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Reducing Mother-to-Child Transmission of Human Immunodeficiency Virus (HIV): Findings from an early Infant Diagnosis Program in Benue State, North Central Nigeria

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Abstract

Introduction*: A critical opportunity to strengthen follow-up of HIV-exposed children and assure early access to ARV treatment for infected children is provided by early infant diagnosis of HIV. This study describes findings from an EID program and the effectiveness of PMTCT intervention in Benue State, Nigeria.*

Methods*: This was a retrospective study. The study population comprised all perinatally HIV exposed children aged six weeks to 18 months who had Dried Blood Spot (DBS) samples taken for a DNA PCR test between January - December 2017 were enrolled for this study. Details of the ARV regimen received to prevent mother-to-child transmission (MTCT), infant feeding, HIV DNA PCR test results and turnaround time (TAT) for results were analyzed using SPSS version 20.*

Results *85.9% of mother-baby pairs received ARVs and 98.4% babies had ever been breastfed. Transmission rates for mother-baby pairs who received ARVs for PMTCT was 1.5% compared to 33% when neither baby nor mother received an intervention. Overall the prevalence of transmission in this study is 3.9% irrespective of intervention. The mean and median turnaround time for test results were 69 days (95% CI: 67.89-70.12) and 56 days respectively*

Conclusions*. Reduction of MTCT of HIV is possible with effective PMTCT intervention, including improved access to ARVs and appropriate infant feeding practices. The PMTCT programme in Benue State was found to be effective and achieved outcomes comparable to similar setting. Triple combination ARV drugs is feasible and resulted in low MTCT rates under routine clinic conditions in resource-limited setting.*

Keywords: *mother-to-child transmission of HIV, early infant diagnosis, breastfeeding, vertical transmission.*

Introduction

Mother-to-child transmission (MTCT) of HIV is one of the biggest challenges of the HIV/AIDS pandemic especially in resource constrained settings (Piot et al,2008; Kahungu et al,2018). Africa has the highest burden of the disease accounting for about 90 percent of paediatric HIV infections (UNAIDS,2018). In 2017, global estimates for HIV stand at 36.9 million (31.1-43.9 million) people living with the virus. From this estimate 35.1 million (29.6 million–41.7 million) are adults and 1.8 million (1.3 million–2.4 million) are children (<15 years). These new infections from children are mostly from MTCT (WHO et al,2004). The prevalence of MTCT is up to 45%; but it is believed that this rate of infection can be reduced to below 5% with effective interventions (Hill et al, 2015; WHO,2016a; Rupali,2007).

It is acknowledged that Nigeria accounts for 30% of the burden of MTCT of HIV in the world (Anoje et al,2012; Ibobo et al,2017). This justifies why Nigeria is one of the 22 focus countries of the Global Plan to Eliminate MTCT (UNAIDS,2011; Adetokunboh OO, Oluwasanu M. (2016). Though the Nigerian Government has implemented PMTCT of HIV program, evidence on the effectiveness of PMTCT remains limited (Anoje et al,2012). Yet, evidence of the effectiveness of PMTCT has been clearly demonstrated in large scale programs that are integrated into routine antenatal care (Stringer et al,2005)

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Early Infant Diagnosis (EID) is part of the service package of PMTCT program. This involves EID testing directly for HIV DNA by Polymerase Chain Reaction (PCR) method and provides definitive diagnosis in children less than 18 months of age. EID makes it possible for early identification and referral of HIV-positive infants. This enables the infants to receive early clinical evaluation and antibiotic prophylaxis against opportunistic infections as well as antiretroviral therapy (Martin & Palladino, 2017; Mateus et al, 2014; Motswere-Chirwa et al, 2014). Furthermore, a review of HIV test results in an EID program provides a unique opportunity for evaluating the success of the PMTCT program and reducing MTCT (Anoje et al, 2012)

This study examined an EID program involving 278 facilities in Benue State of Nigeria using routine program data with a view to evaluating the effectiveness of PMTCT interventions in reducing vertical transmission of HIV.

Methods

Study design

This was a retrospective study using routine early infant diagnosis (EID) program data of infants and children perinatally exposed to HIV aged 6 weeks -18 months from Benue State, Nigeria. 5734 consecutive sample of infants and children identified from the EID laboratory register from January 2017-December 2017 were enrolled for this study.

Study setting

Benue State is one of the six states that make up the north central zone of Nigeria. It lies between latitudes 6Â°25'N and 8Â°8'N and longitudes 7Â°47'E and 10Â°E'. Makurdi is the State capital and also a local Government headquarters. The facilities providing PMTCT services in Benue State are supported by Presidents Emergency Plan for Aids Relief (PEPFAR) through Centres for Disease Control (CDC) and Global Fund (GF). The State has one centralized EID laboratory located at Federal Medical Centre Makurdi where all DBS samples across the state from over 300 facilities are sent and analyzed. The laboratory was set up as a partnership between Government of Nigeria (GoN) and APIN Public Health Initiatives, Nigeria with support from CDC Nigeria. Partners that sent samples during the period under review included Aids Health Care Foundation (AHF), Centre for Integrated Health Programs (CIHP), Caritas Catholic Foundation, Nigeria (CCFN) and GF. The laboratory was set up to strengthen HIV care in children as a continuum of the PMTCT program. EID is a centralized facility and laboratory based program that uses DBS specimens to determine the HIV status of exposed infants at young age (6 weeks to less than 18 months). Through EID outcome treatment for identified HIV infected infants will be facilitated and mortality reduced

Data collection and management

Dried blood spots (DBS) samples are usually collected at the facility level by trained staff designated as EID focal persons. These infants and children were systemically identified in the postnatal clinic through information on their mother's card on her HIV status and during follow up in the clinic where exposure status of children is determined. The DBS samples were collected using special filter paper and the EID PCR laboratory request and result form filled which accompanied the sample to the laboratory. The information collected from the exposed baby included age, sex of the child, breastfeeding status of child and ARV intervention status of mother and baby. The samples are transported directly to the laboratory by the hospital staff. The same process is used to send back the results. This study was based on a review of data routinely collected at 278 partner supported EID sites in Benue. The routine service data was extracted from structured national data collection tools and entered into a Microsoft excel sheet designed for data entry. The national tools used to get data for analysis were the PCR request and result form and the EID register.

Data analysis

Statistical analysis was done with Statistical Package for the Social Sciences (SPSS) version 20.

Descriptive statistics were used to summarize the baseline characteristics. Continuous variables were categorized to facilitate analysis. Transmission rates were estimated for specific PMTCT intervention received by mothers and children. The Chi-square test was used to be used to test for association between categorical variables and the p value < 0.05 was considered statistically significant. Multiple logistic regression model was used to estimate odds ratios along with 95% confidence interval in order to assess correlates of mother-to-child transmission of HIV (relationship between transmission rates and PMTCT ARV intervention received by mother).

Ethical considerations

The study was approved by Texila American University Guyana Institutional Review Board and Benue state ministry of health, Nigeria.

Results

The study population was made up of 49.4% males (n=2688) and 50.6% females (n=2755). The mean age at DBS collection was 11.34 weeks (95% CI: 11.05-11.64). The highest DBS samples representing 58.2% (n=3132) were collected at six weeks of age (Table 1). This is normally the recommended age of DBS collection though it can be collected after that in a program setting. A total of 3.9% of mothers and babies respectively did not receive any ARV medication for preventing mother-to-child transmission of HIV. In relation to infant feeding, the vast majority of children (98.4%) were breastfed.

Table 1. Characteristics of study participants (N=5734)

Characteristics	**Number (%)**
Age at testing	
< 6 weeks	3132 (58.2)
>6 weeks -6 months	1773 (33.0)
>24 weeks-18 months	473 (8.8)
Gender	
Male	2688 (49.4)
Female	2755 (50.6)
Child Breastfeeding status	
Yes	5497 (98.4)
No	87 (1.6)
Maternal ARV	
Yes	5056 (93.9)
No	330 (6.1)
Infant ARV	
Yes	5023(93.7)
No	339 (6.3)
PMTCT ARV Intervention status	
Both	4750 (85.9)
Mother only	317(5.7)
Child only	250 (4.5)
None	250 (4.5)

*Mean age 11.34 weeks (95% CI: 11.05-11.64)

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Analysis of the DNA PCR test results showed that, regardless of infant feeding choice, the transmission rates when both mother and baby received ARV for PMTCT was 1.5%. When neither baby nor mother received an intervention, the transmission rate was 33% (Table 2).

Table 2. Intervention status and transmission rates

Intervention status	Number	Positive result	Transmission rate (%)	OR(95%CI)	p-value
Both	4750	72	1.5	0.153 (0.098-0.239)	
Mother only	317	29	9.1	0.127 (0.080-0.202)	<0.001
Baby only	250	27	10.8	0.031 (0.022-0.045)	
None	215	71	33	1.00	

The transmission rates for HAART started before pregnancy and during pregnancy are 1.5% and 3.6% respectively (Table 3). The odds ratio is significant indicating increased risk of transmission with none initiation of ARV during pregnancy.

Table 3. Maternal ARV and HIV transmission in infants

Maternal ARV	**Number**	**Positive**	**TR (%)**	**OR (95%CI)**	**p-value**
HAART started before pregnancy	3873	58	1.5	1	
HAART started during pregnancy	1183	43	3.6	4 (2.70 – 6.58)	<0.001
None	330	94	28.5	19.54 (14.34 – 26.64)	

The unadjusted odds ratio (OR) of MTCT of HIV was 19 times (95% C.I: 14.1 – 26.26) when mother did not receive any ARV. When adjusted for the impact of variables such as the sex of the baby, age at first PCR testing, and infant feeding choices, HAART, male and breastfed were found to be more likely to get infected (AOR 1.058, 95% CI: 0.761-1.473 and AOR1.007, CI:0.231-4.394)

Table 4a. Mother' PMTCT ARV intervention and transmission rate

Maternal ARV	**Number**	**Positive**	**TR (%)**	**OR (95%CI)**	**p-value**
HAART	5056	101	2.0	1	
None	330	93	28.2	19.25 (14.1 – 26.26)	<0.001

*348 babies had no data on maternal ARV

Table 4b. Estimated adjusted odds ratio and 95% confidence intervals for Mother's ARV regimen

Mother's ARV regimen	AOR
None	1.0
HAART	0.099 (0.72-0.148)
Log10Age	0.150 (0.091-0.248)
Male	1.058 (0.761-1.473)
Breastfeed	1.007(0.231-4.394)

*Mean age 11.34 weeks (95% CI: 11.05-11.64)

The mean and median turnaround time for test results were 69 days (95% CI: 67.89-70.12) and 56 days respectively. The turnaround time for the positive results was found to be < 28 days for 2.8 % (n=6) and

>28 days for 97.2% (n=206) respectively. The turnaround time for 88.6 %(n=4753) of the results was >28 days while 11.4 %(n=611) of the results had a turnaround time of < 28 days. The highest number of samples representing 2.0 %(n=109) had a turnaround of time of 49 days. The recommended turnaround time in a program setting should be < 28 days so that infants and children with positive results can be placed on treatment without delay. However, most of the samples in this program were not processed in line with the recommended time line.

Table 5. Turnaround time for positive HIV DNA PCR Result

		HIV DNA PCR Result		Total
		Positive (%)	Negative (%)	
Turnaround time	<28 days	6(2.8)	605	611
	>28 days	206(97.2)	4547	4753
Total		212	5152	5364

*370 babies had no data turnaround time,
Pearson Chi-Square = 16.026 Pv=0.000

Discussion

A pregnant positive woman must successfully follow the PMTCT cascade for any PMTCT programme to effectively prevent vertical transmission of HIV between mother and baby, beginning with acceptance of HIV counselling and testing to receiving ARV prophylaxis and safe infant feeding practices. Although 98.4% of infants and children in this study are breastfed over 80% of them were under ARV cover in line with the new PMTCT guideline (option B+) of lifelong ART to all pregnant and breastfeeding women(WHO,2016b).

The proportion of HIV infected/exposed mother-infant pairs that received PMTCT ARV intervention is a measure of the PMTCT coverage. Mother-infant pairs that received PMTCT ARV intervention provide a measure for PMTCT coverage which is used as a surrogate marker for effectiveness of the PMTCT program (Stringer, 2009). This program has a coverage of 85.9% which is lower than that of a program in Tanzania with 90% coverage (Kalua et al,2017). This coverage is in line with Nigerian Government's National Strategic Framework goals of at least 80% of PMTCT ARV coverage (Pharr et al,2016). The PMTCT ARV prophylaxis gap for this program is therefore, 14.1% representing HIV positive women who require ARV prophylaxis to reduce MTCT risk but did not receive it. This is slightly lower than the Nigerian national PMTCT gap of 30%. Patient attrition is likely to contribute to this suboptimal uptake of ARV in this study (UNAIDS, 2018). Effectiveness of PMTCT programs is largely dependent on coverage. Coverage requires going through the PMTCT pathway to get ARV prophylaxis. When both the mother and baby received intervention, the transmission rate was 1.5% compared to 9.1% for mother only and 10.8% for baby only. When both did not receive prophylaxis the transmission rate was 33%. This further demonstrates the critical role of ARVs in reducing risk of MTCT and also an indication that PMTCT interventions are effective in a resource-limited program setting. Both mother and infant are required to take their ARV for prophylaxis to be effective to prevent MTCT of HIV. Drugs received by mother alone would not achieve prolonged drug concentrations in the infant if duration of ingestion and delivery is short and if the drugs are only taken by the infant there is little or no efficacy. This underscores the importance of coverage showing that efficacy is of no value without appropriate coverage. Successful PMTCT requires that each mother-infant pair negotiate a critical path that begins with the offering of an HIV test and proceeds through posttest counseling to drug adherence and beyond. Programmatic failures have been found to be common along this path and each site faces its own mix of challenges in maximizing service coverage (Stringer, 2009; Kalua et al,2017; Pharrr et al,2016; Stringer et al,2010). The availability of ARVs to HIV infected mothers during antenatal period is very essential to reduce MTCT though it does not translate to adherence. A safety net is created for HIV positive pregnant women who do not return to the clinic when ARVs are available at first

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contact but this is only possible when HIV counseling and testing is offered with same day result (Torpey et al,2010).

A critical opportunity to strengthen follow-up of HIV-exposed children and initiate early treatment for those who are HIV infected is provided by early diagnosis of HIV in infants. HIV infection in children is associated with very high mortality rates if untreated. The children with HIV early antiretroviral (CHER) study carried out in South Africa showed that early diagnosis and initiation of antiretroviral treatment reduces early infant mortality and HIV progression by 76% and 75% respectively (Anoje et al,2012). The national PMTCT guidelines in Nigeria stipulate that the first DNA PCR test should be conducted at six weeks of age for all HIV exposed infants (FMoH, 2015). The EID testing coverage at 6 weeks is 58.2%. This shows only half of HEI tested at 6 weeks. This is lower than the standard recommendation of 100% (FMoH, 2015). Evidence from systematic review of 44 studies from 15 countries in sub-Saharan Africa showed that between 48 and 81% of HEIs receive EID within 2 months (Wettstein et al,2012), a result comparable to level of EID use in the present study. The opportunity for early HIV diagnosis and ART initiation are missed out, without timely use of EID. It appears timely access to EID is a problem in most sub-Saharan countries. Evidence from a multicenter cohort study in Ethiopia found only 41% of HEIs had EID at 6 weeks and the median age at the time of the testing was 60 days (Kebede et al, 2014). A critical catalyst for EID services utilization is the importance of maternal knowledge of HIV transmission during pregnancy, labor or delivery, and breastfeeding.

The limitations to our study include the purposive nature of the selection of samples. In addition, use of facility based records may have led to selection bias (i.e., study population included those who sought services at facilities). These limitations affected our ability to generalize the findings of this study. Additionally, we acknowledge that our analysis would have been strengthened by including variables such as baseline CD4 counts and viral load, however, the selection of the variables included in our analysis was guided (and thus limited) by what we were able to obtain from the national PMTCT data collection tools used and maintained at the study sites.

Conclusion

The PMTCT programme in Benue State is effective and has achieved outcomes comparable to what is obtainable from similar setting. Triple combination ARV drugs is feasible and resulted in low MTCT rates under routine clinic conditions in resource-limited setting. Commencement of ARV drugs prior to conception or early in conception (in the first and second trimesters of pregnancy) should be emphasized in PMTCT programs. The success of the PMTCT as demonstrated by the EID program data is within the policy framework of the Benue State and the Nigerian government. Low MTCT rates are therefore achievable in Nigeria through rapid scale up of the PMTCT/EID programme. Long TAT can hinder the success of early infant diagnosis (EID) programs. A more efficient process is needed so that caregivers can be provided test results more rapidly, potentially resulting in earlier treatment initiation and better outcomes for HIV-infected infants.

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