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Pregnancy Outcome of ART-experienced and ART-naïve HIV-infected Mothers at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Authors ROU and AUE designed the study protocol and collected the data, Authors ROU and NIP managed the literature searches, performed the statistical analysis of the data and wrote the first draft. All authors read and approved the final manuscript.

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ABSTRACT

Background: Untreated maternal Human Immunodeficiency Virus (HIV) infection is associated with adverse pregnancy outcome including preterm birth, low birth weight, and mother-to-child transmission of the virus. This study aimed to compare the pregnancy outcome between HIV infected mothers who received ART in pregnancy and those who were ART-naïve.
Methods: A cross-sectional study of HIV-infected mothers who brought their infants for follow up between November 2007 and May 2017 at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria. Relevant information obtained include: time of diagnosis, antiretroviral therapy (ART) regimen and when it was commenced, gestational age at delivery and birthweight of child, mode of delivery, infant feeding option and ARV prophylaxis. Infection status of the infant was determined by DNA PCR at 6weeks of age. Based on when ART was commenced, mothers were grouped into three [(HAART experienced (HE) if ART was started before pregnancy, HAART in pregnancy (HIP) and HAART naive (NH) if no HAART was taken in pregnancy]. Main outcome measures were rates of prematurity, low birth weight, mean birth weight, birth defects and mother-to-child transmission.

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Result: A total of 1,640 HIV-exposed infants were seen (716(43.6%) in HE, 360(22.0%) in HIP and 564(34.4%) in NH groups). There were 825(50.3%) males and 815(49.7%) females. Zidovudine/Lamivudine and Nevirapine/Efavirenz was the most frequently used combined ART in 724 (67.3%) mothers. The mean birthweight was 3.12±0.38Kg; range 1.2 – 5.7Kg (3.11±0.58Kg in HE; 3.13±0.53Kg in HIP; 3.18±0.74Kg in NH) Table 3. A hundred and eighty (11.0%) babies were preterm [76(42.2%) in HE; 26(14.4%) in HIP; 78(43.3%) in NH](p=0.007), while 159(9.7%) were LBW [74(46.5%) in HE; 22(13.8%) in HIP; 63(39.6%) in NH](p=0.03). Fourteen (0.9%) babies had birth defects [5(35.7%) in HE; 9(64.3%) in HIP] (p=0.01). The commonest birth defects were neural tube defect 7(50%) and congenital heart defect 4(28.8%). Overall transmission rate was 21.4% [8% in the HE, 4.5% in HIP and 87.5% in NH groups] (p=0.001). The mean birth weights of uninfected babies were higher than their infected counterparts but was not significant (p>0.05).
Conclusion: The benefits of early HAART in reducing mother-to-child transmission must be weighed against the risks of lower birthweight and potential teratogenic effects of drug exposure on the foetus.

Keywords: Pregnancy outcome; ART naïve; ART experienced; preterm delivery; low birth weight; birth defects; MTCT.

1. INTRODUCTION

The Human Immunodeficiency Virus is a known contributor to poor maternal and fetal outcome. Untreated maternal HIV infection is associated with adverse pregnancy outcome including preterm birth, low birth weight, intrauterine growth restriction, stillbirth and mother-to-child transmission as well as maternal mortality with advanced disease [1]. On the other hand, HIV-Infected pregnant women who have received HAART before or early during pregnancy have experienced some adverse outcomes like birth defects (Efavirenz) [2], preterm births and low birth weight (protease-inhibitor) [3] and maternal anaemia (zidovudine)[4].

In the absence of Antiretroviral therapy (ART), the transmission of the virus from mother to child ranges from 25-48%.[5] Despite the benefits of ART, some HIV-Infected pregnant women have never received antiretroviral drugs (antiretroviral naive) thus posing adverse pregnancy outcome in the presence of persistent maternal HIV infection. On the other hand, HIV-infected pregnant women who have received one or more forms of antiretroviral drugs (antiretroviral experienced) usually experience earlier viral suppression which is associated with better pregnancy outcome and lower risk of mother-to-child transmission of HIV. The study sets out to compare the pregnancy outcome (preterm birth, low birth weight, birth defects and mother-to-child transmission) between HIV-infected mothers who are treatment experienced and those who were treatment naïve at the beginning of pregnancy.

2. METHODS

This was a cross-sectional study of HIV-infected mothers who brought their infants for follow up in the Consultant Paediatric HIV specialist Clinic of the University of Port Harcourt Teaching Hospital, Port Harcourt between November 2007 and May 2017. Ethical approval for the study was obtained from the Research and Ethics committee of the University of Port Harcourt Teaching Hospital. All mothers who brought their children within this study period who gave consent for the study were selected for the study. Still births, miscarriages and neonatal deaths were excluded. Relevant information obtained from the mothers include time of HIV diagnosis, antiretroviral therapy (ART) regimen and when it was commenced, mode of delivery, gestational age at delivery, birth weight of infant, infant ARV prophylaxis and mode of infant nutrition. Gestational age was estimated by date of last menstrual period and preterm delivery was defined as delivery before 37 completed weeks of gestation. Low birth weight was defined as weight at birth less than 2.5 kg.

Infection status of the infant was determined by DNA PCR at 6weeks of age. Infants were considered HIV infected if the HIV DNA PCR test was positive and were considered non–HIV-infected if HIV DNA PCR was negative in the absence of any exposure to breast milk. Infants with a negative DNA PCR result but were still being breastfed had a repeat DNA PCR test done 6 weeks after complete cessation of breast feeding and the final result was used to determine the status of the child. A general and systemic physical examination was carried out by

the researchers on all the children and those with birth defects were noted. Those with cardiac murmurs suggestive of congenital heart disease had an echocardiography done to confirm the diagnosis. All patients with identified congenital abnormalities were comanaged and followed up with the various specialists.

Between 2007 and 2010, the national guideline for pregnant women was HAART (triple regimen) only to prevent MTCT. This was changed into Option B+ where the recommendation was that regardless of CD4 count, triple ARVs should be started as soon as diagnosed and continued for life in an effort to provide treatment to control HIV progression in women even after delivery [6]. Based on when ART was commenced, mothers were grouped into three [(HAART experienced (HE) if ART was started before pregnancy, HAART in pregnancy (HIP) if ART was commenced in pregnancy and HAART naive (NH) if she did not receive ART throughout pregnancy]. Depending on the national guidelines at the time, infants received either single dose nevirapine and 6 weeks of zidovudine (2007-2010) or daily nevirapine for 6 weeks (2010-2017) as infant ARV prophylaxis. Main outcome measures were rates of prematurity, low birth weight, mean birth weight, birth defects and mother-to-child transmission.

Statistical Analysis of data was done using SPSS version 20. Ninety-five percent confidence intervals (CIs) for incidence of adverse pregnancy events were calculated and Pearson χ^2-test (Fisher's exact test where applicable) and Analysis of Variance (ANOVA) was used for assessment of potential differences in pregnancy outcomes between ART experienced and ART naïve mothers.

3. RESULTS

Result: A total of 1640 HIV-exposed infants were seen [716 (43.6%) in HE group, 360 (22.0%) in HIP group and 564 (34.4%) in NH group]. There were 825 (50.3%) males and 815 (49.7%) females. The commonest mode of delivery was by spontaneous vaginal delivery (SVD) in 1113(67.9%). More of the infants 736(44.9% were fed with breastmilk substitute only and majority 1098(67%) received infant prophylaxis (Table 1). Zidovudine, Lamivudine and Nevirapine/Efavirenz (the standard of care in Nigeria for much of the study period) were the most frequently used antiretroviral drug combinations in 724(67.3%) mothers (Table 2).

Fig. 1 shows the maternal HAART regimen among mothers who took ARVs. A total of 1076 mothers received ARVs, out of this, 724 (67.3%) received Zidovudine/lamivudine/nevirapine (NVP) or efavirenz (EFV) while 148 (13.7%) received Tenofovir/Lamivudine/ efavirenz (EFV)

There were 20 sets of twins (2 sets of twins in HE group; 14 sets of twins in the HIP group; 4 sets of twins NH group). The mean birth weight of the babies was 3.12±0.38Kg range 1.2 – 5.7Kg (3.11 ± 0.58Kg in HE; 3.13 ± 0.53 Kg in HIP; 3.18 ± 0.74Kg in NH) Table 2. A hundred and eighty (11.0%) of the babies were preterm [76(42.2%) in HE group and 78(43.3%) in NH group](p=0.007) One hundred and fifty-nine (9.7%) were LBW and 74(46.5%) were in HE group (p=0.03). Fourteen (0.9%) babies had birth defects [5 (35.7%) in HE group; 9 (64.3%) in HIP group] (p=0.01). The commonest birth defect was neural tube defect in 7 (50%) and congenital heart defects in 4 (28.8%). Overall transmission rate was 21.4% (351/1640) with 87.5% (307/351) occurring in NH groups, 8% in the HE and 4.5% in HIP (p=0.001). The mean birth weights of uninfected babies were higher than their infected counterparts but it was not statistically significant (p>0.05). Table 2

Table 3 shows the spectrum of the birth defects and the maternal ARV combinations. There was no difference in the risk of birth defects in women on Efavirenz-containing combinations (Fisher's exact test = 0.9; p=0.34)

Preterm birth and LBW rate were not statistically different between women treated with a PI-including regimen and those treated with other regimens (Fisher's exact test = 0.32; p=1.0 and Fisher's exact test = 0.08; p = 0.78 respectively) Table 4.

Comparison of mother-to-child transmission (MTCT) and gender, mode of delivery, infant feeding, and infant ARV prophylaxis showed that MTCT was significantly higher among mothers who received no HAART in pregnancy and delivered vaginally (p=0.001), mixed-fed their infants (p=0.001) and their infants had no antiretroviral prophylaxis (p=0.001). Although more females were infected, the difference was not significant (p=0.30) (Table 5).

Table 1. Distribution of general characteristics of Pregnancy outcome of ART-experienced and ART-naïve HIV-infected mothers

Characteristics	HAART Before pregnancy No (%)	HAART In pregnancy No (%)	No HAART (No (%)	Total No (%)
No	716 (43.6)	360 (22.0)	564 (34.4)	1640 (100.0)
Gender				
Male	359 (21.9)	185 (11.3)	281 (17.1)	825 (50.3)
Female	357 (21.8)	175 (10.7)	283 (17.2)	815 (49.7)
Mode of delivery				
ELCS	198(12.1)	130(7.9)	44(2.7)	372(22.7)
EMCS	81(4.9)	35(2.1)	39(2.4)	155(9.4)
SVD	437(26.7)	195(11.9)	481(29.3)	1113(67.9)
Infant feeding				
Mixed	85(5.2)	44(2.7)	312(19.0)	441(26.9)
EBF	247(15.1)	105(6.4)	111(6.8)	463(28.2)
BMS	384(23.4)	211(12.9)	141.(8.6)	736(44.9)
Infant Prophylaxis				
Yes	644(39.3)	333(20.3)	121(7.4)	1098(67.0)
No	72(4.4)	27(1.6)	443(27.0)	542(33.0)

(ELCS = elective caesarean section; EMCS = emergency caesarean section; SVD = spontaneous vaginal delivery; EBF = exclusive breastfeeding; BMS = breast milk substitute)

Table 2. Pregnancy outcome in relation to mean birth weight, prematurity, LBW, birth defects, mother-to-child transmission

Outcome	HAART (Before Pregnancy)	HAART (in Pregnancy)	NO HAART	ANOVA
Mean birth weight (kg)	3.11±0.58	3.13±0.53	3.18±0.74	0.7942**
Preterm No. (%)	76(42.2)	26(14.4)	78(43.3)	
LBW No. (%)	74(46.5)	22(13.8)	63(39.6)	
Birth defects No. (%)	5(35.7)	9(64.3)	0(0.0)	
Infected No. (%)	28(8)	16(4.5)	307(87.5)	
Mean BWT of infected	2.88±0.84	2.94±0.57	3.15±0.73	0.0812**
Mean BWT of uninfected	3.1±0.57	3.13±0.53	3.21±0.74	0.5266**

***Analysis of variance shows no significant difference between the groups (p>0.05)*
ANOVA: Analysis of Variance (LBW = low birth weight; BWT = birth weight)

Table 3. Spectrum of birth defects and type of ARVs taken by mothers

Birth defects/Type of ARVs	HAART Before pregnancy No (%)	HAART in Pregnancy No (%)	Total N0 (%)
NTD	2 (14.3)	5 (35.7)	7 (50.0)
CHD	2 (14.3)	2 (14.3)	4 (28.6)
Imperforate anus	1 (7.1)	1 (7.1)	2 (14.3)
Cleft lip/palate	0 (0.0)	1 (7.1)	1 (7.1)
Total	5 (35.7)	9 (64.3)	14 (100.0)
ZDV/3TC/NVP	3 (21.4)	6 (42.9)	9 (64.3)
ZDV/3TC/EFV	1 (7.1)	0 (0.0)	1 (7.1)
TDF/FTC/EFV	1 (7.1)	2 (14.3)	3 (21.4)
ZDV/3TC/LPV/r	0 (0.0)	1 (7.1)	1 (7.1)
Total	5 (35.7)	9 (64.3)	14 (100.0)

(Fisher's exact test = 0.9; p=0.34); (NTD = neural tube defect; CHD = congenital heart disease; ZDV = zidovudine; 3TC = lamivudine; NVP = nevirapine; EFV = efavirenz; TDF = tenofovir; FTC = emtricitabine; LPV/r = lopinavir/ ritonavir)

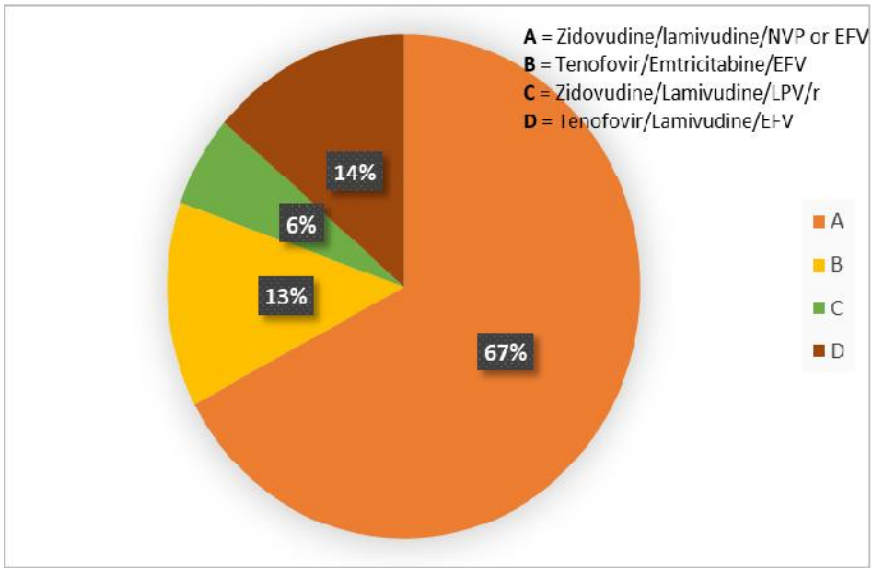

Fig. 1. Maternal HAART regimen among mothers who took ARVs
(NVP = nevirapine; EFV = efavirenz; LPV/r= lopinavir boosted ritonavir)

Table 4. Type of HAART taken by mothers and proportion of preterm/LBW

Characteristics	HAART	HAART		Chi Square/ Fishers Exact	p=value
	Before Pregnancy	In Pregnancy	Total		
ZDV/3TC/NVP or EFV					
Preterm	48 (26.67)	9 (5.00)	57 (31.67)	0.59	0.44
LBW	60(37.73)	16(10.06)	76 (47.79)		
TDF/3TC/EFV					
Preterm	12(6.67)	7 (3.89)	19 (10.56)	0.32	1.00
LBW	1 (0.63)	0 (0.00)	1 (0.63)		
TDF/FTC/EFV					
Preterm	11 (6.11)	10 (5.55)	21 (11.67)	0.08	0.78
LBW	8 (5.03)	6 (3.77)	14 (8.80)		
ZDV/3TC/LPV/r					
Preterm	5 (2.78)	0 (0.00)	5 (2.78)	0.32	1.00
LBW	5 (2.78)	0 (0.00)	5 (2.78)		
No HAART					
Preterm	Not applicable	Not applicable	78 (43.33)		
LBW	Not applicable	Not applicable	63 (39.62)		

(ZDV = zidovudine; 3TC = lamivudine; NVP = nevirapine; EFV = efavirenz; TDF = tenofovir; FTC = emtricitabine; LPV/r = lopinavir/ ritonavir; LBW = low birth weight)

4. DISCUSSION

Pregnant HIV-infected women are potentially at increased risk of adverse pregnancy outcomes, due to a range of factors, including advanced disease and severe immunosuppression from untreated HIV infection on one hand, as well as effects of use of combination antiretroviral therapy (ART) for the treatment of HIV.

Reports on pregnancy outcomes in pregnant women who are on treatment with highly active antiretroviral drugs (HAART) have been conflicting. Whereas some studies have reported that treatment with HAART before pregnancy may be associated with low birth weight or prematurity, [1-3,7] others have not found an association between adverse pregnancy outcomes and treatment with HAART [4]. It is

however a known fact that HIV infection is a relevant risk factor for maternal mortality in the African continent. [5,8] and that antenatal HAART reduces adverse pregnancy outcomes like maternal mortality, fetal demise (abortion/stillbirth) and prematurity in HIV-infected women. [9]. Our study could not assess fetal demise/abortion as a pregnancy outcome as our centre is a tertiary centre and many of the deliveries occurred outside our centre and it was difficult to validate this information based on only verbal information.

The mean birth weight of babies delivered by HAART-experienced and HAART-in pregnancy HIV infected mothers was lower than those delivered by treatment naïve mothers. This was similar to the findings by Joao and colleagues [10] who reported that newborns whose mothers were on ART had slightly lower birth weights than those whose mothers were not on ART. It is possible that these medications have some effects on the weight gain of these fetuses especially in late pregnancy probably by limiting the transport or utilization of macro and micronutrients. This may also be related to the degree of immunosuppression in the mothers but unfortunately viral load estimation was a luxury at our centre as at when this study was carried out.

Namale and colleagues [11] reported on the outcomes of 198 pregnancies from the DART trial of HIV-infected women in Uganda and Zimbabwe a prematurity rate of 11.0% which was similar to the finding in this study but lower than 17.3% reported by Monforte and colleagues [12] who also found that preterm birth rate was higher in the ART experienced group than in the ART naïve group although the difference was not statistically significant.

Table 5. Comparison of MTCT and gender, mode of delivery, infant feeding, and infant ARV prophylaxis

Characteristics	HE No (%)	HIP No.(%)	NH No.(%)	Total No. (%)	X^2	*p*
MTCT	28 (8.0)	16 (4.5)	307(87.5)	351 (100.0)		
Gender						
Male	359 (21.9)	185 (11.3)	281 (17.1)	825 (50.3)		
Infected	10 (2.9)	8 (2.3)	150 (42.7)	168 (47.9)		
Female	357 (21.8)	175 (10.7)	283 (17.2)	815 (49.7)		
Infected	18 (5.1)	8 (2.30	157 (44.7)	183 (52.1)	1.07	0.3
Mode of delivery						
ELCS	198 (12.1)	130 (7.9)	44 (2.7)	372 (22.7)		
Infected	4 (1.1)	5 (1.4)	5 (1.4)	14 (4.0)		
EMCS	81 (4.9)	35 (2.1)	39 (2.4)	155 (9.4)		
Infected	1 (5.3)	2 (10.5)	16 (84.2)	19 (5.4)		
SVD	437 (26.7)	195 (11.9)	481 (29.3)	1113 (67.9)		
Infected	23 (6.50	9 (2.6)	286 (81.5)	318 (90.6)	110.51	0.00001
Infant feeding						
Mixed	85 (5.2)	44 (2.7)	312 (19.0)	441 (26.9)		
Infected	11 (3.1)	4 (1.1)	230 (65.5)	245 (69.8)		
EBF	247 (15.1)	105 (6.4)	111(6.8)	463 (28.2)		
Infected	5 (1.4)	0 (0.0)	41 (11.7)	46 (13.1)		
BMS	384 (23.4)	211 (12.9)	141 (8.6)	736 (44.9)		
Infected	12 (3.4)	12 (3.4)	36 (10.3)	60 (17.1)	418.80	0.00001
Infant Prophylaxis						
Yes	644 (39.3)	333 (20.3)	121 (7.4)	1098 (67.0)		
Infected	19 (5.4)	14 (4.0)	17 (4.8)	50 (14.2)		
No	72 (4.4)	27 (1.6)	443 (27.0)	542 (33.0)		
Infected	9 (2.6)	2 (0.6)	290 (82.6)	301 (85.8)	560.67	0.00001

(HE = HAART experienced; HIP = HAART in pregnancy; NH = No HAART; ELCS = elective caesarean section; EMCS = emergency caesarean section; SVD = spontaneous vaginal delivery; EBF = exclusive breastfeeding; BMS = breast milk substitute)

Alemu et al [7] also observed that ART might be causing adverse birth outcomes like low birth weight (LBW), Preterm Birth (PB) and Small for Gestational Age (SGA) among pregnant women and called for a need to consider regimen types for HIV-infected pregnant women. In contrast to these finding, Bagkeris et al in Ukraine [13] found that HIV infected mothers who were treatment naïve had an increased risk of preterm delivery and low birth weight babies when compared with those who were treatment experienced. This contrasting findings in these studies may also be related to the degree of immunosuppression in these mothers.

Powis et al [14] concluded in their study that PI-based HAART was the most significant risk factor for preterm delivery while Watts et al [15] also concluded that Protease inhibitor use early in pregnancy may be associated with increased risk for prematurity. However, Monforte and colleagues [12] while analyzing antiretroviral therapy (ART) regimens and pregnancy outcomes in naive and ART-experienced HIV-positive women from Italian Cohort found that the preterm birth rate was not associated with protease-inhibitor containing regimen. This was similar to the finding in this study, however, there were few mothers on PI-based HAART in this study, so a higher representation may be required to deduce a definitive conclusion. Concerns about the causal effect between protease inhibitor and prematurity have also been raised by other workers [3,10,14]

The MTCT rate in this study was very high at 21.4%. This was not surprising as majority of the women had many risk factors for transmission which included vaginal or emergency cesarean section delivery, mothers not receiving ART in pregnancy (HAART-naïve), lack of infant prophylaxis, premature delivery, poor infant feeding practices and female gender. However, majority of the MTCT in this study was contributed to by the NH group where 87.5% of babies born to these mothers were HIV infected. In contrast to this and an exception to established fact, French et al [16] found no difference in the risk of mother-to-child transmission between the HAART-naive and HAART-experienced groups although the incidence of mother-to-child transmission was low. The risk of MTCT of HIV is still high in developing countries especially among HAART-naïve mothers where there are still deficient standards of healthcare, lack/poor antenatal care, late diagnosis, lack of ART, and poor or haphazard interventions for Prevention of Mother to Child Transmission (PMTCT) of HIV.

Although most perinatal transmission occur late in pregnancy or during delivery, early and sustained suppression of viral replication is important in reducing the risk of mother-to-child transmission. This makes a case for initiation of HAART in all HIV-infected pregnant women early enough in order to sufficiently suppress viral replication by the third trimester and particularly during the birth process when there is intensive viral exposure.

MTCT was higher among females (52.1%) than males (47.9%) though our study did not show a statistically significant difference between them. This finding support previous observations that girls are either at increased risk of intrauterine HIV infection or that intrauterine-infected boys are at increased risk of fetal death [17]. Also, higher fragility of HIV-infected males in utero disproportionately increases the mortality in them and thus more HIV-infected female infants are born. [17] It may also be due to minor histocompatibility reactions between maternal lymphocytes and infant Y chromosome-derived antigens which reduce the risk of HIV transmission in boys and places girls at higher risk of in utero and perinatal transmission. [18]

This study found an overall MTCT rate of 4.0%, 5.4% and 90.6% among women who delivered by elective CS, emergency CS and vaginally respectively. Further categorization into ART use in pregnancy showed that there was no significant change in the rate of MTCT among the women who had elective CS irrespective of their ART status, however, MTCT was higher among HAART- naïve sub-group who had emergency CS and SVD. The European Collaborative Study [19] also found a similar increasing rate of MTCT of HIV for babies delivered by elective CS, by emergency CS and vaginally as 2.8% (9/319), 6.2% (14/226) and 21.6% (58/268) respectively among preterm babies as was found in this study. The very high rate of MTCT among vaginally delivered babies in this study was contributed mainly from HAART-naïve mothers and may also be due to lack of ANC, poor obstetric delivery practices prevalent in delivery places where HIV and ART services are not routinely offered in pregnancy and more importantly prolonged contact with virus fluid in the birth canal. The European Collaborative Study [19] also found that elective CS and emergency CS were associated with a

reduced MTCT risk versus vaginal delivery, but the emergency CS association was only of borderline significance.

Safe infant feeding practices remain an integral part of prevention of mother-to-child transmission of HIV (PMTCT). The 2010 World Health Organization (WHO) guidelines on infant feeding in the context of HIV infection recommend that infant feeding practices should support the greatest likelihood of infant HIV-free survival, while also protecting against non-HIV morbidity and mortality [6]. Countries were encouraged to support one infant feeding option; either breastfeeding with antiretroviral (ARV) interventions, or avoidance of all breastfeeding by women with HIV [6]. Nigeria then selected one strategy; that of promoting exclusive breastfeeding for women with HIV, and to counsel and support those who opt for exclusive breastmilk substitute. The current recommendation is for women with HIV to breastfeed exclusively for 6 months introducing appropriate complementary foods thereafter, and continue breast feeding at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence [6]. The risk of MTCT of HIV is highest in babies who are mixed feed when compared to those who had exclusive breast feeding or exclusive breastmilk substitute and this risk is highest among mothers who did not receive HAART in pregnancy or who were not virally suppressed [20]. This is in tandem with the findings of this study. This study also found that MTCT was highest in NH group irrespective of the feeding option signifying that in-utero or peri-partum transmission among these mothers was high.

Infant prophylaxis plays a vital role as part of PMTCT of HIV. In this study, it was found that infant ARV alone or in combination with maternal ARV significantly reduced the chances of MTCT of HIV. There was a near equal rate of infection among the children who received ARV irrespective of maternal ARV status (5.4%, 4% and 4.8%), however, 82.6% (290/351) of the babies who did not receive ARV prophylaxis and whose mothers were HAART-naïve in pregnancy were infected. All newborns with perinatal exposure to HIV should receive antiretroviral (ARV) prophylaxis in infancy to reduce perinatal transmission of HIV, with selection of the appropriate ARV regimen guided by the level of transmission risk.

Important factors that influence the risk of HIV transmission to a newborn exposed to HIV are whether the mother has received antepartum antiretroviral therapy (ART) and her viral load. The risk of transmission is increased in the absence of maternal ART or if it was ineffective in producing virologic suppression and higher maternal viral load, especially in later pregnancy. It is therefore not surprising to find a high transmission rate among babies who did not receive ARV prophylaxis and whose mothers had no ARVs in pregnancy as was found in this study.

Fourteen (0.9%) babies had birth defects especially neural tube defects and congenital heart defects. This was similar to the rate of 1.2% reported by Monforte and colleagues [11] and both cases were not associated with efavirenz-containing regimen. Newly gathered evidence has shown a lack of association between efavirenz and newborn malformations leading to the recommendation to continue the drug in pregnant women already on efavirenz combination regimens. [4,6] Namale and colleagues [10] and Watts [21] reported higher rates of 2% and 4.2% of congenital abnormalities among their cohorts respectively. They also observed that ARV use in early pregnancy was not associated with an increased risk of birth defects overall. On the other hand, Knapp [22] reported a congenital anomaly rate of 5.49 % with abnormalities of the cardiovascular system being the commonest. The only specific ARV drug association was with efavirenz.

Florida et al [23] reported a total prevalence of birth defects of 3.2% for infants exposed to antiretroviral drug during the first trimester and 3.4% for infants who had no antiretroviral exposure during the first trimester. No associations were found between major birth defects and first-trimester exposure to any antiretroviral treatment including efavirenz. This further lends support to the assumption that first-trimester exposure to antiretroviral treatment is safe and does not increase the risk of congenital abnormalities.

One limitation of our study was that viral load test was not done and adherence data were not collected in this cohort. Viral load testing only became routinely available in our center from late 2016 and so could not be used to determine the viral suppression at delivery among those on HAART. Also, there was no stratification of prematurity into spontaneous and induced.

5. CONCLUSION

Given the association of earlier viral suppression with lower risk of mother-to-child transmission of HIV, combined ART should be initiated as soon as HIV is diagnosed in women. The benefits of early ART must however be weighed against the risks of preterm delivery, lower birth weight and potential teratogenic effects of drug exposure on the foetus.

CONSENT AND ETHICAL APPROVAL

Ethical approval for the study was obtained from the Research and Ethics committee of the University of Port Harcourt Teaching Hospital. All mothers who brought their children within this study period who gave consent for the study were selected for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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