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### ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF HIV (eMTCT) IN WESTERN NIGERIA: HOW FAR HAVE WE GONE?

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#### ABSTRACT

**Background:** HIV pandemic has continued to be a huge challenge in Nigeria, with the problem of stigmatization reducing the chances of early determination of the HIV status of pregnant women, which may increase the chances of transmission to the child from the mother. Hypotheses tested were the influence of maternal antiretroviral therapy (ART) use and infant's feeding option on baby's final early infant diagnosis (EID) outcome. The study was aimed at determining the trend as well as diagnosis of HIV infection in exposed infants. It will also determine among infants the factors associated with the transmission of the infection from their mothers.

**Methods:** This study was a prospective cohort study of HIV-exposed infants conducted in Ekiti State, South Western Nigeria, between June 2015 and June 2017. Dried Blood Spots (DBS) were analyzed using polymerase chain reaction technique. All data were statistically analyzed, using statistical package for the social sciences (SPSS) and statistical test of significance was performed with Chi-Square test.

**Results:** A total of 200 infants were included in the study, 91 (45.5%) female and 109 (54.5%) male. Three (1.5%) babies were confirmed positive after cessation of all exposures. Maternal antiretroviral therapy (ART) use has significant effect on baby early infant diagnosis (EID) outcome ( $\chi^2 = 65.40$ ,  $df = 2$ ,  $P = 0.001$ ). Infant feeding option has significant effect on baby early infant diagnosis (EID) outcome ( $\chi^2 = 132.67$ ,  $df = 2$ ,  $P = 0.001$ ). Baby's mode of delivery have higher association with the final EID outcome of the baby (OR: 1.018, 95% CI: 0.998 – 1.038).

**Conclusion:** ART administration to both HIV-infected mothers and their babies has demonstrated an effective mechanism in the elimination of mother-to-child transmission (eMTCT), as this is evident in the very low positivity outcome. However, the degree to which Cuba, Armenia, Belarus, and Thailand have eliminated HIV transmission from mother-to-baby is achievable in Nigeria through provision of universal access to health care.

**Key words:** infant, mother, dried blood spot, polymerase chain reaction

### ÉLIMINATION DE LA TRANSMISSION DU VIH (eCTM) DE MÈRE À L'ENFANT DANS L'OUEST DU NIGÉRIA: COMBIEN EN SOMMES-NOUS ALORS?

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## RÉSUMÉ

**Contexte:** Au Nigéria, la pandémie de VIH continue de poser un problème énorme, le problème de la stigmatisation réduisant les chances de déterminer rapidement le statut VIH des femmes enceintes, ce qui peut augmenter les risques de transmission de la mère à l'enfant.

Les hypothèses testées étaient l'influence de l'utilisation du traitement antirétroviral par la mère et de l'option d'alimentation du nourrisson sur le résultat final du diagnostic précoce du nourrisson. L'étude visait à déterminer la tendance ainsi que le diagnostic d'infection par le VIH chez les nourrissons exposés. Il déterminera également chez les nourrissons les facteurs associés à la transmission de l'infection par leur mère.

**Méthodes:** Cette étude était une étude de cohorte prospective menée entre juin 2015 et juin 2017 dans l'État d'Ekiti, dans le sud-ouest du Nigéria, auprès de nourrissons exposés au VIH. Les taches de sang séché ont été analysées à l'aide de la technique de réaction en chaîne de la polymérase. Toutes les données ont été analysées statistiquement, en utilisant un logiciel statistique pour les sciences sociales (SPSS) et un test statistique de signification a été réalisé avec un test de Chi-Square.

**Résultats:** Un total de 200 nourrissons ont été inclus dans l'étude, 91 (45,5%) femmes et 109 (54,5%) hommes. Trois bébés (1,5%) ont été confirmés positifs après la cessation de toutes les expositions. L'utilisation du traitement antirétroviral par la mère a un effet significatif sur l'issue du diagnostic précoce chez le nourrisson ( $ID^2 = 65,40$ ,  $df = 2$ ,  $p = 0,001$ ). L'option d'alimentation du nourrisson a un effet significatif sur l'issue du diagnostic précoce du nourrisson ( $ID^2 = 132,67$ ,  $df = 2$ ,  $p = 0,001$ ). Le mode d'accouchement du bébé est davantage associé au résultat final de l'EID du bébé (OR: 1,018, IC 95%: 0,998 - 1,038). Conclusion: l'administration d'un traitement antirétroviral aux mères infectées par le VIH et à leurs bébés a démontré un mécanisme efficace pour éliminer la transmission mère-enfant (eMTCT), ce qui est évident dans le résultat de très faible positivité. Cependant, il est possible d'atteindre au Nigéria le degré auquel Cuba, l'Arménie, le Bélarus et la Thaïlande ont éliminé la transmission du VIH de la mère à l'enfant grâce à un accès universel aux soins de santé.

**Mots clés:** nourrisson, mère, tache de sang séché, réaction en chaîne de la polymérase

## INTRODUCTION

Prevention of mother-to-child transmission of HIV (PMTCT) is the most successful HIV prevention intervention globally (1). Elimination of mother-to-child transmission of HIV (eMTCT) is key to the global effort to combat sexually transmitted infections (STIs) and to end AIDS by the year 2030. Cuba was the first country validated by the World Health Organization (WHO) in 2015 to have successfully eliminated mother-to-child transmission (MTCT) of HIV and syphilis. Countries such as Thailand, Armenia, Belarus and Republic of Moldova have gone on to join Cuba in 2016 (2). The countries ensured early access to pre-natal care, HIV & syphilis testing for pregnant women and their partners and treatment for women who test positive, as well as their babies. They provided reproductive health information, engaged communities and conducted outreach to marginalized populations, in a manner consistent with basic human rights and gender equality, showing a perfect integration of maternal and child health with sexual & reproduction health and HIV services (2).

Mother-to-child transmission (MTCT) of HIV resulted in approximately 370,000 infant infections worldwide in 2009 (3). The same year, estimated 2.5 million children worldwide were living with HIV, mostly a consequence of MTCT and more than 90% of these children are in Sub-Saharan Africa (3). Mother-to-child transmission of HIV can occur in utero (in-utero), during delivery (intrapartum) or after birth (postnatally) through breastfeeding. Strategies to reduce MTCT focus on these periods of exposure and include the use of antiretrovirals (ARVs), caesarean section before the onset of labour or rupture of membranes and even may involve complete avoidance of breastfeeding (4). The combination of these interventions when effectively followed, reduce the risk of MTCT to as low as 1-2% (5). In the absence of intervention, 30-45% of all infants born to HIV positive mothers will be infected and 10-20% will be infected through breastfeeding (6).

In infants born from HIV-infected women, maternal anti-HIV antibodies cross the placenta and persist in infant blood for up to 18 months. These antibodies usually represent exposure to maternal HIV rather than the true infants less than 18 months by antibody-based tests. Only virological tests can be used for an accurate diagnosis of HIV before 18 months of age (7). A dried blood spot (DBS) is the sampling method used for HIV-exposed infants. Infants can be tested from six weeks of age and sample **collection is from finger, toe or heel depending on the age and weight of the baby (8)**.

A research work published in 2014 on the impact of HIV PMTCT reported 7.0% of the children to be positive, with highest prevalence found among children in age-group 6-18 months (16.1%) (9). An overall prevalence of 16.98% of postnatal HIV was observed in a study on PMTCT published in 2010 (10). In Tanzania, an overall MTCT prevalence rate of 6.3% was reported, with infants on exclusive breastfeeding at the time of first DBS PCR was 86.5% (11). Another research in eastern Cameroon, published in 2013, reported that 50% of the infants were exclusively breastfed and based on the first PCR tests data, an overall prevalence of 11.6% was reported (12). In 2010, a study carried out in Malawi showed that 13.8% of the children born to HIV-positive mothers in 2009 were themselves HIV-positive as infants (13). In China, 4.4% mean HIV-positive rate of exposed infants was reported (14). Meanwhile, only 1.5% & 1.3% of babies within 18-month PMTCT program were confirmed positive in year 2013 & 2014 respectively after all exposure cessation in Western Nigeria (15). This study is therefore designed to determine the diagnosis and trend of HIV infection in exposed infants and the factors associated with mother-to-child transmission (MTCT) among the infants.

## RESEARCH HYPOTHESIS

- Maternal antiretroviral has no significant effect on baby final early infant diagnosis outcome.

- Infant's feeding option has no significant effect on

final early infant diagnosis outcome.

generated for all variables and statistical test of significance was performed with chi-square test. Significance was fixed at  $P < 0.05$  and highly significant when  $P < 0.01$ .

## METHODOLOGY

This study was a prospective cohort study of all HIV-exposed infants enrolled at health facilities in Ekiti State from June 2015 and June 2017. The study population was HIV-exposed infants whose second (i.e. final) early infant diagnosis (EID) result has been determined by HIV nucleic acid testing polymerase chain reaction (PCR) and baby's final outcome (alive/dead) is known. Relevant data such as age, sex, ARV therapy for mother and baby, infants feeding choices, place of delivery, duration of HAART use, HIV DNA results, among others were analysed. Results of samples analysed were received as dried blood spots (DBS) collected from each infant and analysed at the PCR Laboratory at State Specialist Hospital Akure Ondo State with an automated real-time amplification and detection of DNA using a qualitative DNA polymerase chain reaction (PCR) analyser by (Roche Molecular Diagnostics, Basel, Switzerland). HIV testing was also done at the Federal Teaching Hospital Ido Ekiti, State Specialist Hospital Ikere Ekiti & Ekiti State University Teaching Hospital Ado Ekiti.

The data analysis was done using statistical package for the social sciences (SPSS) for windows version 23.0 software (SPSS Inc; Chicago, IL, USA). Frequency counts were

## RESULTS

A total of 200 infants were included in the study with mean age (in months)  $13.80 \pm 1.20$ , 91 (45.5%) female and 109 (54.5%) male. The research outcomes showed that majority of the children were breastfed exclusively, with the main mode of delivery being spontaneous vaginal delivery (SVD), 173 (86.5%) while one hundred and seven (53.5%) of the mothers had antiretroviral therapy started during pregnancy. Nearly 60% of the mothers used recommended first line regimen Tenofovir/Lamivudine/Efavirenz while most of the babies took single dose nevirapine.

Three (1.5%) babies were confirmed positive after cessation of all exposures, largely breastmilk. Maternal antiretroviral therapy (ART) use was found to have a significant effect on baby early infant diagnosis (EID) outcome ( $\chi^2 = 65.40$ ,  $df = 2$ ,  $P = 0.001$ ) while infant feeding option also had significant effect on baby early infant diagnosis (EID) outcome ( $\chi^2 = 132.67$ ,  $df = 2$ ,  $P = 0.001$ ). Baby's mode of delivery was also found to have higher association with the final EID outcome of the baby (OR: 1.018, 95% CI: 0.998 – 1.038).

The full results are captured in tables:

**TABLE 1: CHARACTERISTICS OF INFANTS AND MOTHERS**

CHARACTERISTICS	Frequency	%
<b>BABY AGE (MONTHS)</b>		
12	22	11.0
13	73	36.5
14	54	27.0
15	31	15.5
16	15	7.5
17	5	2.5
<b>SEX</b>		
Male	109	54.5%
Female	91	45.5%
<b>MODE OF DELIVERY</b>		
Spontaneous Vaginal Delivery (SVD)	173	86.5%
Caesarean Section (C/S)	27	13.5%

<b>PLACE OF DELIVERY</b>		
Mission	7	3.5
Primary Healthcare Centre	23	11.5
Private Clinic	12	6.0
Secondary Healthcare Facility	26	13.0
Tertiary Healthcare Facility	132	66.0
<b>MATERNAL ENROLMENT TO CARE</b>		
Yes	196	98.0
No	4	2.0
<b>MATERNAL ENROLMENT/ART</b>		
HAART started before pregnancy	89	44.5
HAART started during pregnancy	107	53.5
No HAART taken	4	2.0
<b>MATERNAL OUTCOME</b>		
Alive	197	98.5
Dead	3	1.5
<b>TYPE OF ARV USED BY MOTHER</b>		
Zidovudine/Lamivudine/Nevirapine	78	39.0
Tenofovir/Lamivudine/Efavirenz	118	59.0
None	4	2.0
<b>INFANT ARVs (NEVIRAPINE TAKEN)</b>		
Yes	199	99.5
No	1	0.5
<b>INFANT EVER BREASTFED</b>		
Yes	196	98.0
No	4	2.0
<b>BABY FEEDING OPTION</b>		
Exclusive Breastfeeding (EBF)	194	97.0
Breastmilk Supplement (EBS)	4	2.0
Mixed Feeding (MF)	2	1.0
<b>FIRST EID DONE</b>		

Yes	200	100
No	0	0
<b>FIRST EID RESULT</b>		
Negative	197	98.5
Positive	3	1.5
<b>SECOND EID DONE</b>		
Yes	200	100
No	0	0
<b>SECOND EID RESULT</b>		
Negative	197	98.5
Positive	3	1.5
<b>RAPID TEST RESULT AT SECOND EID</b>		
Negative	197	98.5
Positive	3	1.5
<b>BABY FINAL OUTCOME</b>		
Alive	200	100
Dead	0	0

TABLE 2 - CHI SQUARE RESULT SHOWING EFFECT ON BABY EARLY INFANT DIAGNOSIS (EID) OUTCOME

VARIABLES (HYPOTHESES)	$\chi^2$	df	Critical value	Decision	P-Value
Maternal Antiretroviral Therapy (ART) use does not have significant effect on baby early infant diagnosis (EID) outcome	65.40	2	5.99	Rejected	0.001
Infant feeding option does not have significant effect on baby early infant diagnosis (EID) outcome	132.68	2	5.99	Rejected	0.001

The null hypothesis is rejected when the test statistic is greater than the tabled value or critical value.

TABLE 3 – ODDS RATIO (OR) TABLE

Variables	OR	95% CI
Estimated odds that mode of baby delivery have effect on baby final EID outcome	1.018	0.998 – 1.038

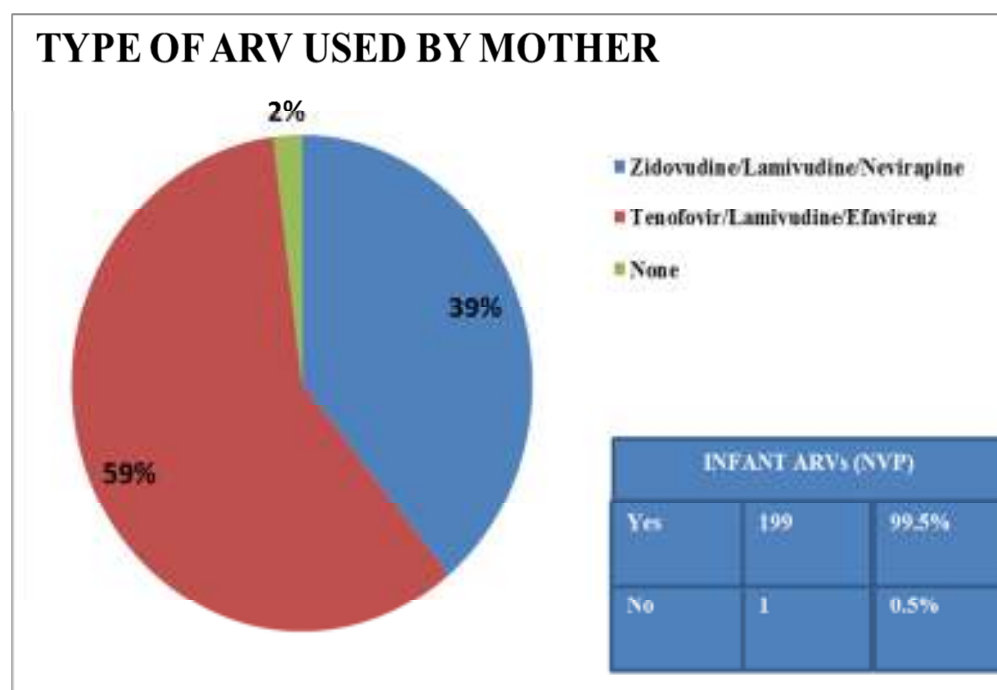


FIGURE SHOWING THE TYPE OF ARV USED BY MOTHER

## DISCUSSION

The outcome of this study reveals a positivity rate of 1.5% after second EID test. The positivity rate is similar to previous research outcome in Western Nigeria where 1.5% & 1.3% of babies within 18-month PMTCT program were confirmed positive in year 2013 & 2014 respectively after all exposure cessation in Western Nigeria (15). It is however lower than those reported in various other studies such as 7.0% reported in 2014 & 16.98% reported in 2010 respectively (9, 10), 6.3% positivity reported in Tanzania (11), 11.6% reported in Eastern Cameroon in 2013 (12), 13.8% & 4.4% positivity rates reported in Malawi & China (13, 14). This prevalence outcome is a great improvement over most of the previous studies although very similar to the previous Western Nigeria study outcome. The low positivity rate might be attributed to enhanced spread of programmes now targeting the elimination of HIV infection to children through the mothers especially with utilization of

updated guidelines where most positive mothers are on antiretroviral (ARV) therapy either before pregnancy or commenced during pregnancy, with 98.0% of the mothers on ARV therapy and infants even born to mothers with HIV who are at high risk of acquiring HIV now receive dual prophylaxis for extended period showing strict adherence to the new national guidelines, with its main role in reducing HIV transmission. This outcome suggests therefore that the commencement of ARV prior or during pregnancy had a great impact on the babies' status outcome. Moreover, another contributory factor is the fact that the babies receive treatment as soon as possible after birth, mostly a single-dose nevirapine, from birth for a period of six weeks, after which the drug is replaced with cotrimoxazole. Infections to these few babies could be due to poor viral suppression which could not be ascertained in this study, as the HIV viral load, used to determine how well antiretroviral therapy (ART) is controlling the virus, was not included as part of the study objectives

as it was just beginning to be fully optimized during the course of this study. It is therefore recommended that mixed feeding especially within the first 6 months, should be highly discouraged.

The Chi Square analysis in table 2 shows that maternal antiretroviral therapy use ( $\chi^2 = 65.40$ ,  $df = 2$ ,  $P = 0.001$ ) & infant feeding option ( $\chi^2 = 132.68$ ,  $df = 2$ ,  $P = 0.001$ ) have significant effect on baby early infant diagnosis (EID) outcome, indicating that the antiretroviral therapy used before or during pregnancy and exclusive breastfeeding being the most common baby feeding option in this study cohort enhanced the baby eventual outcome after the second EID result. It is thus recommended that partial breastfeeding with complimentary food, should be in

place after 6 months to enhance HIV-free child survival.

#### CONCLUSION:

ART administration to both HIV-infected mothers and their babies has demonstrated an effective mechanism in the elimination of mother-to-child transmission (eMTCT), as this is evident in the very low positivity outcome. However, the degree to which Cuba, Armenia, Belarus, and Thailand have eliminated HIV transmission from mother-to-baby is achievable in Nigeria through provision of universal access to health care.

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