

Pregnancy Outcome of HIV Positive Mothers on Antiretroviral Therapy in a Tertiary Health Institution in Abuja, Nigeria.

Adewole ND.¹ Okechukwu AA.² Offiong RA¹

¹Department of Obstetrics and Gynaecology, University of Abuja Teaching Hospital, Abuja-FCT, Nigeria.

²Department of Paediatrics, University of Abuja Teaching Hospital, Abuja-FCT, Nigeria

Corresponding author: Adewole, Nathaniel D:

Department of Obstetrics and Gynaecology, University of Abuja Teaching Hospital, Abuja-FCT, Nigeria.

Abstract

Background: Highly active antiretroviral therapy has remained the main strategy in use for the prevention of mother to child transmission of HIV. There are however conflicting reports of poor pregnancy outcomes following its use in HIV positive pregnant mothers in resource limited settings. We therefore conducted this study to evaluate the effect of these drugs on pregnancy outcome of positive mothers in our health institution.

Materials and Methods: A retrospective analysis of medical records of HIV positive mothers on highly active anti-retroviral therapy who attended the antenatal care services in our health institution was done over a ten-year period of January 2010 to December 2019 for the above objective. The pregnancy outcomes evaluated were the 5 minutes Apgar score, preterm deliveries, number of low birth weight, status of the new born (dead or alive), and the status of the mother (dead or alive).

Results: Of the total of 19,645 deliveries conducted during the 10-year review period, 330 (1.7%) were HIV positive. The mean age of the positive mothers, their parity, gestational age, and place of residence were 31.1 ± 4.7 years, 2.0 ± 1.6 , 38.6 ± 3.1 weeks, and 82.7% vs 17.3% for rural and urban dwellers. Most of the positive mothers 80.0% were Christians, 88.8% were from middle socio-economic class, and all were married. Most 80.3% started their highly active antiretroviral therapy before conception, 51.5% and 42.7% were on zidovudine+lamivudine+nevirapine, and tenofovir+lamivudine+lopinavir boosted ritonavir combinations respectively. Majority 67.0% and 51.0% had their viral load and CD4 cell count of between 20 to 1000 copies/mls, and >500 cells/ μ l. The pregnancy outcomes were 2.4% neonatal and maternal deaths each, 6.3% preterm deliveries, 9.6% low birth weights, and 4.5% Apgar score of <7 at 5 minutes. The two maternal variables significantly associated with poor pregnancy outcome were place of residence, χ^2 of 6.12, $p=0.013$, and HIV related morbidity χ^2 of 245.9, $p<0.0001$. Maternal HIV related morbidity was also associated with low 5 minutes Apgar score of <7 , χ^2 of 245.9, $p<0.0001$.

Conclusion: The effect of antiretroviral therapy on pregnancy outcome of HIV positive mothers in this study was minimal, however social, economic, medical empowerment is required of mothers residing in rural communities and those with HIV associated morbidities in order to minimize poor neonatal outcome seen in such mothers.

Key words: HIV positive, pregnancy, mothers, anti-retroviral therapy, outcome

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I. Introduction

Human immunodeficiency virus (HIV) infection still remains a global pandemic, with sub-Saharan Africa being worst hit, and having the highest incidence of 4.2% among its adult population.¹ Nigeria ranks second to South Africa in this global burden, with over 3.19 million of its people living with HIV (PLWH).^{2,3} Pregnant women and children under the age of 5 years also bear the greatest burden of PLWH globally, and Nigeria accounts for over 80% of this global burden.^{2,3} Approximately 1.4 million of pregnant women are living with HIV infection in low- and middle-income countries,⁴ while over 90% of children acquire this infection from their mothers during pregnancy, labour, delivery or during breastfeeding.³

Antiretroviral therapy (ART) during pregnancy is considered the most effective method of reducing the risk of vertical transmission, this method has however been reported to be associated with poor pregnancy outcomes in developing countries when compared to their developed counterpart.⁵ It also reported to have over 7 times poorer outcome when compared to non HIV-infected pregnant mothers.⁶ Such fetal/neonatal consequences include miscarriages, low birth weight, intra-uterine growth restriction, stillbirth, preterm delivery, low birth weight, decreased neural function and 5-minute Apgar score of less than 7.^{5,7-12} Contributing factors include poor access to ART, limited HIV counselling and testing for pregnant mothers, and inadequate/overwhelmed

trained health workers to identify women who requires treatment initiate, monitoring, and counselling during pregnancy.¹³

Over the years, there have been changes in the regimen of ART in WHO/Nigerian guidelines.¹⁴ Initially, all pregnant women with HIV were given single dose nevirapine (NVP) only, later, zidovudine (AZT) based combination was introduced comprising of AZT, lamivudine (3TC) and NVP. (AZT+3TC+NVP) between 2005 and 2010.¹⁴ For the past ten (10) years, our centre has also changed HAART regimen according to WHO and national guideline.¹⁵ Currently pregnant women are on two nucleoside reverse transcriptase inhibitors (NRTI), tenofovir (TDF) +3TC, plus one non-nucleoside reverse transcriptase inhibitor (NNRTI), efavirenz (EFV), or one protease inhibitor (PI) lopinavir boosted ritonavir (LPV/r). Integrase inhibitors, dolutegravir (DTG) has also just been added to the regimen in 2020 after the review year.¹⁵ Little is known of the pregnancy outcome of these HIV positive pregnant women on HAART in our environment. We therefore conducted this 10 year review to determine pregnancy outcomes of both booked and un-booked pregnant mothers started on HAART before pregnancy, during early, mid and late pregnancy, and at delivery for the above objective(s).

II. Materials and Methods

A 10 year retrospective review of medical records of HIV positive pregnant mothers who attended antenatal clinical services at the hospital prevention of mother-to-child transmission (PMTCT) unit was carried out to document the pregnancy outcome of such mothers on HARRT.

Study Design: A retrospective study.

Study Location: At the prevention of mother-to-child transmission (PMTCT) unit of the antenatal clinic of University of Abuja Teaching hospital (UATH), Gwagwalada, in Federal Capital Territory (FCT), Abuja, Nigeria.

Study Duration: January 2010 to December 2019.

Sample size: 330 HIV positive mothers and their 333 new born infants

Sample size calculation: All the HIV positive mothers. seen during the 10 year review period.

Subjects & selection method: The medical history and pregnancy outcome of HIV positive pregnant mothers who received prevention of mother-to-child transmission (PMTCT) services at the antenatal clinic of the University of Abuja Teaching hospital (UATH), Gwagwalada was collected. The PMTCT service area of the antenatal clinic not only provides routine antenatal clinical services for HIV positive pregnant mothers, but also provides pre and post HIV counselling services, rapid HIV testing, adherence counselling and distribution of routine antenatal drugs, and HAART to the mothers. It has consulting rooms for the doctors, the nurses, and adherence counsellors. Record clerks, pharmacists, laboratory technicians, and scientist were also at their disposal on week days (Monday-Friday, from 7.30 am to 4 pm.). UATH is a 350 bed capacity referral hospital, sub-serving the people of FCT Abuja, and four neighboring states of Nasarawa, Kogi, Kaduna and Niger. Is one of the first centers to start offering free HIV/AIDS services in the country, courtesy of Federal Government of Nigeria (FGN), and United States of America (USA) President Emergency Plan for AIDs Relief (PEPFAR) since 2005.

Inclusion criteria:

1. HIV pregnant positive mothers with or without HIV related morbidity.
2. Multiple gestation

Exclusion criteria:

1. HIV negative pregnant women

Procedure methodology: The data for the subjects were collected from the database of the PMTCT unit, antenatal clinic database, delivery records, and new born database at the Paediatric Special Treatment Clinic (PSTC) of the hospital where exposed/infected babies/children and adolescents are treated and monitored. Each folder was identified using the hospital number, and parameters assessed were based on WHO/UNAIDS definition of adverse outcome reported in HIV-positive women.¹⁶

A structured questionnaire, in line with the objectives of the research was developed and pre-tested to ensure that it could retrieve all relevant information from the patients' records. Such information collected included socio-demographic profile of the mothers, the newborns and maternal characteristics. The mother's characteristics collected included: Her age, history of miscarriages, preterm deliveries, stillbirth, maternal mortality, and morbidity. Other demographics characteristics collected were her weight, level of education, husband's occupation, whether married or single, her parity, gestational age at booking, type of HARRT being used, whether 1st line or 2nd line, duration of use of HARRT, time of commencement of HARRT, whether before pregnancy, at early pregnancy, at mid or late pregnancy or at the point of delivery, her packed cell volume (PCV), CD4 cell count, and viral load (VL). Mode of delivery, gestational age at delivery, PCV after birth, and whether the mother was dead or alive were also collected. For their new-born information, data collected

included: Apgar scores at 5minutes, estimated gestational age at birth, their birth weight, and weather the new born was alive or dead.

HIV testing was done using Determine TM and Uni-gold TM test kits, CD4 cell count was measured using automated Partec Cyflow easy count kit (*Partec code no. 05-8401 Western Germany*), VL was measured with (*Roche Smp /prep /cobs Taqman 96, USA*), while adult Seca beam weighing scale accurate to the nearest 0.01 kg and paediatric beam weighing was used for measuring the weight of the mother, and the new born. Analysis of social class was based on Olusanya et al ¹⁷ classification of mother’s level of education, and husband occupation.

Statistical analysis

This was done using SPSS version22 that generated frequency tables, mean, and standard deviation. Student t test was used to compare group means, while chi-square was used to analyse categorical data. Same tests used for test of association, and p value of <0.05 was considered statistically significant.

Ethical issues

Ethics approval was obtained from the Health Research and Ethics Committee of the hospital before the commencement of the study, and principles of research ethics wasmeticulously followed

III. Results

Table I depicts the characteristics of the 330 HIV positive mothers studied. Of the total 19,645 deliveries conducted during the 10-year review period, 330 (1.7%) were HIV positive. The mean age of positive mothers was 31.1±4.7 years, their mean parity, gestational age, VL, and CD4 cell count were 2.0±1.6, 38.6±3.1 weeks, 2953.02± 1619.9 copies/ml, and 543.63±283.7 cells/μl respectively. Most positive mothers 273 (82.7%) were rural dwellers, 175 (53.0%) had secondary level of education, all (100.0%) were married, majority 293 (88.8%) were from middle socio-economic class (SEC), 265 (80.3%) were already on HARRT before the index pregnancy, and mean duration of HARRT was 8.3±2.8 years. Majority 170 (51.5%), and 141 (42.7%) were on AZT/3TC/NVP, and TDF/3TC/EFV based combinations, 311 (94.2%) were still on 1st line HARRT, while majority 173 (52.4%) were on AZT based regimen.

Table 1: Shows the demographic variables of the 330 HIV positives pregnant study population

Variable	Frequency(%)	Mean ±SD
Maternal age (years)	-	31.1± 4.7
Maternal parity	-	2.0 ±1.6
Gestational age(weeks)	-	38.6± 3.1
Viral load (copies /ml)	-	2953.02± 1619.9
CD4 cell count (cells/μl)	-	543.63± 283.7
Residence		
Rural	273(82.7)	-
Urban	57(17.3)	-
Maternal level of education		
No formal education and Primary	35(10.6)	-
Secondary	175(53.0)	-
Tertiary	120(36.4)	-
Religion		
Christianity	264(80.0)	-
Islam	66(20.0)	-
Maternal marital status		
Married	330(100.0)	-
Socio-economic status		
Low	31(9.4)	-
Middle	293(88.8)	-

High	6(1.8)	-
Time of Commencing HAART		
Before pregnancy	265(80.3)	-
During first trimester	24(7.3)	-
During mid trimester	28(8.5)	-
During last trimester	11(3.3)	-
At delivery	2(0.6)	-
Mean duration on HAART (years)	-	8.3±2.8
Type of HAART		
ABC/3TC/LPV/r	3(0.9)	-
AZT/3TC/NVP	170(51.5)	-
AZT/3TC/LPV/r	3(0.9)	-
TDF/3TC/EFV	141(42.7)	-
TDF/3TC/LPV/r	13(4.0)	
1 st or 2 nd Line regimen		
1 st line	311(94.2)	
2 nd line	19(5.8)	
Type of regimen		
AZT based	173(52.4)	
TDF based	157(47.6)	

Table II showed the maternal clinical characteristics at antenatal booking and neonatal outcome. Most positive mothers 211(63.9%) had PCV of greater than 30% at booking, majority 221(67.0%) and 128(51.0%) had VL and CD4 cell count of 20-1000 copies/ml, and >500 cell/μl. Majority 303(91.8%) had body weight of <90kg, majority 287(86.9%) also had spontaneous vertex delivery (SVD), while only 6(1.8%) had HIV related morbidity, and maternal death of 8(2.4%). For the neonatal outcome; 8(2.4%) neonatal deaths were also recorded, 15(4.5%) had Apgar score of <7 in 5 minutes, 21(6.3%) were delivered at <37 weeks, 32(9.6%) had birth weight of <2.5kg, and their mean birth weight of 3.0±1.1kg.

Table II: Shows maternal clinical characteristics at antenatal booking and neonatal outcome

Maternal Variable (N=330)	Frequency (%)
Pack cell volume (%)	
<30	119(36.1)
≥30	211(63.9)
Viral Load (copies/ml)	
<20	82(24.8)
20-1000	221(67.0)
>1000	27(10.8)
CD4 Cell Count(cells/μl)	
<200	23(9.2)
200-500	179(39.8)
>500	128(51.0)
Maternal outcome	
Alive	322(97.6)
Dead	8(2.4)
Mode of delivery	
Caesarean section	43(13.0)
Spontaneous Vertex Delivery	287(86.9)
HIV related morbidity	
Yes	6(1.8)
No	324(98.2)
Neonatal outcome (N=333)	
Alive	325(97.6)
Dead	8(2.4)
Apgar score at delivery	
<7 at 5 minutes	15(4.5)

>7 at 5 minutes	318(95.5)
Sex of the baby	
Female	145(43.5)
Male	188(56.5)
Birth weight (kg)	
<2.5	32(9.6)
≥2.5	301(90.4)
Mean birth weight (kg)	*3.0±1.1
Gestational age	
<37	21(6.3)
>37	312(93.6)

Table III (a& b) showed the relationship between maternal variables and neonatal outcome (alive or dead) for table III(a), and mean maternal/ neonatal variables and neonatal outcome for table III(b). The two maternal variables that had statistically relationship with neonatal outcome (alive or dead) were place of residence, and HIV associated morbidity: χ^2 of 6.12, $p=0.013$ for place of residence, and χ^2 of 245.9, $p<0.0001$ for HIV related morbidity. The other variables had no significant relationship with neonatal outcome, their p values were >0.05 . For table III (b), no mean maternal/ neonatal variables(maternal age, duration on ART, gestational age, parity, birth weight, VL, and CD4 cell count) had any significant relationship with neonatal outcome, p values were also >0.05 .

Table III(a): Shows relationship between maternal variables and neonatal outcome

Variable	Neonatal outcome		χ^2	P value
	Alive(%)	Dead(%)		
Residence				
Rural	265(98.5)	4(1.5)		
Urban	57(93.4)	4(6.6)	6.12	0.013
Maternal level of education				
No formal education and Primary	35(100.0)	0(0.0)		
Secondary	172(98.3)	3(1.7)	2.73	0.436
Tertiary	115(95.8)	5(4.2)		
Socio-economic status				
Low	31(100.0)	0(0.0)		
Middle	285(97.3)	8(2.7)	1.05	0.6
High	6(100.0)	0(0.0)		
Time of commencing HAART				
Before pregnancy	257(97.0)	8(3.0)		
During first trimester	23(100.0)	0(0.0)		
During mid trimester	27(100.0)	0(0.0)	1.93	0.748
During last trimester	10(100.0)	0(0.0)		
At delivery	2(100.0)	0(0.0)		
Regimen base				
AZT based	168(97.1)	5(2.9)		
TDF based	156(99.4)	1(0.6)	2.2	0.142
Mother's weight (kg)				
<90	297(98.0)	6(2.0)		
>90	27(100.0)	0(0.0)	0.533	0.469
Pack cell volume (%)				
<30	116(97.5)	3(2.5)		
>30	206(97.6)	5(2.4)	1.07	0.301
HIV related morbidity				

Yes	0(0.0)	6(100.0)		
No	322(98.4)	2(0.6)	245.9	<0.0001*
Mode of delivery				
Caesarean Section	43(100.0)	0(0.0)		
Spontaneous Vertex Delivery	281(97.9)	6(2.1)	1.008	0.315
Baby's gender				
Female	142(97.9)	3(2.1)		
Male	183(97.3)	5(2.7)	0.009	0.926

Table III (b): Shows the relationship between mean maternal and neonatal variables and neonatal Outcome

Variables	Neonatal outcome		T	P value
	Alive	Dead		
Maternal age (years)	31.08±4.7	32.6±6.5	0.9	0.36
Duration on ART (years)	8.3±3.1	8.3±2.5	0.06	0.948
Gestational age (weeks)	38.6±3.1	36.6±3.0	1.42	0.155
Parity	2±1.6	2±1.8	0.173	0.863
Birth weight (kg)	241.1±69.4	219.8±36.0	0.864	0.388
Packed cell volume (%)	32.4±5.2	28.9±3.3	1.8	0.07
Viral load(copies/ml)	3075.5±16516.2	28.3±14.15	0.487	0.627
CD4 cell count ((cells/µl))	550.8±281.8	417.4±28.0	1.23	0.218

Table IV depicts relationship between maternal/neonatal categorical variables and Apgar score. The only maternal variable that had significant relationship with Apgar score is maternal HIV related morbidity, χ^2 of 42.3, $p < 0.0001$, the other variables recorded p values of > 0.05 .

Table IV: Shows relationship between maternal variables and Apgar score

Variable	Apgar Score		χ^2	P value
	<7 at 5 minutes(%)	>7 at 5 minutes(%)		
Residence				
Rural	17(6.2)	256(93.7)		
Urban	3(5.3)	54(94.7)	0.09	0.765
Maternal level of education				
No formal education and Primary	2(5.7)	33(94.3)		
Secondary	9(5.1)	166(94.9)	0.5	0.919
Tertiary	5(4.2)	115(95.8)		
Socio-economic status				
Low	1(3.2)	30(96.7)		
Middle	14(4.8)	279(95.2)	0.387	0.824
High	0(0.0)	6(100.0)		
Time of commencing HAART				
Before pregnancy	12(4.5)	253(95.5)		
During first trimester	0(0.0)	24(100.0)		
During mid trimester	2(7.1)	26(92.9)	3.49	0.48
During last trimester	1(9.1)	10(90.1)		
At delivery	0(0.0)	2(100.0)		
Regimen base				

AZT based	7(4.0)	166(96.0)		
TDF based	6(3.8)	151(96.2)	0.009	0.921
Mother weight (kg)				
<90	13(8.1)	290(91.9)		
>90	0(0.0)	27(100.0)	1.32	0.251
Packed cell volume (%)				
<30	5(4.2)	114(95.8)		
>30	9(4.3)	202(95.7)	1.7	0.193
HIV related morbidity				
Yes	4(66.7)	2(33.3)		
No	11(3.4)	313(96.6)	42.3	<0.0001*
Mode of delivery				
Caesarean section	3(7.0)	40(93.0)		
Spontaneous vertex delivery	11(3.8)	276(96.2)	0.487	0.485
Baby sex				
Female	7(4.8)	138(95.2)		
Male	8(4.3)	180(95.7)	0.635	0.426

IV. Discussion

The low HIV prevalence of 1.7% among pregnant mothers in this study was comparable to 3.0%, and 4.0% reported from Port Harcourt,¹⁸ and Damaturu¹⁹ both in Nigeria, and current national sero-prevalence of 1.4%.²⁰ This was however far much lower than reported 7.7% from Ogun state,²¹ 8.2% from Jos,²² 11.5% from Abuja,²³ 26.4% from Ibadan,²⁴ also from Nigeria studies, and 6.2% from Addis Ababa.²⁵ This varying prevalence across Nigeria, and other countries may be a reflection of the differences in sexual practices and behaviour, awareness of HIV infection and testing, socio-cultural practices, and accessibility to healthcare services to the populace, an increasing trend if not properly addressed will pose a particular risk to the foetus, and the newborns.²⁶

Pregnancy outcomes in HIV infected women on ART remains skewed with poor outcome reported mainly from developing countries. The outcome in the present study appeared minimal with preterm delivery of 6.3%. This was however lower than 14.1% from UK study,²⁷ and Nigerian studies of 15.2% from Port Harcourt,²⁸ 22.2% from Maiduguri,²⁹ 21.6% from Nnewi.³⁰ and 35.5% from Ilorin.²⁶ The lower outcome of preterm delivery in this study might be to the early commencement of HARRT prior to the conception by most mothers in the study (80.3%), together with adequacy of monitoring during pregnancy as suggested by Onakewhor et al.³¹ Adeniran et al,²⁶ in their study on pregnancy outcomes in booked HIV positive women initiating HARRT equally documented higher preterm deliveries in those that started HARRT during pregnancy than those start before pregnancy (31.5% vs. 1.9%, OR 24.35, 95% CI 7.15-91.26, p<0.01). While administration of HARRT during pregnancy is essential for preventing MTCT of HIV, and maintaining good maternal health in positive women,³² the use of HAART may induce preterm delivery by the modulation of the immune system via cytokine mediated effect, and changing circulating cytokine levels through antiretroviral-associated immune reconstitution.^{33,34} Protease inhibitor is well known for its associated risk of preterm delivery as a result of its immunological induced complication, and disruptions in progesterone synthesis.³⁵ However, part of the lower number of preterm deliveries in the study might also be lower number of mothers (5.8%) on protease inhibitors containing HARRT.

Low birth weight (LBW) of 9.6%, low Apgar score of <7 in 5 minutes (4.5%), neonatal and maternal mortality (2.4%) for each was also recorded as part of the pregnancy outcome of this study. These findings were comparable to <7 Apgar score in 5 minutes of 7.6% from Port Harcourt,²⁸ LBW of 9.3% from same study, and no record of maternal or neonatal deaths.²⁸ Similar findings were also reported by Young et al.³⁶ from Uganda who also found no relationship between use of HAART in positive pregnant mothers and adverse pregnancy outcomes, thus buttressing Onakewhor et al,³¹ report of untreated HIV mothers having more adverse obstetric and perinatal events than those who received HAART. This result and other studies^{28,36,37} support the notion that use ART can be very beneficial not only in the prevention of mother-to-child transmission of HIV, but also in the minimization of adverse birth outcomes in treated HIV mothers especially when initiated as early as possible.

The two maternal variables that had significant relationship with neonatal death, and low Apgar score in this study was place of residence, and HIV related morbidity. χ^2 of 6.12, $p=0.013$ place of residence, χ^2 of 245.9, $p<0.0001$ for HIV related morbidity for neonatal death, and χ^2 of 245.9, $p<0.0001$ for HIV related morbidity for low Apgar score. The poor neonatal outcome seen with place of residence in this study could be because greater percentage (82.7%) of HIV positive pregnant women resides in rural areas. Yang et al³⁸ from China equally observed 92.0% of their positive mothers to have come from rural areas where maternal HIV infection, rural residence, and pregnancy history were noted to be the three indicators associated with adverse pregnancy outcomes, and suggested medical, and social support for maternal-infant duo from such areas because of poor transportation services, limited education of the mothers, economic and other social complications of such environment. This could equally be same case of mothers in this study where majority of HIV positive women are from rural communities, with poor transportation services, poor social amenities, and inadequate or poor medical services very common in such environment. HIV associated morbidity of which pulmonary tuberculosis was the commonest co-morbidity among our study population was statistically associated with neonatal deaths and low 5 minutes Apgar score. This was equally reported in other studies where opportunistic infections with low CD4 cell count and high VL load played a significant role.^{38,39}

V. Conclusion

The effect of HARRT on pregnancy outcome of HIV positive mothers in this study was minimal, however social and medical support is required for mothers residing in rural communities and those with HIV associated morbidity in order to minimise adverse pregnancy outcome associated with these two conditions.

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