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## **A Review and Analysis of Outcomes from Prevention of Mother-to-Child Transmission of HIV Infant Follow-up Services at a Pediatric Infectious Diseases Unit of a Major Tertiary Hospital in Nigeria: 2007-2020**

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### **ABSTRACT**

**Background and Objective:** Above 90% of childhood HIV infections result from mother-to-child transmission (MTCT). This study examined the MTCT rates of HIV-exposed infants enrolled in the infant follow-up arm of the prevention of mother-to-child transmission (PMTCT) program in a teaching hospital in Southeast Nigeria.

**Methods:** This was a 14-year review of outcomes of infants enrolled in the infant follow-up arm of the PMTCT program of Nnamdi Azikiwe University Teaching Hospital Nnewi, Nigeria. The majority of subjects were enrolled within 72 hours of birth and were followed up until 18 months of age according to the National Guidelines on HIV prevention and treatment. At enrollment, relevant data were collected prospectively, and each scheduled follow-up visit was recorded both electronically and in physical copy in the client's folders. Data were analyzed using SPSS version 20. The major outcome variable was final MTCT status.

**Results:** Out of 3,784 mother-infant dyads studied 3,049 (80.6%) received both maternal and infant Antiretroviral (ARV) prophylaxis while 447 (11.8%) received none. The MTCT rates were 1.4%, 9.3%, 24.1%, and 52.1% for both mother and infant, mother only, infant only, and none received ARV prophylaxis respectively. There was no gender-based difference in outcomes. The MTCT rate was significantly higher among mixed-fed infants ( $p < 0.001$ ) and among those who did not receive any form of ARVs ( $p < 0.001$ ). Among dyads who received no ARVs, breastfed infants significantly had a higher MTCT rate compared to never-breastfed infants (57.9% vs. 34.8%;  $p < 0.001$ ). The MTCT rate was comparable among breastfed (2.5%) and never-breastfed (2.1%) dyads who had received ARVs. After logistic regression, maternal ( $p < 0.001$ , OR: 7.00) and infant ( $p < 0.001$ , OR: 4.00) ARV prophylaxis for PMTCT remained significantly associated with being HIV-negative.

**Conclusion and Global Health Implications:** Appropriate use of ARVs and avoidance of mixed feeding in the first six months of life are vital to the success of PMTCT programs in developing countries. PMTCT promotes exclusive breastfeeding and reduces the burden of pediatric HIV infection, thereby enhancing child survival.

**Keywords:** • HIV-Exposed Infants • Antiretroviral Prophylaxis • Mixed Feeding • PMTCT Outcome • Exclusive Breastfeeding • Early Infant Diagnosis • Mother-Infant Pairs • Nigeria

## **I. Introduction**

### **1.1. Background of the Study**

The high burden of mother-to-child transmission of Human Immunodeficiency Virus (HIV) in sub-Saharan Africa including Nigeria is due to high rates of heterosexual transmission, high prevalence of HIV in women of reproductive age, high total fertility rate, characteristically prolonged breastfeeding culture, sub-optimal infection prevention measures during labor and delivery, and limited access to general HIV prevention interventions.<sup>1</sup> According to the National Agency for the Control of AIDS (NACA), Nigeria accounted for 37,000 of the world's 160,000 new cases of babies born with HIV in 2016.<sup>2</sup> A high burden of infection in women naturally translates to an increase in that of infants and young children as vertical or mother-to-child transmission (MTCT) accounts for upwards of 90% of infections. MTCT can occur during pregnancy, birth, or through breastfeeding. Without any interventions during these stages, MTCT rates range between 15% and 45%, increasing with the duration of breastfeeding.<sup>3</sup> However, the risk of MTCT can be reduced to less than 2% with a package of evidence-based interventions which constitute prevention of mother-to-child transmission (PMTCT) strategies.<sup>3</sup> PMTCT services are offered to women of childbearing age living with or at risk of HIV to maintain their health and prevent their infants from acquiring HIV. These services include preventing unwanted pregnancies among women living with HIV; safe childbirth practices; life-long antiretroviral (ARV) drug therapy to mothers once their status is ascertained, irrespective of CD4 cell counts; ARV prophylaxis to infants from birth; infant feeding counseling and appropriate choices; early infant virologic diagnosis of HIV post-partum and during the breastfeeding period.<sup>3</sup>

Since PMTCT commenced in 2001 in Nigeria, the National PMTCT guidelines, in collaboration with the World Health Organization, have undergone frequent evidence-based modifications. Maternal ARV therapy moved from 'when pregnant only' for those not immunosuppressed to 'lifelong irrespective of CD4 counts' and 'treat all.' Infant feeding moved from mandatory 'no breastfeeding' to 'exclusive

breastfeeding in the first 6 months of life, then appropriate complementary foods plus continued breastfeeding until 12 months, in a bid to enhance child survival.<sup>4-6</sup> Nigeria has a prevalence of 1.4%, and currently takes the fourth position among countries battling with HIV.<sup>7,8</sup> However, prevalence varies in the constituent states (highest in Akwa Ibom 5.5%, Benue 5.3%, Rivers 3.8%, Taraba 2.9%, Anambra 2.4%, lowest in Katsina and Jigawa 0.3% each, among others).<sup>7,8</sup> Anambra is one of the states with a high prevalence of HIV, and the Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi is the largest center offering HIV care in the state. NAUTH was one of the first PMTCT centers in Nigeria and has continued to expand its service delivery to a vast clientele covering Anambra and neighboring states, such as Imo, Benue, Enugu, and Delta. An initial review of the Early Infant Diagnosis services in the center,<sup>9</sup> yielded an MTCT rate of 3.6% in spite of PMTCT. Since then, breastfeeding has been encouraged, more so with prolonged duration up to age 12 months, and most mothers are accessing ARVs.

### **1.2. Objectives of the Study**

The objective of this study was to audit the PMTCT infant follow-up services offered by the Pediatric Infectious Diseases Unit of NAUTH over a 14-year period (January 2007 – December 2020).

### **1.3. Specific Aims and Hypothesis**

Specifically, the study: a) determined the MTCT rate in the milieu of maternal and infant ARV drugs; b) assessed the impact of infant feeding on the rate of MTCT; c) assessed if sociodemographic factors such as the timing of infant ARV, initial PCR test and gender affected PMTCT outcomes. It was hypothesized that maternal and infant ARV administration, infant feeding options, and timing of initial PCR tests would affect PMTCT outcomes.

## **2. Methods**

### **2.1. Study Location**

Nnamdi Azikiwe University Teaching Hospital (NAUTH) is located in Nnewi, the industrial hub of the southeast of Nigeria. It is a tertiary health facility that provides services for Anambra and surrounding

communities in Imo, Delta, and Enugu States. NAUTH is one of the largest centers for HIV Care in Nigeria. Organized HIV Care Services commenced in this center by 2001. Moreover, the program received support from the President's Emergency Plan for AIDS Relief (PEPFAR) under the auspices of the Institute of Human Virology (IHVN) domiciled in Nigeria from 2005. However, in 2013 IHVN was replaced by Family Health International (FHI), which has continued to support the activities. The PCR Laboratory has been analyzing dried blood spot samples for Early Infant Diagnosis (EID) of HIV and Viral load assays since 2007. The infant follow-up clinic is manned by pediatricians, pediatric resident doctors, medical officers, well-trained nurses, and counselors.

## 2.2. Subjects, Interventions, and Data collection

The study population consisted of mother-infant pairs who were seen at the infant follow-up arm of the NAUTH Nnewi PMTCT program. The majority of the mothers were enrolled during pregnancy and benefited from antenatal PMTCT interventions as well as follow-up for their infants. However, some infants who were enrolled in the infant follow-up program at different ages after delivery had not benefited from PMTCT intervention *in utero* and sometimes neither the infant post-exposure prophylaxis.

HIV-positive women were enrolled in the PMTCT program at different stages of pregnancy depending on the gestational age at initial presentation. The mothers were offered ART interventions for PMTCT, infant feeding counseling, support, and modified obstetric care. The infants were commenced on post-exposure prophylaxis as soon as possible (within 72 hours of life). Maternal and Infant ARV prophylaxis was based on Nigeria's National Guidelines for HIV prevention and treatment. Over the years, the guidelines were reviewed in line with prevailing evidence and WHO recommendations. This resulted in variations in maternal/infant ARV prophylaxis received. Generally, the infants received syrup nevirapine and or zidovudine, the duration of which depended on the risk of MTCT.

Over the years, infant feeding practices varied according to the National Guidelines. During the

“pre-rapid advice” era (prior to the implementation of the 2009 WHO guideline), HIV-infected mothers were required to practice either EBF or replacement feeding during the first six months of their infant's life depending on their ability to meet the AFASS criteria. (Breastmilk substitute must be Acceptable, Feasible, Affordable, Sustainable, and Safe). Subsequently, breastfeeding was promoted as the preferred infant feeding option for HIV-positive mothers in Nigeria. All breastfeeding mothers were on ARVs during the period of breastfeeding. Avoidance of mixed-feeding was emphasized at each follow-up visit. Free infant formula was not provided for mothers who chose to formula-feed. The infants also received co-trimoxazole prophylaxis for *Pneumocystis jiroveci* pneumonia, early infant diagnosis (EID) using HIV DNA PCR technique on DBS sample, and monitoring for vaccination, developmental and nutritional status. EID was done at 6 weeks of age and 6 to 8 weeks after all cessation of exposure to breastmilk. Those who tested positive were immediately linked to HIV treatment services. However, if the infants were healthy and had an HIV-negative rapid test at 18 months of age, they were discharged from the unit.

At enrollment, each mother-infant pair had a proforma completed documenting demographic data, birth details, use of ARV prophylaxis in mother and infant, infant feeding practice, etc. Subsequently, the mother-infant pairs were seen on scheduled appointments during which their health, nutritional, vaccination, developmental, and HIV status were assessed and documented both electronically and in physical folders. Tracking was done through phone calls after each missed appointment to ensure continued engagement in care. The list of those who were lost to follow-up was handed over to the Home-Based Care Unit at intervals for continued tracking and home visits where feasible. Data were abstracted from the electronic record of the subjects which was prospectively updated at each clinic visit.

## 2.3. Study Variables

The dependent variable was final HIV status (by DNA PCR [ $<18$  months] and rapid tests [at  $\geq 18$  months]), while the independent variables were maternal or

infant ARV prophylaxis, infant feeding practice, the timing of DNA PCR test, and gender of the infant.

Mother-infant pairs were recruited at various infant ages into the Infant Follow-Up arm of PMTCT of HIV at the Pediatric HIV Unit of Nnamdi Azikiwe University Teaching Hospital, Nnewi, from January 2007 to December 2020. Mothers-infant pairs may or may not have received all components of the NAUTH PMTCT package depending on the timing of presentation.

#### 2.4. Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 21 (IBM Corp., Armonk, NY). The characteristics of the infants were presented as categorical variables in frequency tables. The primary outcome was the HIV status of the infants that were discharged from the HIV-exposed infant follow-up program. The association between the primary outcomes (HIV positive, HIV negative, or inconclusive HIV status) and infants' characteristics were examined using the Chi-square test. Factors significantly associated with the final outcome in bivariate analysis were further analyzed using multinomial logistic regression analysis. A P-value less than 0.05 was considered statistically significant. Ethics approval was obtained from the Research and Ethics Committee of NAUTH, Nnewi, Anambra state. All data obtained during the study was kept confidential.

### 3. Results

#### 3.1. Sociodemographic Characteristics

A total of 3,784 mother-infant pairs were enrolled. The infants had a male to female ratio of 1.04:1. Nearly two-thirds (62.5%) of infants were never breastfed. Among the 1,419 infants who were breastfed, 1,053 (74.2%) received breastmilk for 6 months or less. The majority (3,145 [83.1%]) of mothers and infants (3,240 [85.6%]) received some form of ARVs for PMTCT. Both mother and infant in a mother-infant dyad received ARVs in 80.6% of cases. Mothers were mostly on the combination of Nevirapine or Efavirenz/Lamivudine/Zidovudine. The prophylaxis given to the infants is shown in Table 1. The majority of the infants received either single

dose Nevirapine plus 6 weeks of Zidovudine (sdNVP, 6wkZDV) [40.22%] or 6 weeks of Nevirapine (6wkNVP) [43.71%]. There was no gender-based difference in the outcome.

#### 3.2. Maternal and Infant ARV Therapy and MTCT Rate

Infants who did not receive any form of ARVs for post-exposure prophylaxis (PEP) were significantly more likely to have MTCT of HIV. This was higher where mothers received no ARVs compared to infants of mothers who received any form of ARVs (52.1% vs. 9.3%) (see Table 2). Table 3 shows that 3,337 mother-baby pairs received some form of ARV Prophylaxis, out of which 74 (2.2%) babies turned out HIV positive. This was further reduced to 1.4% (44/3,048) where both mother and infant pairs benefited from PMTCT interventions according to the National Guidelines. In other words, the true PMTCT failure rate at the NAUTH center is 1.4%. The MTCT rates were 1.4%, 9.3%, 24.1%, and 52.1% for both mother and infant, mother only, infant only and none received ARV prophylaxis respectively.

#### 3.3. Infant Feeding and MTCT Rate

Breastfed infants who did not benefit from any form of ARV prophylaxis significantly had a higher rate of MTCT compared to their never breastfed counterparts (57.9% vs. 34.8%). However, among infants who received ARV prophylaxis, there was a slight difference in the MTCT rate between the breastfed (2.5%) and never breastfed (2.1%). Infants who were mixed-fed were significantly more likely to become infected via MTCT.

Table 4 shows that among the ARV-naïve mother-infant pairs MF in the first 6 months resulted in 61.7% MTCT as against 35.5% in those not mixed-fed. The MTCT rate was reduced to 28.6% in the mixed-fed and 1.4% in the non-mixed fed where both mothers and infants received ARVs.

After multinomial logistic regression analysis factors that remained significantly associated with being HIV-negative were maternal ARV prophylaxis for PMTCT ( $p < 0.001$ , OR 7); ARV prophylaxis for infants ( $p < 0.001$ , OR 4).

**Table 1: Characteristics of mother-infant pairs**

Characteristic	Number (N=3,784)	Percentage
<b>Gender</b>		
Females	1,856	49
Males	1,928	51
<b>Breastfeeding status</b>		
Never breastfed	2,367	62.50
Breastfed	1,417	37.50
<b>Duration of breastfeeding</b>		
Never breastfed	2,367	62.50
<3 months	403	10.70
3 – 6 months	650	17.20
>6 – 12 months	332	8.80
>12 months	32	0.80
<b>Infant feeding pattern</b>		
Never mixed fed	3,360	88.80
Mixed fed in the first 6mo only	137	3.60
EBF first 6mo, then Continued Breastfeeding beyond age 6mo	137	3.60
Mixed fed in first 6 months, then Continued Breastfeeding after 6mo	150	4
<b>Maternal ARV Status</b>		
No ARV	639	16.90
ARV in labor only	9	0.20
ARV during index pregnancy only	1,140	30.10
ARV prior to and during index pregnancy	1,996	52.80
<b>ARV Prophylaxis for Mother &amp; Infant</b>		
Neither mother nor infant	447	11.80
Mother only	97	2.60
Infant only	191	5
Both mother and infant	3,049	80.60
<b>Details of Infant Prophylaxis</b>		
None	544	14.38
SdNVP	3	0.08
SdNVP, 6wkZDV	1,522	40.22
6wkZDV	10	0.26
6wkNVP	1,654	43.71
6wkNVP, 6wkZDV	2	0.05
12wkNVP, 12wkZDV	4	0.11
Very late prophylaxis (>72hours)	33	0.87
Any other combination	12	0.32
<b>Age of infant at first DNA PCR test</b>		
≤ 2months	2,428	64.2
>2 months	1,356	35.8

(Contd...)

Table 1: (Continued)

Characteristic	Number (N=3,784)	Percentage
<b>Final outcome of HEI</b>		
Negative (HIV-free)	3,074	81.2
Positive (HIV-infected)	307	8.1
Lost to follow-up (Inconclusive)	403	10.7

EBF = Exclusive breastfeeding; sdNVP = Single dose Nevirapine; ZDV=Zidovudine

Table 2: Type of PEP given to the baby in the milieu of maternal ARV and final outcome in babies

Mother's ARV Status	PEP given to Infant	Final Outcome				P-Value (X <sup>2</sup> test)
		Negative	Positive	Inconclusive (LTFU)	Total	
<b>No ARV</b>	None	178 (39.8)	233 (52.1)	36 (8.1)	447 (100)	0.000
	SdNVP, 6wkZDV	85 (84.1)	12 (11.9)	4 (4.0)	101 (100)	
	6 wkZDV	2 (100)	0 (0.0)	0 (0.0)	2 (100)	
	6 wkNVP	58 (78.4)	9 (12.2)	7 (9.4)	74 (100)	
	6 wkNVP, 6 wkZDV	0 (0.0)	0 (0.0)	1 (100)	1 (100)	
	Very late PEP (>72 hours)	11 (91.7)	0 (0.0)	1 (8.3)	12 (100)	
	Any other combination	2 (100)	0 (0.0)	0 (0.0)	2 (100)	
	Total	336 (52.6)	254 (39.7)	49 (7.7)	639 (100)	
<b>Some form of ARV</b>	None	79 (81.4)	9 (9.3)	9 (9.3)	97 (100)	0.000
	SdNVP	3 (100)	0 (0.0)	0 (0.0)	3 (100)	
	SdNVP, 6 wkZDV	1,353 (95.2)	28 (2)	40 (2.8)	1,421 (100)	
	6 wkZDV	8 (100)	0 (0.0)	0 (0.0)	8 (100)	
	6 wkNVP	1,269 (80.3)	14 (0.9)	297 (18.8)	1,580 (100)	
	6 wkNVP, 6 wkZDV	1 (100)	0 (0.0)	0 (0.0)	1 (100)	
	12 wkNVP, 12 wkZDV	3 (75)	0 (0.0)	1 (25)	4 (100)	
	Very late PEP (>72 hours)	14 (66.7)	2 (9.5)	5 (23.8)	21 (100)	
	Any other combination	8 (80)	0 (0.0)	2 (20)	10 (100)	
	Total	2,738 (87.1)	53 (1.7)	354 (11.2)	3,145 (100)	

Percentages in parentheses; LTFU=lost to follow-up

Table 3: Breastfeeding status in the milieu of ARV Prophylaxis and final outcome in the infants

ARV Prophylaxis Status of Mother-Infant Dyad	Breastfeeding Status of Infant	Final Outcome				P-Value (X <sup>2</sup> test)
		Negative	Positive	Inconclusive	Total	
• No ARV Prophylaxis	Breastfed	105 (31.3)	194 (57.9)	36 (10.8)	335 (100)	0.000
	Never breastfed	73 (65.2)	39 (34.8)	0 (0.0)	112 (100)	
	Total	178 (39.8)	233 (52.1)	36 (8.1)	447 (100)	
• Some form of ARV Prophylaxis	Breastfed	690 (63.7)	27 (2.5)	367 (33.8)	1,084 (100)	0.000
	Never breastfed	2,206 (97.9)	47 (2.1)	0 (0.0)	2,253 (100)	
	Total	2,896 (86.8)	74 (2.2)	367 (11)	3,337 (100)	
• Total	Breastfed	795 (56)	221 (15.6)	403 (28.4)	1,419 (100)	0.000
	Never breastfed	2,279 (96.4)	86 (3.6)	0 (0.0)	2,365 (100)	
	Total	3,074 (81.2)	307 (8.1)	403 (10.7)	3,784 (100)	

Percentages in parentheses

**Table 4: Infant feeding and outcome amidst ARV Prophylaxis for mother and baby**

ARV for mother and infant	Infant Feeding Category	Final Outcome				P-Value (X <sup>2</sup> test)
		Negative	Positive	Inconclusive	Total	
<b>Neither mother nor infant</b>	No MF	126 (58.9)	76 (35.5)	12 (5.6)	214 (100)	0.000
	MF in 1 <sup>st</sup> 6 mo then SBF	27 (25.2)	66 (61.7)	14 (13.1)	107 (100)	
	MF from 1 <sup>st</sup> 6 mo then CBF	25 (19.8)	91 (72.2)	10 (7.9)	126 (100)	
	Total	178 (39.8)	233 (52.1)	36 (8.1)	447 (100)	
<b>Mother only</b>	No MF	73 (83)	7 (8)	8 (9.1)	88 (100)	0.385
	MF in 1 <sup>st</sup> 6 mo then SBF	4 (57.1)	2 (28.6)	1 (14.3)	7 (100)	
	EBF 1 <sup>st</sup> 6 mo & CBF>6 mo	2 (100)	0 (0.0)	0 (0.0)	2 (100)	
	Total	79 (81.4)	9 (9.3)	9 (9.3)	97 (100)	
<b>Infant only</b>	No MF	156 (84.3)	18 (9.7)	11 (5.9)	185 (100)	0.003
	MF in 1 <sup>st</sup> 6 mo then SBF	1 (50)	1 (50)	0 (0.0)	2 (100)	
	EBF 1 <sup>st</sup> 6 mo & CBF>6 mo	1 (50)	0 (0.0)	1 (50)	2 (100)	
	MF from 1 <sup>st</sup> 6 mo then CBF	0 (0.0)	1 (50)	1 (50)	2 (100)	
	Total	158 (82.7)	20 (10.5)	13 (6.8)	191 (100)	
<b>Both Mother and Infant</b>	No MF	2,520 (87.7)	39 (1.4)	314 (10.9)	2,873 (100)	0.000
	MF in 1 <sup>st</sup> 6 mo then SBF	12 (57.1)	6 (28.6)	3 (14.3)	21 (100)	
	EBF 1 <sup>st</sup> 6 mo & CBF>6 mo	116 (87.2)	0 (0.0)	17 (12.8)	133 (100)	
	MF from 1 <sup>st</sup> 6 mo then CBF	11 (50)	0 (0.0)	11 (50)	22 (100)	
	Total	2,659 (87.2)	45 (1.5)	345 (11.3)	3,049 (100)	
<b>Total</b>	No MF	2,875 (85.6)	140 (4.2)	345 (10.3)	3,360 (100)	0.000
	MF in 1 <sup>st</sup> 6 mo then SBF	44 (32.1)	75 (54.7)	18 (13.1)	137 (100)	
	EBF 1 <sup>st</sup> 6 mo & CBF>6 mo	119 (86.9)	0 (0.0)	18 (13.1)	137 (100)	
	MF from 1 <sup>st</sup> 6 mo then CBF	36 (24)	92 (61.3)	22 (14.7)	150 (100)	
	Total	3,074 (81.2)	307 (8.1)	403 (10.7)	3,784 (100)	

MF=Mixed feeding; EBF=Exclusive breastfeeding; SBF=Stopped breastfeeding; CBF=Continued breastfeeding; Percentages in parentheses

**Table 5: Age at first test and final outcome in the background of PMTCT interventions**

PMTCT Status of Mother-Infant Dyad	Age at first DNA PCR test	Final Outcome				P-Value (X <sup>2</sup> test)
		Negative	Positive	Inconclusive	Total	
<b>No PMTCT</b>	≤8 weeks	41 (54.7)	28 (37.3)	6 (8)	75 (100)	0.012
	>8 weeks	137 (36.8)	205 (55.1)	30 (8.1)	372 (100)	
	Total	178 (39.8)	233 (52.1)	36 (8.1)	447 (100)	
<b>Some form of PMTCT</b>	≤8 weeks	2,039 (86.7)	28 (1.2)	286 (12.2)	2,353 (100)	0.000
	>8 weeks	857 (87.1)	46 (4.7)	81 (8.2)	984 (100)	
	Total	2,896 (86.8)	74 (2.2)	367 (11)	3,337 (100)	
<b>Total</b>	≤8 weeks	2,080 (85.7)	56 (2.3)	292 (12)	2,428 (100)	0.000
	>8 weeks	994 (73.3)	251 (18.5)	111 (8.2)	1,356 (100)	
	Total	3,074 (81.2)	307 (8.1)	403 (10.7)	3,784 (100)	

Percentages in parentheses

**Table 6: Characteristics of HIV-Exposed Infants who failed PMTCT interventions**

Characteristics	Frequency (n=74)	Percent
<b>Age at first test</b>		
≤2 months	28	37.8
>2 months	46	62.2
<b>Result of initial DNA PCR</b>		
Negative	2	2.7
Positive	72	97.3
<b>Breastfeeding status</b>		
Never breastfed	47	63.5
Breastfed for <3 months	11	14.9
Breastfed for 3-6 months	15	20.3
Breastfed beyond 6 months	1	1.4
<b>Mixed feeding status during first 6 months of life</b>		
Never mix-fed	65	87.8
Mix-fed	9	12.2
<b>ARV prophylaxis for PMTCT</b>		
Mother only	9	12.2
Infant only	20	27
Both mother and infant	45	60.8
<b>Maternal ARV for PMTCT</b>		
None	21	28.4
Only during index pregnancy	33	44.6
Before and during index pregnancy	20	27
<b>Infant ARV prophylaxis</b>		
None	9	12.2
Sd NVP+6wk ZVD	40	54.1
6wk NVP	23	31.1
Late PEP initiation (>72 hours of birth)	2	2.7

### 3.4. Age of Infant at Initial DNA PCR Test and PMTCT Outcomes

The younger the age at the first PCR test, the more likely it is that PMTCT interventions were accessed and also final outcome being HIV negative. However, this also meant a higher tendency for loss to follow up, especially among the breastfed infants (Table 5).

### 3.5. Failed PMTCT Cases

Two infants turned out to be HIV positive after an initial negative test, following cessation of breastfeeding. One of the infants had the initial negative test at 8 weeks and after EBF for 3 months retested positive. The mother had received ARVs for

3 years before conception and all through pregnancy, however, her adherence to the program was poor. The second infant had the initial negative test at 3 months (after having been mix-fed (MF) from birth) but when retested at 8 months, after a total of 6 months of breastfeeding the result was positive. The mother had received ARVs in the index pregnancy only. Both infants had ARV prophylaxis. Table 6 gives the characteristics of the infants with PMTCT failure.

Among the infants who became HIV positive despite any form of PMTCT intervention for mother-baby pair, 97.3% had a positive initial DNA PCR. Approximately two-thirds had the initial PCR test after the recommended 6-8 weeks (62.2%). The majority were never mix-fed (87.8%) and approximately two-thirds were never breastfed (63.5%). Both mothers and infants in each pair received ARV prophylaxis for PMTCT in 60.8% of cases. Only 27% of their mothers were on ARVs before index pregnancy, and more than half (54.1%) of the MTCT occurred during the era of sdNVP + 6wkZDV use for infant PEP.

## 4. Discussion

The risk of MTCT of HIV if the mother has no ARVs, ranges from 30%-45% depending on breastfeeding duration. One of the important goals of the Global Plan is to reduce the risk to less than 5% among breastfeeding populations, and less than 2% among non-breastfeeding populations.<sup>10</sup> In this study, this target was met with the MTCT rate after PMTCT interventions being 1.4%. Other large cohorts have also reported successful PMTCT implementation with rates of below 1% in Johannesburg, South Africa,<sup>11</sup> 2.0% in Zambia,<sup>12</sup> 2.8% in the AIDS Prevention Initiative Nigeria (APIN)-supported sites in Nigeria,<sup>13</sup> 3.5% in eight centers in North Central Nigeria,<sup>14</sup> and 4.1% in Senegal.<sup>15</sup> However, reports from Kenya (6.9%)<sup>16</sup> and Southwest Nigeria (6.3%<sup>17</sup> and 8.2%<sup>18</sup>) document reduced rates yet to achieve the optimum.

Where no ARVs were used for both mother and infant, a large proportion (52.1%) of the infants had an HIV-positive outcome. This has been reported by Saounde et al.<sup>19</sup> in Cameroon (31.3%), and Anoje et al.<sup>20</sup> in south-south Nigeria (19.5%). This study's

MTCT rate was 24.1% where no maternal ARVs were received and 9.3% when the infants only did not avail of ARVs. Infants whose mothers had no ARVs were seven times more likely to get infected. This was nine times more in a Zambian study,<sup>12</sup> and eight times as reported by Anoje et al.<sup>20</sup> In this study, maternal ARVs remained essentially the same, while the infant's prophylactic ARVs varied in kind and timing of administration. It was noted that the MTCT rate while using nevirapine seemed to be superior to the sdNVP and 6-week ZDV regimen. However, the timing of initiation of ARVs in the infants seemed to have no effect on the outcome. Infants who did not receive ARVs were four times more likely to be infected than those who availed.

Breastfed infants with no ARV prophylaxis had a higher MTCT rate compared to the never-breastfed (57.9% vs. 34.8%). When the effect of breastfeeding was evaluated in the milieu of ARV prophylaxis, there was just a slight difference between the rates in breastfed (2.5%) compared to never-breastfed (2.1%). This buttresses the fact that ARVs are paramount to achieving a low MTCT rate, irrespective of breastfeeding status. This was also observed in other studies.<sup>21-24</sup>

Among the ARV naïve mother-infant pairs mixed-feeding (MF) in the first 6 months resulted in 61.7% MTCT, as against 35.5% with no MF. However, with both mothers and infants getting ARVs MTCT reduced to 28.6% in the MF and 1.4% in those, not MF. MF was still a significant factor in MTCT despite the administration of ARVs. This was attested to by other studies showing MTCT rates in excess of 20% with MF,<sup>20, 25</sup> and even up to 60%.<sup>26</sup> Afolabi et al.<sup>27</sup> noted MF as an important predictor in which the risk of MTCT was about two times higher compared to EBF. When infants were EBF in the first 6 months and breastfeeding continued thereafter, there was no risk of MTCT in the mother-infant pairs who received ARVs. This is a very cheering observation, more so in the developing world where breastmilk is the bedrock of infant nutrition as many mothers cannot afford infant formula. It behooves the healthcare workers to assist mothers to achieve viral suppression and encourage continued breastfeeding for infant survival and nourishment.

Early Infant Diagnosis (EID) deals with qualitative detection of viral DNA in dried blood spot samples taken within 6 weeks of birth.<sup>28</sup> This becomes the basis for enrollment of the infants into a lifelong ARV therapy. About two-thirds of the infants had their first DNA PCR test done at age 8 weeks and below. Among those who had no PMTCT interventions and those that had, the younger the age at first test is the lesser the rate of MTCT (37.3% vs. 55.1%, and 1.2% vs. 4.7%, respectively). When taken together (whether received interventions or not), infants aged 8 weeks and below had an MTCT rate of 2.3% against those older than 8 weeks with 18.5%. The younger the age at first PCR test the more likely PMTCT services were accessed hence greatly reducing the chances of the infant's outcome being HIV-Positive. Dakum et al.<sup>29</sup> evaluating a large sample of HIV-exposed infants (HEI) in North-central Nigeria also believed that HEI tested earlier than 20 weeks of age had significantly greater odds of a negative HIV result. The blight on early recruitment and EID was the loss to follow up and burgeoned inconclusive outcomes.

Our findings highlight the need to intensify efforts at ensuring that all infants of HIV-infected mothers benefit from PMTCT interventions and are engaged in care until the recommended time of exit from the PMTCT program. This is crucial in heavy burden countries like Nigeria where treatment programs record high attrition rates and poor outcomes.<sup>30</sup>

#### 4.1 Limitations of the Study

The inability to incorporate maternal viral load results due to logistic difficulties is a limitation. There was an appreciable number of inconclusive outcomes, especially among the infants that were breastfed beyond six months due to a high rate of loss to follow-up. Tracking the lost mother-infant dyads proved an insurmountable task with limited communication support and a lack of home visits.

### 5. Conclusion and Global Health Implications

The determining factor for being HIV-negative hinged on mother-infant pairs receiving ARVs (especially maternal ARVs) and not necessarily the breastfeeding status. However mixed feeding

remained an important factor in MTCT of HIV. This study portrayed an inalienable need for intensification of efforts on the prompt diagnosis of HIV and enrollment into care for women of childbearing age before conception, as well as effective tracking to forestall disengagement from the PMTCT continuum of care.

### Compliance with Ethical Standards

**Conflicts of Interest:** All authors declare no conflicts of interest. **Financial Disclosure:** All authors have no financial disclosures to declare. **Funding/Support:** This study received no funding support. **Ethics Approval:** The Nnamdi Azikiwe University Teaching Hospital New Research and Ethics Committee approval for the study was obtained. **Acknowledgments:** None. **Disclaimer:** None.

### Key Messages

- ▶ All women of childbearing age need to know their HIV status and be on ARV drugs, if required, well before conception.
- ▶ Exclusive breastfeeding and avoidance of mixed feeding should be the norm in the first 6 months in HIV-exposed infants in developing countries.
- ▶ Breastfeeding is relatively safe for HIV-exposed infants in developing countries, where recommendations for ARV prophylaxis are adhered to.

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