PROGRESS TOWARDS ELIMINATING MOTHER-TO-CHILD TRANSMISSION OF HIV IN THE MACHA AREA IN ZAMBIA FROM 2010-2018

Abstract

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Abstract

Prevention of mother-to-child transmission of HIV (PMTCT) services is important in achieving national targets as well as global targets for 90% coverage and less than 5% mother-to-child transmission of HIV. In Zambia, there has been evidence of improvement in PMTCT coverage at national level with fewer studies done at local level. The study aims to address the gap, by assessing improvement in PMTCT coverage in Macha area. Cross-sectional study was conducted of HIV-infected mothers bringing their infants for early infant diagnosis at Macha Hospital from 2010 to 2018. Data from 1,175 mother-infant pairs was analysed. The majority of the mothers (85%) and infants (75%) received ARVs. The proportion of mothers that received combination antiretroviral therapy (cART) increased from 2010 (28%) to 2018 (91%). The proportion of infants testing positive decreased from 12% in 2010-2013 to 4% in 2016-2018 (P< 0.0001) and differed significantly by maternal receipt of PMTCT (38% vs. 2% for none and cART respectively [P<0.0001]). Comparing data collected at different time periods indicates that significant improvement has been made in Macha from 2010-2018. To continue with these gains, a concerted focus will be needed to target and improve on the integration of new guidelines into clinical practice at a facility level.

Introduction

A number of children that are living with HIV are infected through mother-to-child transmission (MTCT), during pregnancy, at delivery or through breastfeeding; which is often referred to as 'parent-to-child transmission or vertical transmission'[1]. Transmission of HIV from the mother to the child can be significantly minimized if expecting mothers have access to PMTCT services during pregnancy, delivery and breastfeeding [2]. Scaling up of antiretroviral therapy is said to be on a fast-track trajectory which has surpassed expectations [2] leading to a significant decrease in the number of infants that are becoming newly infected with HIV. A major challenge, nevertheless, still remains in the transmission of HIV from mothers to their infants [3]. At the end of 2017, an estimated 36.9 million people were living with virus; with 1.8 million being newly infected globally. In 2017, the proportion of HIV-infected adults and children (aged between 0 to 14 years) who were receiving ART was 59% and 52%, respectively, and the ART global coverage for pregnant HIV-infected women and breastfeeding mothers was 80% [2]. In 2017, an estimated 180, 000 children were living with HIV and 130,000 of these children live in Eastern and Southern Africa [4]. In 2017 in Zambia, 92% of women infected with HIV were receiving antiretroviral drugs for PMTCT, and 46,100 children between 0-14 years of age were on ART, accounting for 64% coverage [5].

Without having any intervention put in place, in low and middle income countries where breastfeeding is very common MTCT rates are approximately 25-45%. In industrialized countries where infant replacement feeding is more readily available MTCT rates are approximately 15-25% [6]. At the height of the epidemic, paediatric HIV threatened to reverse the achievements that had been made in managing child mortality in African countries with a high HIV prevalence. In southern Africa, 20% of child mortality was due to HIV whereas globally it was 3% [6]. The international community recognized the threat, which spurred advocacy and financial and political resources to minimize and eventually eliminate transmission of HIV from the mother to the child [7]. Impressive declines of vertical transmission rates have been due to changes in treatment regimens over the past years with regards to PMTCT. In 2015, a majority of pregnant women that had HIV were given antiretroviral drugs. Most PMTCT programs are evaluated through measurement of process leading indicators, such as the accepting pace to test for HIV and be counselled and the percentage of women who are found with the HIV virus and are given ARV drugs.

Changes in PMTCT guidelines

Starting from 2010, Zambia, like many other countries, based its PMTCT national policies on interventions put forward by the World Health Organization (WHO). WHO recommendations were that pregnant women infected with HIV and have a CD4 count M350 cells/mm3 or clinical stage 3 or 4 were being treated with a triple ART regimen. There were two options for prophylaxis for those whose CD4 counts were >350 cell/mm3and clinical stage 1 or 2: Option A included zidovudine (AZT) which was started in the antepartum as early as 14 weeks of gestation, individual dose nevirapine (NVP) and beginning of AZT/3TC (lamivudine) in the intrapartum and a continuation in the postpartum periods with AZT/3TC for 7 days [8]. A triple ART regimen was included in option B, which was started during gestation as early as 14 weeks and this, was continued till after giving birth or 1 week after cessation of breastfeeding (WHO 2010). With both

options, infants received ARV prophylaxis. During the 19th International AIDs Conference in Washington DC (AIDS 2012), there was a call by UNICEF that ART programmes be transformed into PMTCT programmes in order for the HIV targets to be met globally. Evidence was mounting that a new model for preventing HIV transmission from the mother to the child was more effective than either Options A or B: starting lifelong ARV treatment in pregnant women infected with HIV, regardless of their CD4 count [9]. Option B+ was adopted by the WHO; which is a single universal regimen for treating pregnant women infected with HIV prescribed as soon as they are found positive with HIV (done at any stage of development during pregnancy age); treatment continues for life in settings which have the capacity to initiate and monitor the mother on triple therapy [9]. The model minimized obstacles and delays in initiating treatment in settings with low resources, thereby lowering risks of drug resistance developing with interruptions in ART with each pregnancy [8]. The intention for this significant change was that maternal health should be optimized, and that HIV transmissions should be prevented during current and future pregnancies. In 2015, WHO recommended that all HIV-infected pregnant women be provided with Option B+ .

Improvement in PMTCT coverage

In recent years there has been a general increase in the number of women accessing PMTCT programmes. The percentage of HIV-infected pregnant women receiving ART in 21 of the 22 priority countries in the global plan doubled from 36% in 2009 to 80% in 2015. Of more importance is that 93% of pregnant women were receiving ARVs for treatment, an increase from 73% in 2014 [1]. Zambia adopted the Option B+ model on January 14, 2013, although some areas within the country lagged behind in implementation. Findings show that there was an increase in the number of pregnant women accessing PMTCT from87% in 2016 to 92% in 2017, resulting in a reduction in the risk of mother-to-child transmission (MTCT) [1].

Studies from sub-Saharan African countries have documented the impact of these policy changes on PMTCT uptake and the rate of MTCT. Kenya has seen a decline in the number of infected infants due to PMTCT policy changes. A study done by Ruby and colleagues provides evidence on how hospitals in Kenya are moving in the right direction in regards to coverage of PMTCT, provision of Option B+, and earlier ART initiation. He says compared to the earlier analysis, a higher proportion of mothers received any ART regimen (83.1% in 2010-2013 and 91.1% in 2013-2016), as well as desired Option B+ regimen (19.6 vs 56.2 2010-2013 and 2013-2016 respectively) This resulted in a decrease in the number of HIV-infected infants being born (from 5.9% in 2010-2013 to 4.3% in 2013-2016) [8].

South Africa has experienced impressive PMTCT outcomes during a period in which PMTCT guidelines were implemented. A study done by Goga and colleagues provides evidence of triple ART coverage of U93% by 2015/16. Nationally, the rate of MTCT plummeted from 25-30% before 2001 to an estimated 1.4% in 2016 [10].

Methods

Study design

A cross-sectional study of the data drawn from the three studies (DBS, EID and NSEBA) of HIV-infected mothers bringing their infants for EID at Macha Hospital.

Study setting

The study utilized secondary data collected from three studies that were done at the ART clinic at Macha Mission Hospital in Choma District of Southern Province, Zambia between 2010 and 2018. Macha Mission Hospital is approximately 72 kilometres and 350 kilometres from Choma and Lusaka towns respectively. The area is primarily inhabited by subsistence farmers who live in small, scattered homesteads [11]. Macha Mission hospital is managed by the Brethren in Christ Church (BIC) but functions within the Ministry of Health Zambia's health care system. It is a district level hospital with a catchment of 150, 000 persons and also serves as a referral hospital for the surrounding rural health centres that are within the radius of 80 kilometres (12). Macha Mission Hospital has been operating an ART clinic which provides PMTCT programmes, care and treatment of HIV-infected people since 2005 (12). Since 2008, EID has been accessible with HIV DNA testing being done from the central laboratory, first in Lusaka and later in Livingstone. Pregnant and breastfeeding HIV-infected mothers and their infants' access care in line with the MOH Zambia and WHO guidelines[13] [14].

Study procedure

Data from three studies conducted at Macha Hospital was used for this study; all mother-infant pairs that visited the ART clinic from August 2010 to August 2018 and had complete data, were included in the analysis.

The DBS Study

A chart review was done at the ART clinic in Macha. Data abstraction was done from the laboratory log books for all the dried blood spot (DBS) specimens that were collected at the clinic for HIV diagnosis in infant between 2010 August and 2013 March. The information that was collected routinely in the DBS tracking register included file number, date of birth, sex, sample collection date, date sample arrived at the central laboratory in Lusaka, and date when the specimen were processed. A medical chart review was done on all the infants that had DBS specimens collected. This was done to be sure of the infant's sex, date of birth and collection of maternal and infant receipt of drugs for PMTCT information. Data was entered in duplicate using EpiInfo.

The EID and NSEBA Study

The Early Infant Diagnosis (EID) study was done at the ART clinic at Macha Mission Hospital from April 2013 to October 2015. The Novel Screening for Exposed Babies (NSEBA) study was done at the ART clinic at Macha Mission Hospital from February 2016 to August 2018. Both studies followed similar procedures. All mother-infant pairs who presented for early infant diagnosis were eligible and approached for enrolment. A written informed consent was obtained from all the women agreeing to take part in the study. A questionnaire was administered after enrolment by study assistants to obtain demographic data and a medical chart review was done. Information collected included: antenatal care attendance, PMTCT received or not by the mother/infant and PMTCT regimen. Blood was collected from the infant by means of heel stick as part of clinical requirement for care and stored as a dried blood spot card in the laboratory. DBS cards were sent in batches to the central laboratory for HIVDNA testing using the Roche Amplicor HIV-1 DNA test v1.5 (Roche Molecular System, Switzerland).

Information recorded in the laboratory log book as the DBS was being collected was recorded for the study and included date of birth for the child, clinic number and date sample collected. When the DBS results (these are usually in batches) were brought to the clinic, the results were also recorded for the study. All the data collection forms for the study were double entered in EpiInfo and compared for discrepancies as a way of ensuring data quality management.

Sample size and selection

The three studies used a convenience sample of participants for the study. This is a method where participants who are readily available or accessible to the research are selected [9]. While information on all pregnant women infected with HIV and their infants was desirable, only women accessing services for EID were enrolled due to feasibility and logistical constraints. All participants with completed data from the three studies were included in the analysis.

The formula used for calculating the sample size was as shown below:

$$= Z^2 * P(1-P)/e^2$$

Where:
Z ==Z-score
P = population proportional or sample proportional
e = margin of error and N = the population size.

Data management and analysis

Data from the three studies were exported from EpiInfo to excel files, cleaned and merged into one dataset. The PMTCT regimen for each mother was classified as none, single dose nevirapine, short course ART (when a mother would take one or two ARV drugs for a short period during pregnancy until delivery or breastfeeding), and triple regimen ART (when a mother initiates combination antiretroviral therapy (cART) prior to or during pregnancy). Children were considered diagnosed with HIV if they have a positive HIV DNA test. Descriptive statistics, inclusive of chi-square tests for variables that are categorical, were used for the analysis to compare the proportion of women receiving each regimen and the proportion of infants diagnosed with HIV diagnosed with HIV was compared by PMTCT regimen. All analyses were conducted using SPSS Version 16 and Stata Version 12 statistical packages.

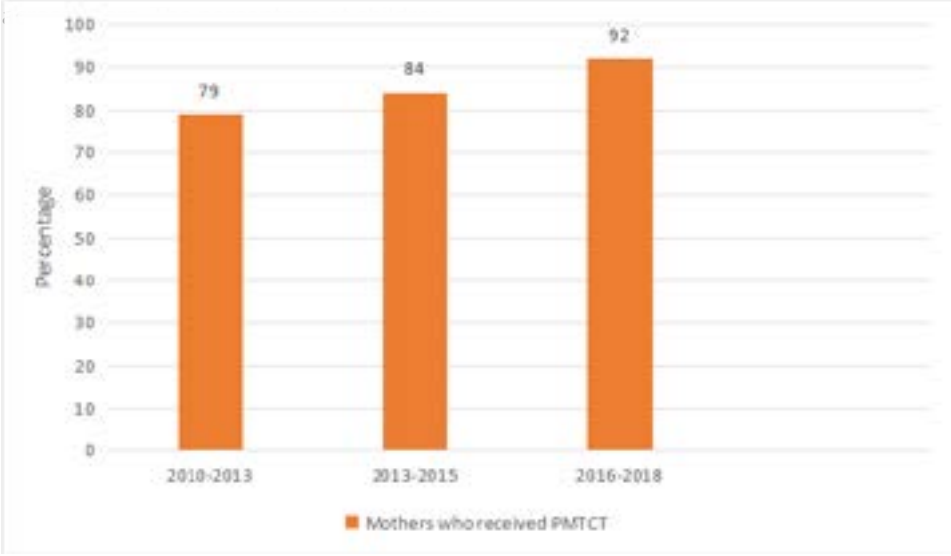

Figure 1: Proportion of HIV-infected mothers who received PMTCT in the Macha area by time period.

Ethical Consideration
The DBS, EID and NSEBA studies were approved by the Institutional Review Boards at the Johns Hopkins Bloomberg School of Public Health and Macha Research Trust. The studies were additionally approved by the Ministry of Health of Zambia (DBS and EID studies) and the National Health Research Authority (NSEBA study- MH/101/23/10-1).
Clearance and approval for this analysis was received from the University of Lusaka under the Department of Public Health and the Principal Investigators at Macha research Trust and Johns Hopkins Bloomberg School of Public Health.

Results

A total of 1,205 mother-infant pairs were enrolled in the three studies (403 from the DBS study, 502 from the EID study and 300 from the NSEBA study). For this study 1,175 mother-infant pairs with available HIV DNA test results were included in the analysis; 394 from the DBS study (2010-2013), 494 from the EID study (2013-2015) and 287 from the NSEBA study (2016-2018). The median age for the infants was 6 months (interquartile range [IQR]: 2.4, 7.2), with 592 (50%) being males. The characteristics of the mothers and infants are presented in (Table 1).

Adherence to PMTCT guidelines from 2010-2018

A large number of mothers (992, 84%) were receiving ART at time their infants were tested. Most mothers (997, 85%) mothers received ARVs for PMTCT, with 772 (66%) receiving cART, 216 (18%) receiving short course ART, and, 9 (1%) receiving single dose nevirapine (Table 1). Only 177 (15%) of mothers did not receive PMTCT (one mother was missing information on PMTCT). Similarly, most infants 884 (75%) received their postpartum ART prophylaxis.

Trends in PMTCT guidelines

The number of HIV-infected mothers that received any PMTCT increased per time period; from 79% in (2010-2013) to 92% in (2016-2018).

The distribution of PMTCT regimens was different by time period (Figure 2); in 2010-2013, the majority of mothers were receiving short course ART. By 2016-2018, the majority of the mothers were receiving cART. The proportion of mothers receiving cART increased from 28% in 2010-2013 to 92% in 2016-2018 (P<0.0001).

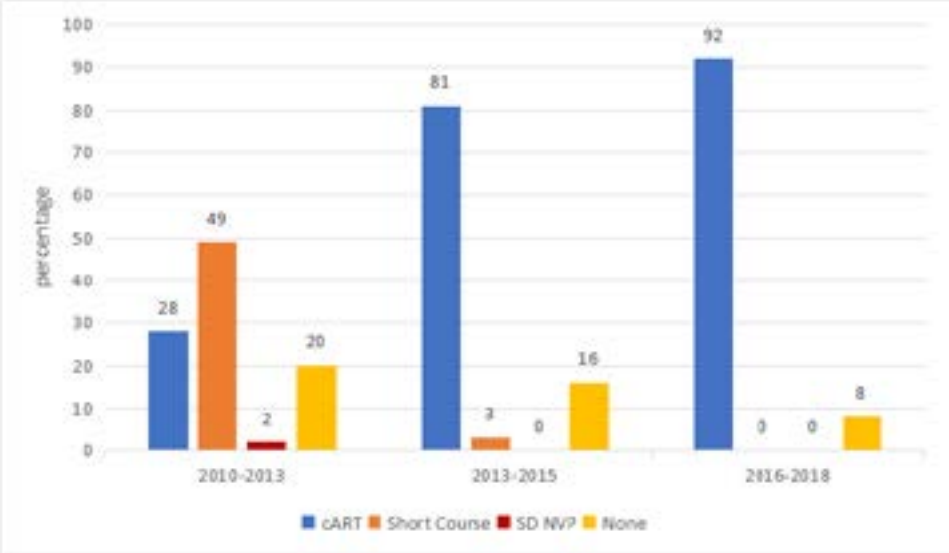

Figure 2: Distribution of maternal PMTCT regimens by calendar year

Note: One mother (2010-2013) was missing information on PMTCT (0.25%). None were on SD NVP (2013-2015), short course and SD NVP (2016-2018).

Using 95% CI, the sample size for this study was found to be 598. The sample size was done to demonstrate the minimum sample to be studied, but since the study used secondary data more participants were included in the analysis so as to improve the power of the study for statistical inference. Source: https://www.surveymonkey.com/mp/sample-size-calculator

Estimated population size for Macha	150,000
Margin of error	4%
Z-score at 95% confidence interval (CI)	1.96
Population proportional	0.5

Table 2: Characteristics of HIV-infected mothers and HIV-exposed children in the Macha area, 2010-2018

Characteristics of the mother	N (%)
Mother currently on ART	992 (84%)
Mother received PMTCT	
None	177 (15%)
Short course	216 (18%)
cART	772 (66%)
Single dose NVP	9 (1%)
Missing information on PMTCT	1 (0.1%)
Characteristics of the Child	
Male sex	592 (50%)
Median age in months (IQR)	6 (2.4, 7.2)
Child received PMTCT	884 (75%)
HIVDNA results- positive	101 (9%)

Trends in infant HIV testing and transmission

From 2010-2018, 101 (9%) infants tested positive for HIV (1% had an invalid test result). The proportion of infants testing positive decreased from 12% in 2010-2013 to 4% in 2016-2018 (P<0.0001; Figure 3).

The proportion of infants who tested positive differed significantly by maternal receipt of PMTCT. Among infants whose mothers did not receive any PMTCT, 38% tested positive, compared to 2% among infants whose mothers received cART for PMTCT (P<0.0001).

Discussion

Data from this study showed that there was improvement in PMTCT coverage in the Macha area from 2010 to 2018. The proportion of mothers who received any ART regimen during pregnancy increased significantly per time period from 79% in 2010-2013 to 92% 2016- 2018. This was due to policy changes which occurred from 2010-2018. We see that the distribution of PMTCT regimens differed by time period (Figure: 2); in 2010-2013 the majority of the mothers (49%) were receiving short course ART and this is because in 2010 Zambia based its PMTCT national policy on the World Health Organization recommendations that only pregnant women infected with the virus and have a CD4 count M350 cells/mm3 or clinical stage 3 or 4 could be treated with a triple ART regimen. By 2016-2018, the majority of the mothers (92%) were receiving cART as Zambia changed its PMTCT national policy guidelines to adopt Option B+ on January 13, 2013. Option B+ is a single universal regimen for treatment of pregnant women infected with HIV.

prescribed as soon as they are found positive with HIV (done at any stage of development during pregnancy age); treatment continues for life [9].

The Macha area has seen a decline in MTCT of HIV (12% in 2010-2013 to 4% in 2016-2018- Figure 3) along with the changes in maternal PMTCT regimen. The decline seen is due to formulation of aggressive political led multi-sectorial efforts; the prevention efforts that were put in place such as coming up with a structure within the Zambian government

to provide policy direction in relation to HIV and the coordination for the multi-sectorial efforts, scaling up of HIV testing and counselling, ART and PMTCT and the rolling out of EID and strategies to improve its use [9]. Infants born to mothers that did not receive any PMTCT regimen where more likely to test positive compared to infants born to mothers that received any PMTCT regimen (38% vs. 3% respectively). This in itself clearly shows that the Macha area is on the right track in scaling up PMTCT programmes, and is contributing towards the UNAIDs 90-90-90 targets (of having 90% of the people living with HIV knowing their status and 90% of those people who know their status accessing ART and 90% of those accessing ART with a suppressed viral load) [14] of ending the AIDS epidemic by the year 2030.

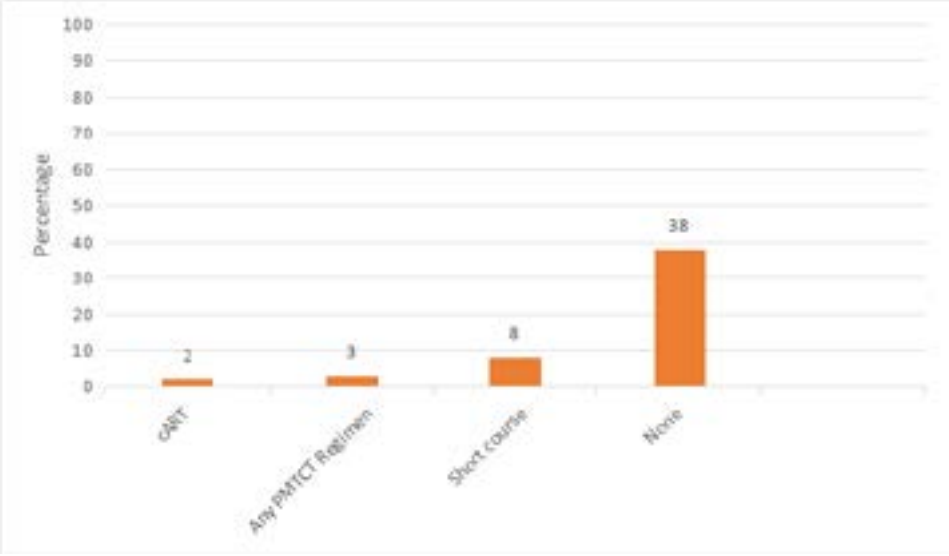

Figure 4: Proportion of infants diagnosed with HIV by maternal PMTCT regimen
Note: Mothers who took SD NVP or had missing information no infant was diagnosed with HIV

Although these data indicate achievement of 90% coverage of PMTCT in the Macha area, ensuring more widespread and consistent use of the Option B+ regimen is needed to make further progress. Continuous coverage of PMTCT and achieving early initiation of Option B+ in pregnancy should remain an important focus for Zambia [9]. Concerted efforts are required to achieve the goal of universal access to ARV drugs, treating and preventing HIV, and ultimately ending the HIV epidemic by 2030 [15].

Conclusion

This study provides evidence that the Macha area is moving in the right direction with regard to PMTCT coverage, provision of infant ARV prophylaxis and recommended Option B+ regimen. The majority of the infants received HIV prophylaxis and the most important thing to note is that there was a significant decrease in the proportion of infants that tested positive.

The government of Zambia, through the Ministry of Health, should protect these gains in their PMTCT services and strengthen strategies to improve on eMTCT.

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