Original Article

Decline in positivity rates among HIV-exposed infants with changes in prevention of mother-to-child transmission antiretroviral regimens in Nigeria: Evidence from 7 years of field implementation

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ABSTRACT

Objective: Demonstrate if the introduction of more and more efficacious antiretroviral (ARV) combinations for prevention of mother-to-child transmission (PMTCT) over time translated into a declining HIV-infection among HIV-exposed infants. **Methods:** This was a retrospective review of routinely collected PMTCT service data from 2008 to 2014 in 682 secondary and tertiary health facilities across Nigeria. The ARV regimen was measured by the proportions of different ARV regimens received by HIV-positive pregnant women each year and the HIV-infection among infants was determined by the rate of HIV-positive polymerase chain reaction tests each year. The District Health Information Software (DHIS) was used to extract data from health facilities. The same DHIS was used to aggregate and analyze data. **Results:** Maternal HIV positivity rates varied from 4.1% in 2008, 2.9% in 2011, and 3.2% in 2012, then declined steadily to 1.9% in 2014. The total number of pregnant women who tested positive for HIV and received different ARV regimen for PMTCT during the period (2008–2014) was 63,774; ranging from 7506 in 2008 to 10,388 in 2014. Uptake of single dose nevirapine by the positive pregnant women was 34.4%, 41.6%, and 45.9% in 2008, 2009, and 2010, respectively. HIV positive pregnant women on triple ARVs (prophylaxis or treatment) increased from 22% in 2008 to 99% in 2014. Infant HIV positivity rates showed a steady decline over the years, from 38% in 2008 to 6% in 2014 ($P < 0.001$). **Conclusions:** We demonstrated the declining trend of HIV-infection among HIV-exposed infant in Nigeria as more and more efficacious ARV regimens were available for HIV-positive pregnant women. We conclude that if current efforts were sustained and coverage widened, an alignment of the country's PMTCT program with the best available scientific evidence could lead to the elimination of mother to child transmission.

Key words: Child, early infant diagnosis, healthcare, HIV transmission, Nigeria, pregnancy, retrospective studies

INTRODUCTION

The risk of mother to child transmission of HIV (MTCT) in Nigeria is high due to a combination of factors which include; a high fertility rate of 5.5%;[1] HIV prevalence of 4.1% among women attending antenatal clinic (ANC);[2] and low coverage of prevention of mother-to-child transmission (PMTCT) services (30% as at end of 2013).[3] The 51,000 new HIV infections recorded in Nigeria in 2013 accounted for one-quarter of all new HIV infections among children in the 21 Global Plan priority countries.[4,5] MTCT is responsible for the majority of these HIV infections among children.[6] Without antiretroviral drugs (ARVs), the rate of MTCT is estimated to be

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about 15–45%, with more than half of the HIV-infected infants dying before the age of 1 year.[7]

Evidence from controlled studies has shown that the use of ARVs and other interventions have the potential to reduce pediatric HIV infections to <2%.[8,9] This has created the optimism that MTCT can be eliminated. Accordingly, PMTCT programs have provided ARVs to an increasing number of HIV-infected pregnant women. In Nigeria for example, the number of health facilities providing PMTCT services increased from only 6 in 2004 to 6000 in 2014.

As countries scaled up PMTCT services, scientific evidence was also evolving leading to changes in recommended ARVs for PMTCT to more efficacious regimens. Nigeria's PMTCT program has evolved over the years with changes in guideline recommendations, including cut-off for antiretroviral therapy (ART) eligibility and transition from monotherapy (single dose nevirapine [sdNVP]) to the use of more efficacious triple ARVs for PMTCT.[10-12] These changes are summarized in Table 1.

Although clinical trials have been and continue to be very helpful in advancing practice,[13-23] they, however, offer only limited insight into what may happen in the program implementation setting where events are subject to much more varying "un-controlled" conditions. A number of authors have described PMTCT outcomes in nontrial settings.[24-28] The scope of these publications vary from single hospitals to country level evaluations. Some have used models applied to local data to estimate impact.[29]

We found a study that evaluated the impact of changes of national guidelines on PMTCT outcomes in a single South African clinic.[30] This is a step in the right direction. Nigeria has only recently in December 2014, launched a new set of integrated national guidelines for HIV prevention, treatment, and care. We are yet to come across any publication from Nigeria that relates infant positivity rates to changes in ARV regimen over time. It is, therefore, imperative to evaluate how PMTCT program has performed with regards to changes in ARV regimen and accompanying MTCT rates.

We conducted a desk review of PMTCT program implementation data from 2008 to 2014. The objective was to demonstrate changes in HIV transmission rates among exposed infants as the ARV regimen changed over time.

METHODS

This was a retrospective review of routinely collected PMTCT program implementation data collected using the District Health Information Software (DHIS), from 2008 to 2014.

Study setting

Data used for this review were collected from ANCs in 682 health facilities as part of PMTCT projects funded by the President's Emergency Program for AIDS Relief, through the United States Agency for International Development (USAID) Nigeria, and implemented by FHI360 across Nigeria's 36 states and the Federal Capital Territory. The period covered was from 2008 to 2011 through the Global HIV/AIDS Initiative in Nigeria (GHAIN) project; and 2011–2014 through the Strengthening Integrated Delivery of HIV/AIDS Services (SIDHAS) project.

PMTCT program implementation in all project supported health facilities were based on the national PMTCT guidelines and protocols. The technical details of these PMTCT interventions have varied over the years as the guidelines changed.[10-12] Key changes and current interventions are summarized in Table 1.

National data collection tools/registers are used to document information from HIV-positive pregnant women and their babies: General ANC, PMTCT HIV testing and counseling, PMTCT ARV, maternal follow-up, delivery, and child follow-up registers. The delivery register is used to collect information from all HIV-positive pregnant women during labor and immediately after delivery while the child follow-up register is used to document information during the follow-up of HIV-exposed infants. The national PMTCT monthly summary form (MSF) aggregates all the key PMTCT indicators. All information on the PMTCT MSF is transcribed into the DHIS on a monthly basis.

Data source and data analysis

We used routine monitoring and evaluation aggregate data from the DHIS reported through 184 of 185 facilities supported by the GHAIN project from 2008 to 2011; and 498 of 2593 facilities supported by the SIDHAS project from 2011 to 2014. The DHIS PMTCT data set were complete for all of the facilities included in this review. Indicators of interest were a percentage

Table 1: Summary of key changes in national guidelines between 2005 and 2014 [10,11]

PMTCT service	Guideline			
	2005	2007	2010	2014
Antenatal				
Testing and counseling for HIV	Opt-out	PITC	PITC	PITC
HAART eligibility assessment	Stage IV disease regardless of CD4 Stage III disease with CD4 <350 Stages I or II with CD4 <200 Stage II with TLC <1200	<200	CD4 <350 irrespective of clinical stage Stages III and IV disease irrespective of CD4 count	<500 irrespective of clinical stage Stages III and IV disease irrespective of CD4 count
Provision of antenatal ARV prophylaxis as eligible	ZDV from 28 weeks, or ZDV + 3TC from week 34-36	ZDV from 28 weeks or ZDV + 3TC from week 34-36	Option A: ZDV from 14 weeks Option B: Triple ARV	Option B: Triple ARV
Provision of antenatal HAART as eligible	Delay ARV use in first trimester Triple regimen (NVP + 2 NRTIs if CD4 <250 or EFV + 2 NRTIs if CD4 >250); ZDV preferred NRTI	Triple regimen (after the first trimester). ZDV preferred NRTI	Triple regimen (after the first trimester)	Triple (irrespective of GA). TDF preferred NRTI and EFV preferred NNRTI
Infant feeding counseling and support	Recommended	Recommended	Recommended	Recommended
Subsequent retesting for those who initially test negative	Recommended	Recommended	Recommended	Recommended
Family planning and reproductive health services	Recommended	Recommended	Recommended	Recommended
Intrapartum (labor and delivery)				
Encouragement of facility-based delivery and delivery with a skilled attendant	Recommended	Recommended	Recommended	Recommended
Safe delivery techniques	Recommended	Recommended	Recommended	Recommended
PITC for HIV (intrapartum)	Recommended - offer routine HIV testing in early labor with the right to opt out - for unbooked clients and women of unaware of their status	Recommended - offer routine HIV testing in early labor with the right to opt out - for unbooked clients and women unaware of their status	Recommended - testing for all women of unknown status and those who tested negative during pregnancy	Recommended- for all women of unknown HIV status including those who tested negative during pregnancy
Intrapartum ARV prophylaxis or continuation of HAART as eligible	Continue ZDV during labor, plus single-dose NVP at onset of labor Continuation of HAART as eligible	sdNVP + ZDV + 3TC at onset of labor Continuation of HAART as eligible	ZDV + 3TC 12 hourly during labor, plus single-dose NVP at onset of labor and ZDV + 3TC 12 hourly for 7 days postpartum Continuation of HAART as eligible	Continuation of triple ARV prophylaxis or HAART as eligible
Infant feeding counseling and support (intrapartum)	Recommended	Recommended	Recommended	Recommended
Postpartum/postnatal				
Maternal postpartum ARV prophylaxis or continuation of HAART as eligible	NVP + 2 NRTIs (ZDV preferred)	ZDV + 3TC for 7 days postpartum	Triple regimen (ZDV/TDF-based) till 1 week after cessation of breastfeeding or lifelong continuation of HAART if eligible	Triple regimen TDF based preferred) till 1 week after cessation of breastfeeding or lifelong continuation of HAART if eligible
PITC for HIV (postpartum)	VCT (not mandatory/ opt-out)	PITC - Recommended	PITC - Recommended	PITC - Recommended
Infant cotrimoxazole prophylaxis	Recommended for 6 weeks to 18 months of age. Discontinued if infants tests negative at 18 months	Recommended from 6 weeks to 18 months of age. Discontinued if infants tests negative at 18 months	Recommended from 6 weeks till HIV status is determined - if positive, continue, if negative, stop cotrim	Recommended from 6 weeks till HIV status is determined - if positive, continue, if negative, stop cotrim

Contd...

Table 1: Contd...

PMTCT service	Guideline			
	2005	2007	2010	2014
Infant ARV	Single-dose NVP as soon as possible after birth, plus ZDV for 6 weeks	Single dose NVP as soon as possible after birth plus ZDV for 6 weeks	NVP suspension recommended from birth to 6 weeks	NVP suspension recommended from birth to 6 weeks
EID	DNA PCR done 6-8 weeks after birth	DNA PCR from 6 weeks after birth	Recommended from 4-6 weeks after birth (for first DNA PCR) and 6 weeks after cessation of breastfeeding (for second DNA PCR)	Recommended from 4-6 weeks after birth (for first DNA PCR) and 6 weeks after cessation of breastfeeding (for second DNA PCR)
HIV rapid test to determine final HIV status of infant	Recommended after 18 months and at least 3 months after breastfeeding	Recommended after 18 months and at least 3 months after breastfeeding	Recommended at 12-18 months of age	Recommended at 12-18 months of age
Infant feeding support and adherence	EBF/replacement feeding for 6 months. Abrupt cessation thereafter	EBF/replacement feeding for 6 months. Abrupt cessation thereafter	EBF for 6 months. Complimentary feeding from 6 months. Cessation of all breastfeeding at 12 months. ARV cover by mother or infant for duration of breastfeeding till 1 week after breastfeeding has ceased	EBF for 6 months. Complimentary feeding from 6 months. Cessation of all breastfeeding at 12 months. ARV cover by mother or infant for duration of breastfeeding till 1 week after breastfeeding has ceased
Links to care, treatment, and support	Recommended as 4th prong of PMTCT	Recommended as 4th prong of PMTCT	Recommended as 4th prong of PMTCT	Recommended as 4th prong of PMTCT
Family planning and reproductive health services (postpartum)	Recommended	Recommended	Recommended	Recommended
Community				
Community services	Recommended-peer support and stigma reduction	Recommended-peer support and stigma reduction	Recommended-peer support and stigma reduction	Recommended-peer support and stigma reduction

PITC: Provider-initiated testing and counseling, EID: Early infant diagnosis, EBF: Exclusive breastfeeding, NNRTIs: Nonnucleoside reverse transcriptase inhibitor, PMTCT: Prevention of mother-to-child transmission, PCR: Polymerase chain reaction, ZDV: Zidovudine, sdNVP: Single dose nevirapine, VCT: Voluntary counseling and testing, HAART: Highly active antiretroviral therapy, ARV: Antiretroviral, 3TC: Lamivudine, TDF: Tenofovir, GA: Gestational age

of pregnant women who received various ARV regimens and infant HIV positivity rates. Chi-square test was used to compare infant positivity rates across the review period. A $P < 0.05$ was considered statistically significant.

Ethical considerations

All data were collected at an aggregate level and do not include any identifiers, and the data used were those collected routinely as part of PMTCT service delivery in all the study focus health facilities.

RESULTS

The data we reviewed indicated that the total number of pregnant women counseled and tested for HIV rose steadily from 280,123 in 2008 to 600,670 in 2014; whereas maternal HIV positivity rates varied from 4.1% in 2008, 2.9% in 2011, 3.2% in 2012, then declined steadily to 1.9% in 2014 [Figure 1].

The total number of pregnant women who tested positive for HIV and received different ARV regimen for PMTCT during the period (2008–2014) were 63,774; ranging from 7506 in 2008 to 10,388 in 2014. Uptake of sdNVP by the positive pregnant women was 34.4%, 41.6%, and 45.9% in 2008, 2009, and 2010, respectively. In 2014 however, of all the positive pregnant women that received ARVs, 49% received triple ARV prophylaxis, whereas 50% received ART. Uptake of option A ranged from 9.0% in 2011 to 0.6% in 2014. HIV-positive pregnant women on triple ARVs (prophylaxis or treatment) increased from 22% in 2008 to 99% in 2014. Infant HIV positivity rates showed a steady decline over the years, from 38% in 2008 to 6% in 2014 ($P < 0.001$).

DISCUSSION

We observed a steady decline in the HIV positivity rates among exposed infants across our program as

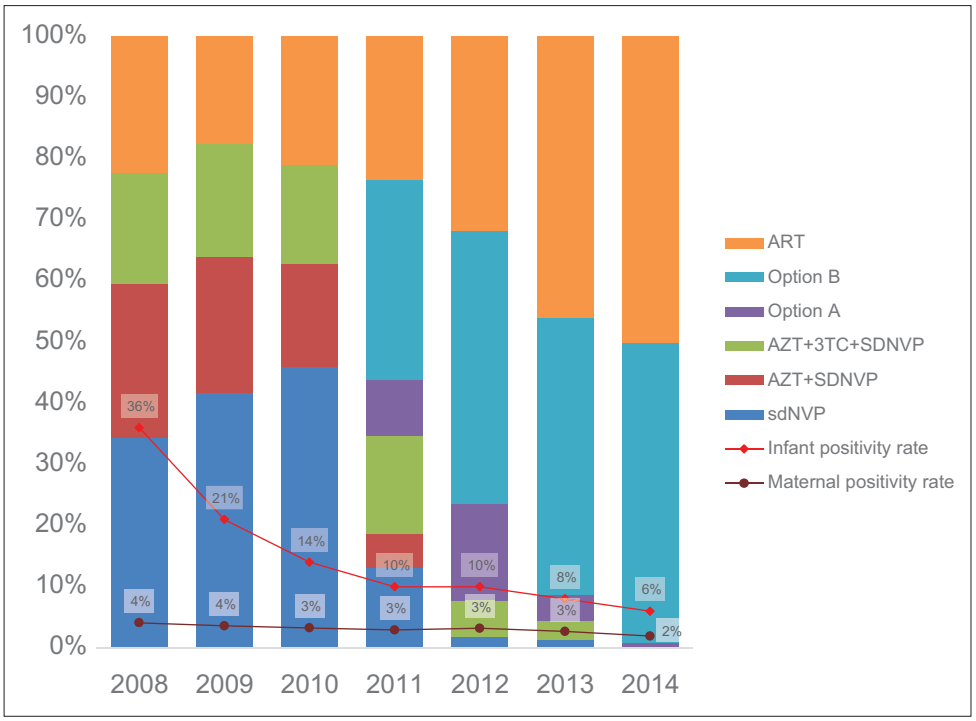

Figure 1: Changes in infant HIV positivity rates with changes in antiretroviral regimen

the country transitioned to more efficacious PMTCT ARV regimens. We also observed a steady but less steep decline in maternal HIV positivity rates within the same timeframe. The study design may not allow for direct attributions as in a controlled trial, but using data from early infant diagnosis is one of the five recommended approaches to evaluating the impact of national PMTCT programs.[31] Given the multifactorial influences that are present in everyday settings, our data show that changes in regimen coincide with a decline in positivity rates among HIV-exposed infants at the program level.

The rate of new infections among infants when considered at the population level, can be influenced by the four prongs of PMTCT described by the United Nations and included in the Nigeria national guidelines.[11,32] These four prongs are: (1) Primary prevention of HIV infection in women of reproductive age group and their partners; (2) prevention of unintended pregnancies among HIV-positive women; (3) prevention of HIV transmission from HIV-infected mothers to their infants; and (4) care and support for HIV-infected mothers, their infants and family members.[11] It is estimated that achieving the targets for prongs 1 and 2 would contribute a 13% reduction in new infant infections. Implementing prong 3 with more effective ARV prophylaxis or treatment would contribute an additional 60% reduction, with a further 6% decrease resulting from limiting breastfeeding to 12 months.[33] When the group in focus is, however, HIV-exposed infants as considered in this paper, the positivity rates are mainly influenced by prong 3.

At a population level, the rate of decline in new infections in Nigeria is not keeping up with the rest of the world. The number of new HIV infections among children in Nigeria has declined by only 19% since 2009 compared to 50% or more in other African countries such as Botswana, Ethiopia, Ghana, Malawi, Mozambique, Namibia, South Africa, and Zimbabwe.[5] This may be due to the time lag in adopting new guidelines as well as the limited coverage of interventions. The latter possibly being a stronger factor.

Our finding of declining maternal infections in Nigeria corroborates findings in national surveys and reports from other authors.[2,34,35] This decline in maternal infections will ultimately contribute to a population level overall decline in new pediatric HIV infections. Successes in prongs 1 and 2 as described earlier may be contributory.[35,36]

While changes in regimen may not be the only varying factor that has impacted the declining infant positivity rates described in this paper, we opine that

it lies in the prong – prong 3 – that has witnessed the most remarkable changes during the period under consideration. The 6% positivity among the HIV-exposed babies in 2014, is a clear indication that the goal of elimination of MTCT of HIV is achievable in Nigeria. However, challenges with low ANC attendance and hospital delivery[1] must be addressed to close the gaps created by several missed opportunities within the PMTCT continuum.

A review of the 32% decline of all new infections between 2005 and 2013 reported by United Nations Programme on HIV/AIDS shows that decline in new pediatric HIV infections were 63% while adult infections have only declined by 23%.[5] This supports data presented here and presents real hope that if current efforts were sustained and coverage widened, an alignment of the country's PMTCT program with the best available scientific evidence could lead to real progress.

CONCLUSIONS

We conclude that the evidence here discussed shows that while progress may be slow and challenges a myriad, the country is moving in the right direction with her PMTCT program. The country must therefore not rest on its oars but continue to advance its PMTCT program as well as align with available best scientific evidence.

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Conflicts of interest

There are no conflicts of interest.

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