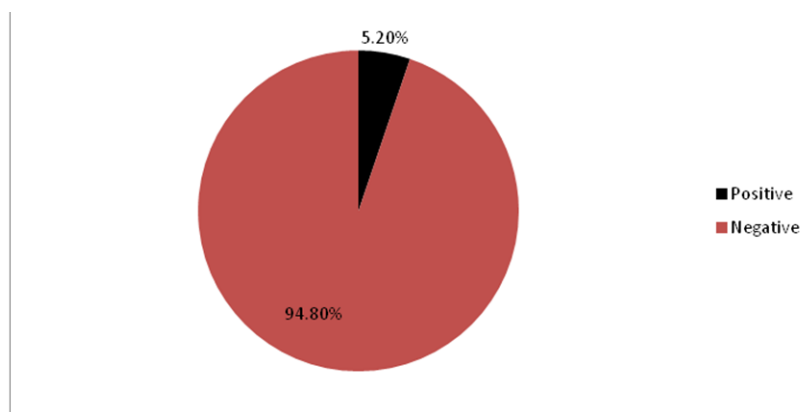


Figure 2: Result of PCR tests on HIV exposed children

DISCUSSION

The study intended to pair mother and child but it was found out that the records of the children were kept separate from those of the mothers and there was no way of linking most of the children to their mothers. If the linkage were done the study would have benefited from looking at associations between mothers' prophylaxis and the babies HIV status. The PMTCT in Faith Alive Foundation relied on PCR test performed for all the children born to HIV positive mothers. This has helped the Foundation know the children's status early in life for the purpose of instituting interventions on time. This is the recommended test for infants as it has no interferences from the mothers' HIV antibody that may be found in the baby which makes ELISA tests unreliable in such age groups.

All the women that were studied were on triple ARVs for their own diseases or for

the purposes of prevention of mother-to-child transmission. This finding was in keeping with the WHO recommended option B for PMTCT which advocates that the pregnant woman be placed on triple ARV made up of 2 NRTIs and 1 NNTRI. This provided a reduction in the viral load of the mother thus reducing the risk of vertical transmission to the baby. The use of NVP for a long time is known to increase the risk of treatment failure due to drug resistance by the virus. This treatment failure has been shown even when the mother was exposed to only a single dose NVP (Coovadia *et al.*, 2009).

The post-exposure prophylaxis that was administered to the children was a single dose of nevirapine given within 72 hours of delivery and a 7 day course of zidovudine. This treatment was administered irrespective of whether the child was breast feeding or not and was in keeping with the recommendations

for PMTCT in resource limited settings. The test result showed that 94.8% of the children were prevented from contracting the HIV infection vertically through the post exposure prophylaxis they received. This gives the percentage of babies that tested HIV positive as 3.6% and that is close to the discovery by De Cock and co workers that ARV prophylaxis is able to reduce mother- to- child infection to between 2-5% (De Cock *et al.*, 2000). The outcome of the PMTCT interventions in this study (5.2% transmission rate) is better than the 8.8% transmission rate found in Khayelitsha, South Africa (Coetzee *et al.*, 2004) and the about 16% transmission recorded in some hospitals in Kampala Uganda by Bajunirwe (Bajunirwe 2004). Of the 8 babies that were not given post exposure prophylaxis, 3 (37.5%) of them tested positive for HIV. This again was in agreement with the findings of DeCock *et al.* (2000) that for women not on treatment for their disease they have about 25- 45% chance of infecting their infants (Msellati *et al.*, 1995). Of the children that had post exposure prophylaxis 8 (3.6%) of them tested positive for HIV. From the studies it is difficult to place a finger on why the protection was not 100% but some reasons might include infection of the fetus before delivery due to compromise in the placental protection. Other reasons might be post-prophylaxis exposure to HIV either through breast milk or through other invasive procedures that were not reported.

The study results indicated that 35.8% of the children were either breastfed exclusively or mixed with infant formula while only 21% of the children were fed exclusively with infant formula prior to the tests. The preferred feeding option for HIV exposed children is exclusive infant formula as it is known to provide the best protection in combination with ARV prophylaxis (WHO PMTCT Briefing Note 2007). The study result revealed that there was no major difference in the protection of breast fed

children and those who were not breast milk as the protection was 95.2% and 91.8% respectively. If one considers the fact that one of the risk factors for vertical infection from mother to child is through breast feeding (Dunn *et al.*, 1992). This was another further proof that the HAART regimen the mother was on helped to protect the child from the maternal HIV in breast milk. This study could not capture the effect of the duration of breastfeeding on the prevention of mother- to-child transmission as it is known that the longer the child is on breast milk the higher the risk of vertical transmission.

There was no level of association computed between the test outcomes and the 47 mother-baby pairs because all the 47 babies tested negative. However the treatment regimens that the mothers were on for their HIV infection were in accordance with the National guidelines and by extension the WHO guidelines. The mothers' demographics such as literacy rate, religion and occupation could not be related to the outcome of the PMTCT because of the inability to pair them with their babies. The study showed that 80.7% of the women knew of their HIV status before pregnancy. This means that HIV positive women were either on treatment before pregnancy or were immediately placed on triple ARV for their disease and for the protection of their unborn baby. It has been established that the earlier the treatment is commenced in pregnancy the better the prevention of vertical transmission.

The study indicates that of the women reviewed, 34.8% had CD4+ cell count of $< 350/\text{mm}^3$ and 62.2% had CD4+ cell count $>350 /\text{mm}^3$. In keeping with the WHO guideline which provides that those women with CD4+ count $>350 \text{ cells}/\text{mm}^3$ should only be given prophylactic ARV regimen. The women were all placed on triple ARVs immediately they presented to the antenatal clinic which gave the baby a better protection.

Even though this study targeted a minimum sample of 135 pairs of mothers and their babies or more, the mothers and babies records were kept independent of each other hence the disparity in the mothers' figures of 135 and the children's sample of 232. Painstaking efforts were made to pair them but could only get 47 pairs and this denied this study some important cross tabulations. There were some variables in the data collection form that could not be entered because they were not available and these included; mode of delivery and post delivery procedures that may have been confounding factors in the study. Being a clinical study it might be inadequate to make a generalized country wide deduction on the result. After the initial PCR tests conducted on the children, there were no records available of subsequent follow up tests to see the effects of the PMTCT on the overall HIV free child survival rate. A longer prospective study could serve to shed more light on the impact on child survival.

The study has helped us to know that ARV drugs intervention for PMTCT can work even in our own environment if the recommended guidelines are followed. The study also serves as a motivation for similar studies to be conducted in other PMTCT centers so as to give feed back to policymakers and other funding agencies about the effectiveness of their support.

Conclusion. This study revealed that of the 135 pregnant women reviewed, all of them were on triple ARV and that the 221 children that had post exposure prophylaxis were all placed on NVP after birth and 7 day course of AZT thereafter. The antiretroviral regimens used in the prevention of mother- to- child transmission in Faith Alive Foundation were in keeping with the National and WHO Guidelines as at the time of study. Even though it was difficult to pair mother and child for most of the children, the PCR test results showed that 96.4% of the children

given post-exposure prophylaxis were HIV negative. Within the limitations of this study one can conclude that antiretroviral drugs prophylaxis has been effective in preventing vertical transmission of HIV from the infected mother to the child.

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