

OBSTETRIC AND NEWBORN OUTCOMES AND RISK FACTORS FOR LOW BIRTH WEIGHT AND PRETERM DELIVERY AMONG HIV-INFECTED PREGNANT WOMEN AT THE UNIVERSITY COLLEGE HOSPITAL IBADAN

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ABSTRACT

There remains uncertainty about the impact of HIV on pregnancy outcomes and effects of highly active antiretroviral therapy on fetal development. This study describes obstetric outcomes among HIV positive parturients at the University College Hospital, Ibadan. HIV positive parturients were identified in the birth register. During the 30-month period, 318 of 6203 deliveries were HIV positive (5.1%) with 97.6% record retrieval. The mean age of the HIV positive parturients was 31.66 years (± 4.66); the mean gestational age at delivery was 38.02 weeks (± 2.75) and the mean birth weight 2.85kg (± 0.59). There were 35.8% (109) preterm births, 2.9% stillbirths and 21.5% low birth weights. The regimen most commonly (198, 64.5%) used was a non-nucleoside reverse transcriptase (NNRTI) based HAART. Preterm births were similar following spontaneous vaginal delivery (31.5%) and elective section (31%) but higher (41.3%) with emergency section ($p=0.4$).

On univariate analysis, the preterm infants had lower mean birth weights (2.46 ± 0.61 vs 2.96 ± 0.44 ; $p=0.000$). The proportion of preterm births was higher among Low birth weight infants (71.9% vs 28.1%; $p=0.00$). Variables with more preterm births were age >35 years (51.6%), 6 years of schooling (51.5% vs 48.4%) and being on combination ARV (PI, 37.5% or non-PI, 36.2%). However, these differences did not attain statistical significance. Low birth weight infants had mothers who had higher mean ages (33.28 years ± 4.59

vs 31.28 years ± 4.59 , $p=0.02$), lower mean gestational age at delivery (35.72 weeks ± 3.16 vs 38.49 weeks ± 2.1 , $p=0.00$). Variables with more low birth weight include <12 years of schooling and being on mono/ dual therapy (31.8%). These differences were not statistically significant.

On logistic regression, factors that retained an

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association with low birth weight were mean maternal age at delivery ($\rho=0.002$; $\beta=0.904$; 95% CI, 0.848 – 0.966) and being on mono/ dual therapy ($\rho=0.039$; $\beta=3.042$; 95% CI, 1.055 – 8.768). The only factor that retained an association with preterm birth was mean maternal age at delivery ($\rho=0.015$; $\beta=0.935$; 95% CI, 0.886 – 0.987).

HIV positive (especially older) women, have high rates of preterm deliveries and low birth weights. The beneficial effects of HAART on mother-to-child transmission are indisputable but monitoring antiretroviral therapy in pregnancy remains a priority and antenatal surveillance should include fetal growth assessment.

INTRODUCTION

Nigeria, with a 4.1% HIV prevalence reported among pregnant women in the 2010 national sentinel survey, contributes significantly to the global HIV burden¹. Because women account for about 60% of the total HIV burden in Nigeria, the coexistence of HIV and pregnancy is a common finding¹. The result is that 315,00 to 625,00 children are delivered annually to HIV infected mothers in Nigeria, with an estimated 63,000 to 125,000 infants acquiring HIV from their mothers each year². The result is that Nigeria contributes approximately 10% of the global burden of mother-to-child transmission of HIV infection^{3,4}.

Some studies⁵ have associated HIV in pregnancy with higher rates of adverse pregnancy outcomes such as stillbirths and low birth weight, while others^{6,7} have found no adverse effects of HIV infection on pregnancy outcome. In addition, while prevention of mother-to-child transmission of HIV (PMTCT) interventions can reduce the vertical transmission rate of HIV to as low as 1 – 2%⁸ and antiretroviral therapy (ART) provides clear benefits, the evidence for the effect of highly active antiretroviral therapy (HAART) on adverse pregnancy outcomes is conflicting. While studies from Europe have provided support for an association between receipt of ART during pregnancy and an increased risk of preterm birth (PTB) and low birth weight (LBW)⁹⁻¹¹, studies from the United States have not consistently associated maternal receipt of ART during pregnancy

with these adverse pregnancy outcomes¹²⁻¹⁴.

The large number of HIV positive women who require PMTCT services and the uncertainty regarding the pattern of pregnancy outcomes among this group of parturients therefore necessitates the need for constant review. Thus, the objective of this study was to review the pregnancy outcomes – maternal and fetal – among HIV-positive pregnant women who delivered at the labour ward of the University College of Hospital, Ibadan.

METHODS

This retrospective cross-sectional study was conducted at the labour ward of the University College Hospital (UCH), Ibadan. The study period, over 30 months, was from January 2011 to June 2013. The birth register was reviewed and the records of all women identified as HIV positive in this period were retrieved. Information that was obtained was as follows: selected socio-demographic and neonatal characteristics, gestational age at delivery, mode of delivery etc.

The University College Hospital Ibadan offers prevention of mother-to-child transmission (PMTCT) services in the Anti-retroviral Clinic supported by the AIDS Prevention Initiative in Nigeria (APIN) program and the President's Emergency Plan for AIDS Relief (PEPFAR) program. HIV positive pregnant women access

these services having being referred from the UCH antenatal clinic and other clinics in the environs. PMTCT services provided include opt-out system of HIV testing in pregnancy, antiretrovirals for PMTCT, infant feeding counseling and family planning counseling. In addition women are monitored by regular assay of CD4 count and viral load. Caesarean delivery is offered at no cost to the patient if there are obstetric indications or viral load above 1,000 copies per ml close to term (>36weeks gestational age).

Until April 2011, patients were either commenced on zidovudine (AZT) monotherapy or combination therapy of zidovudine and lamivudine (Combivir, CBV) for prophylaxis if CD4 count was more than 200 cells per ml. Women with CD4 count less than 200 cells per ml or symptomatic women with CD4 200-249 cells /ml were commenced on the national first-line regimen of nevirapine (NVP)-based Highly Active Antiretroviral Therapy (HAART). Symptomatic women with CD4 count 250cells/ml and above or women on 2nd line were placed on protease inhibitor (PI) based HAART therapy. Genotypic testing for antiretroviral resistance was not routinely available. After April 2011, all women were commenced on efavirenz based HAART following adoption of the WHO recommendations. Women on second line drugs were placed on PI based HAART. Approval was obtained from the joint UI/UCH ethics committee.

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS Inc, Chicago, Ill). Data was summarized with frequency tables and mean (\pm standard deviation). Information analysed included maternal demographic characteristics and antiretrivoral drug (ARV) type. The pregnancy outcomes evaluated were LBW (<2500 g) and PD (gestational age <37completed weeks).Chi-square (χ^2) test was used for analysis of categorical variables. Continuous variables were analyzed using student's T-test or analysis of variance (ANOVA) for

groups more than two. Significance was defined as p value <.05. These variables were examined within two groups divided by birth weight (<2500 g and 2500 g) or gestational age (<38 weeks and 37 weeks) for statistical significance by Logistic regression analysis. Multivariate Logistic regression analysis was used to explore the potential risk factors for LBW/PD. All variables in the univariate analysis with *P* value <0.25 and those deemed clinically significant were entered into multivariate models using stepwise logistic regression. Variables were held in the models if they reached a significance level of *P*<0.05.

RESULTS

During the study period, there were 6203 deliveries. Three hundred and eighteen women (318) were HIV positive giving a prevalence of 5.1%. Of these 307 casenotes were retrieved giving a retrieval rate of 97.6%. Fifty- four of the women were unbooked in UCH, being newly discovered to be HIV positive in labor. The mean age of all the parturients was 31.66 years (\pm 4.66), while the mean gestational age at delivery was 38.02 weeks (\pm 2.75). The mean birth weight was 2.85kg (\pm 0.59).

Over half (214, 69.7%) of the patients were in the age range 26 to 35 years (see table 1). While most (236, 76.9%) had at least 12 years of education only 2 patients reported being single. Although, over half (190, 61.2%) of the patients presented at term, the prevalence of preterm delivery was 35.8% (109). Elective cesarean section was the mode of delivery in 27.4% (84) of the patients. The drug regimen most commonly (198, 64.5%) used by the parturients was a non-nucleoside reverse transcriptase (NNRTI) based HAART.

The gestational age at delivery following spontaneous vaginal delivery compared to deliveries after caesarean section showed a similar proportion of preterm deliveries; 31.5% after

vaginal delivery and 31% after elective cesarean delivery (see table 2). In contrast women who had emergency delivery had more preterm deliveries (41.3%). These differences were however not statistically significant ($\rho=0.4$). Review of neonatal characteristics revealed a male sex preponderance of 54.7% (see table 3). There were 2.9% stillbirths and 21.5% low birth weights.

Over a third (35.8%) of the infants were born preterm (see figure 1). Table 4 shows the factors that were associated with preterm delivery. The mean birth weight of the preterm infants was lower (2.46 ± 0.61 vs 2.96 ± 0.44). The difference was statistically significant ($\rho=0.000$). The mean age of the mothers with preterm babies was higher. Compared to the other age groups, mothers older than 35 years had a higher proportion of preterm infants (51.6%). Women with six years or less of schooling also had higher proportion of preterm deliveries (51.5% vs 48.4%). Other factors that demonstrated higher proportion of preterm infants include having emergency CS (42.1%), being low birth weight (71.9% vs 28.1%) and being on combination ARV (PI, 37.5% or non-PI, 36.2%). However, only being low birth weight achieved statistical significance. The differences observed in the other factors did not attain statistical significance.

Table 5 shows the factors that were associated with low birth weight. The mean age of the mothers with low birth weight babies was higher (33.28 years ± 4.59 vs 31.28 years ± 4.59 , $\rho=0.02$). The mean gestational age at delivery was also lower (35.72 weeks ± 3.16 vs 38.49 weeks ± 2.1 , $\rho=0.00$). These differences were statistically significant. Mothers older than 35 years had a higher proportion of low birth weight infants (35.9%). Women with twelve years or more of schooling had lower proportion of low birth weight infants. Other factors that demonstrated higher proportion of low birth weight infants include being preterm (42.6%) or being on

mono/ dual therapy (31.8%). However, the factors that were statistically significant were the age of the mother and preterm birth.

On logistic regression the factors that retained an association with low birth weight were mean maternal age at delivery ($\rho=0.002$; $\beta=0.904$; 95% CI, 0.848 – 0.966) and being on mono/ dual therapy ($\rho=0.039$; $\beta=3.042$; 95% CI, 1.055 – 8.768) while the factor that retained an association with preterm birth was only mean maternal age at delivery ($\rho=0.015$; $\beta=0.935$; 95% CI, 0.886 – 0.987).

DISCUSSIONS

The mean age of the parturients was 31.66 years (± 4.66). This is similar to the mean age of 30.1 years (± 5.1) reported by van der Merwe et al from South Africa¹⁵. Majority (78.8%) of the women were in the age group 20-34 years, similar to the values reported by Ezechi et al from Lagos (84.7%) and Onah et al in Enugu, (72.6%) both in Nigeria^{1,8}. HIV infection in this relatively younger age group has a negative impact on the economy, especially in developing countries. This is on account of this group being sizeable in the workforce.

The overall preterm delivery rate of 35.8% in this cohort of HIV positive women is much higher than the rate of 11.1% reported by Ezechi et al¹, 13.5% by Townsend et al working in England¹⁶ and 13.6% by Taguebue et al who worked in Cameroon¹⁷. All of these worked with groups of HIV positive women. Mokuolu et al reported a rate of 11.8% among the general obstetric population in a teaching hospital in Southern Nigeria¹⁸. In Europe and the US, studies in the general obstetric populations have reported preterm delivery rates of 5-10%¹⁹⁻²¹ and 12.5%^{18,22} respectively. In our cohort of HIV positive women, only older maternal age at delivery and being low birth weight were found to be statistically significant in their association with preterm delivery. The finding of maternal age being

associated with preterm delivery in this study is contrary to the findings of Ezechi et al²³ and Szyld et al.²⁴ who found no association between maternal age and preterm delivery in the groups of HIV positive women they studied. However, it has been noted that pregnancy in the parturient of advanced age is associated with significant increase in maternal and fetal risk²⁵. This is on account of their demonstrating an increased rate of pre-gestational chronic medical complications such as type 2- diabetes mellitus and chronic hypertension.²⁵⁻²⁹

Although some concordance exists between birth weight and gestational age, they are not interchangeable. Only around two thirds of low birth weight infants are preterm³⁰. Term infants maybe of low birth weight because they are 'small for gestational age' or 'light for date' infants. Preterm infants may also be small for gestational age. Thus, they may have neonatal problems additional to those related to shortened gestation, particularly if they are small because of intrauterine growth restriction³⁰. In this cohort of HIV positive women, of the 190 term infants 28.1% were LBW while of the LBW infants 9.6% were delivered at term.

There was a higher proportion of preterm birth among women with fewer years of education, although this did not attain statistical significance. Different variables including occupation, type of housing and years of education have been used by different authors as proxy socioeconomic variables³¹⁻³³. Level of education maybe used as a proxy for socioeconomic status. Poor economic background of the mother has been described as one of the most important predictors of spontaneous preterm delivery³⁰. The interaction of many factors that contribute to the association of preterm birth with socioeconomic status has been described as being complex. For example mothers who smoke cigarettes are twice as likely as non-smoking mothers to deliver before 32 weeks of gestation. However,

while antenatal smoking cessation programs can lower the incidence of preterm birth, other interactions such as better antenatal care, dietary advice or increased social support during pregnancy have not been shown to improve perinatal outcomes or reduce the social inequalities in the incidence of preterm delivery³⁰.

Patients on combination HAART demonstrated higher preponderance of preterm births. This, however, did not achieve statistical significance. The effect of antiretroviral therapy on prevalence of preterm birth among HIV positive women remains unclear with conflicting data from various research settings. While some demonstrated increased risk of preterm delivery with antiretrovirals^{1,9,15,16} others demonstrated no such increase^{24,34}. The workers who demonstrated an association between antiretrovirals and preterm delivery have reported this association with the initiation of combination therapy before pregnancy or during the first trimester of pregnancy^{1,9,15,35,36}.

Various reasons have been proffered for the association of preterm births with HIV and antiretrovirals^{16,37}. One of them is the Th2 to Th1 cytokine shift associated with HAART administration. Successful pregnancies are characterised by an increase in Th2 cytokines and suppression of Th1 cytokine production, a Th1 to Th2 cytokine shift³⁷. A similar shift is also observed in the disease progression of HIV infection. Fiore et al (2006) hypothesised that the increased risk of premature delivery reported in HIV-infected, HAART-treated pregnant women is mediated through changes in the cytokine environment in pregnancy³⁷. They investigated the levels of interleukin IL-2 (Th1) and IL-10 (Th2) in peripheral blood mononuclear cells (PBMCs) 49 HIV-infected women. They were able to demonstrate favourable immunomodulation induced by HAART with increased IL-2 (Th1) and

decreased IL-10 (Th2). They showed that each unit increase in IL-2-PHA slope was associated with an 8% increased risk of premature delivery (AOR, 1.08; 95% CI, 1.0-1.17; $p=0.005$). They concluded that HAART use in pregnancy while providing significant benefits in delaying HIV disease progression and reducing the risk of mother-to-child-transmission, may however be counterproductive in terms of successful pregnancy outcome.

It must however be noted that preterm birth may also be associated with a multitude of factors that include family and psychosocial histories. For example, other factors reported by Ezechi et al in their group of HIV positive women include multiple pregnancies, stressful work, and presence of opportunistic infection at delivery¹. Of particular interest in this cohort is the stratification of gestational age at delivery by mode of delivery. The rate of preterm delivery among women delivering per vaginam was similar to those delivered by elective cesarean delivery. Women delivered by emergency cesarean section however had a higher rate of preterm delivery. Women delivering per vaginam having opted for this mode of delivery antenatally are probably a better reflection of the true prevalence of preterm delivery among HIV +ve women. The prevalence of preterm delivery in this group was 35.5% which is still quite higher than the rate reported in the general obstetric population by Mokuolu et al¹⁸. Other studies do not perform these stratifications often including all births no matter the mode of delivery.

The prevalence of low birth weight in this group of HIV positive women was 21.5%. This is higher than the rates of 9.4% and 13.0% reported respectively by Ezechi et al²³ and Haeri et al³⁶. However, it is similar to the rates of 19.6% and 22.4% reported respectively by van der merwe et al¹⁵ and Yu et al³⁴. All four groups worked with HIV positive pregnant women. The conference of Paediatric Association of Nigeria

(PANCORF) has reported a LBW prevalence of 14% in the general Nigerian obstetric population³⁸. Ahmadu et al. working in Maiduguri reported a prevalence of 12.9% LBW³³, while Ugboma and Onyearugha reported a prevalence of 8.3%³⁹. The latter two groups also worked with the general obstetric population.

Only older maternal age at delivery and being preterm were found to be statistically significant in their association with LBW. Links between rising maternal age and LBW especially among blacks have been reported^{33,39,40}. Possible reasons for this include the fact that mothers at this age may have less physiologic reserve compared to younger mothers. This is because older mothers are more likely to be multiparous which has a depleting effect on their nutrient store³³. In addition, as previously noted, this group of mothers are likely to have pregestational chronic medical illnesses²⁵.

As previously stated, the level of education of the mothers was used as proxy for socioeconomic class (SEC) with lower class being associated with fewer years of education. Women with more years of education had a lower proportion of LBW. It has been suggested that the effect of low SEC factors start at the time of conception through low physiologic reserves, inadequate medical care, poor diet and high risk of infectious diseases^{33,41,42}. In addition, women with more years of education could be exposed to information on the importance of prenatal health care coupled with personal and environmental cleanliness, which has been found to reduce the toll of infectious disease^{33,41}. Promoting these practices among women, including HIV +ve women, may lower the possibility of mothers giving birth to LBW babies⁴¹.

Interestingly, women on mono/dual therapy had higher proportion of low birth weight infants. This is in spite of their having fewer preterm infants. Various studies have attempted to evaluate the

effect of maternal ART regimens on adverse infant outcome such as LBW. While some workers have demonstrated increased odds of LBW among HIV +ve women on HAART^{16,36} others have found no association between HAART and LBW, no matter the treatment group^{9,24,34}. A possible explanation for the increased odds of LBW among HIV positive women on HAART maybe found in the effect of HAART on preeclampsia. An association between HAART and an increased risk of pre-eclampsia has been observed⁴³⁻⁴⁵, and the association of hypertension and pre-eclampsia with increased risks of preterm birth and LBW is well recognized^{46,47}. We must caution that our study is an overall evaluation of perinatal outcomes in HIV positive parturients. Our retrospective study design precluded an optimal assessment of medication compliance within this population. In addition, no data was collected on duration of receipt of ART prior to pregnancy. In addition, preterm birth has been associated with a multitude of factors that include family and psychosocial histories for which we could not account. Despite these limitations, we conclude that HIV positive women who use HAART may be at increased risk for preterm birth and low birth weight. Antenatal surveillance in HIV positive mothers should therefore include serial fetal growth assessment by USS. An HIV-infected woman of child bearing age is in the unique position of making treatment decisions which will not only impact on her own health, but may also affect her future children^{48,49} (1, 8). Thus health care providers need to discuss future plans with HIV positive women when deciding what kind of antiretroviral therapy to initiate.

Table 1: Characteristics Of HIV Positive Mothers Delivered At UCH Ibadan

| Maternal Characteristic | Frequency (307) | Percentage (100.0 %) |
|------------------------------------|------------------|----------------------|
| Age of mother | | |
| <20 | 1 | 0.3% |
| 20-25 | 28 | 9.1% |
| 26-30 | 101 | 32.9% |
| 31-35 | 113 | 36.8% |
| 36-40 | 55 | 17.9% |
| >40 | 9 | 2.9% |
| Educational level | | |
| Tertiary | 105 | 34.2% |
| Secondary | 131 | 42.7% |
| Primary | 24 | 7.8% |
| None | 10 | 3.3% |
| Others | 25 | 8.1% |
| Not stated | 12 | 3.9% |
| Marital status | | |
| Single | 2 | 0.7% |
| Married | 303 | 98.7% |
| Not stated | 2 | 0.7% |
| Gestational age at delivery | | |
| <28 | 1 | 0.3% |
| 28-33 | 18 | 5.9% |
| 34-37 | 91 | 29.6% |
| = 38 | 190 | 61.2% |
| Not stated | 7 | 2.9% |
| Mode of delivery | | |
| Vaginal del. | 113 | 37.1% |
| ELCS | 84 | 27.4% |
| EMCS | 110 | 35.5% |
| Drug type | | |
| Mono/ dual | 22 | 7.2% |
| NonNNRTI | 198 | 64.5% |
| PI-based | 33 | 10.7% |
| Unknown | 54 | 17.6% |

Table 2: Gestational age at delivery by mode of delivery

| Gest. age at delivery | SVD (N=111) | ELCS (N=84) | EMCS (N=109) | |
|----------------------------|---------------|---------------|---------------|------------------------|
| <28 | 1 (.9%) | 0 (.0%) | 0 (.0%) | P-value- 0.395 |
| 28-33 | 6 (5.4%) | 1 (1.2%) | 9 (8.3%) | χ ² - 8.405 |
| 34-37 | 29 (26.1%) | 25 (29.8%) | 36 (33.0%) | |
| 38-42 | 71 (64.0%) | 56 (66.7%) | 61 (56.0%) | |
| >42 | 4 (3.6%) | 2 (2.4%) | 3 (2.8%) | |
| Mean GA at delivery | 38.01(± 2.99) | 38.8 (± 1.52) | 37.51(± 2.82) | p=0.153 |

Table 3: Characteristics of Infants Delivered To HIV Positive Mothers at UCH Ibadan

| Neonatal Characteristic | Frequency (307) | Percentage (100.0 %) |
|--------------------------------|------------------|----------------------|
| Sex of neonate | | |
| Male | 168 | 54.7% |
| Female | 137 | 44.6% |
| Not stated | 2 | 0.7% |
| Status at delivery | | |
| Alive | 294 | 95.8% |
| Dead | 9 | 2.9% |
| Not stated | 4 | 1.3% |
| Birth weight of infants | | |
| <1.5 | 8 | 2.6% |
| 1.5-2.49 | 58 | 18.9% |
| 2.5-3.9 | 231 | 75.2% |
| >3.9 | 5 | 1.6% |
| Not stated | 5 | 1.6% |
| Prematurity | | |
| Preterm | 110 | 35.8% |
| Not preterm | 190 | 61.9% |
| Post term | 7 | 2.3% |
| Low birth weight | | |
| Low birth weight | 66 | 21.5% |
| Not LBW | 236 | 76.8% |
| Not stated | 5 | 1.6% |

Table 4: Factors Associated With Preterm Birth

| Maternal Characteristic | Preterm (N=110) | | Not Preterm(N=190) 95% CI | |
|----------------------------------|-----------------|--------------------|---------------------------|----------------|
| | | | | p-value |
| Mean maternal age (years) | 32.61±5.09 | 31.19±4.32 | +0.323 to -2.517 | 0.089 |
| Mean birth weight (kg) | 2.48±0.61 | 2.96±0.44 | -0.596 to -0.354 | 0.000 |
| Age of mother | Preterm | Not Preterm | χ2 | p-value |
| <25 | 9, 33.3% | 18, 66.7% | 1.062 | 0.587 |
| 26-30 | 28, 28.3% | 71, 71.9% | | |
| 31-35 | 41, 36.6% | 71, 63.4% | | |
| >35 | 32, 51.6% | 30, 48.4% | | |
| Educational level | | | | |
| Tertiary | 35, 34.3% | 67, 65.7% | 6.616 | 0.158 |
| Secondary | 44, 34.1% | 85, 65.9% | | |
| Primary/ none | 17, 51.5% | 16, 48.5% | | |
| Others | 9, 36% | 16, 64.0% | | |
| Mode of delivery | | | | |
| Vaginal del. | 39, 35.5% | 71, 64.5% | 2.428 | 0.297 |
| ELCS | 26, 31.3% | 57, 68.7% | | |
| EMCS | 45, 42.1% | 62, 57.9% | | |
| Sex of baby | | | | |
| Male | 58, 35.6% | 105 (64.4%) | 0.53 | 0.718 |
| Female | 51, 37.8% | 84, 62.2% | | |
| Birth weight at delivery | | | | |
| LBW | 46, 71.9% | 18, 28.1% | 44.128 | 0.00 |
| Not LBW | 62, 26.7% | 170, 73.3% | | |
| Drug type | | | | |
| Mono/ dual | 5, 25.0% | 15, 75.0% | 1.064 | 0.587 |
| NonNNRTI | 71, 36.2% | 125, 63.8% | | |
| PI-based | 12, 37.5% | 20, 62.5% | | |

Table 5: Factors Associated With Low Birth Weight (LBW)

| LBW (N= 66) | Not LBW (236) | 95% CI | p-value |
|---------------------------------------|---------------|----------------|--------------------------|
| Maternal Characteristic | | | |
| Mean maternal age (years) | 33.28±4.59 | 31.28±4.59 | +0.729 to +3.28 0.02 |
| Mean gest. Age at del. (weeks) | 35.78±3.16 | 38.49±2.10 | -3.365 to -2.047 0.000 |
| Age of mother | LBW | Not LBW | χ2 p-value |
| <25 | 4, 13.5% | 25, 86.2% | 13.137 0.004 |
| 26-30 | 13, 13.1% | 86, 86.9% | |
| 31-35 | 26, 23.4% | 85, 76.6% | |
| >35 | 23, 35.9% | 41, 64.1% | |
| Educational level | | | |
| Tertiary | 18, 17.6% | 84, 82.4% | 2.247 0.690 |
| Secondary | 28, 21.4% | 103, 78.6% | |
| Primary/ none | 9, 27.3% | 24, 72.7% | |
| Others | 7, 28.0% | 18, 72.0% | |
| Mode of delivery | | | |
| Vaginal del. | 26, 23.2% | 86, 76.8% | 2.616 0.27 |
| ELCS | 13, 15.7% | 70, 84.3% | |
| EMCS | 27, 25.0% | 81, 75.0% | |
| Sex of baby | | | |
| Male | 33, 19.9% | 133 (80.1%) | 0.643 0.254 |
| Female | 32, 23.7% | 103, 76.3% | |
| Gestational age at delivery | | | |
| Preterm | 46, 42.6% | 62, 57.4% | 44.128 0.00 |
| Not LBW | 18, 9.6% | 170, 90.4% | |
| Drug type | | | |
| Mono/ dual | 5, 31.8% | 15, 68.2% | 1.557 0.459 |
| NonNNRTI | 42, 21.4% | 154, 78.6% | |
| PI-based | 6, 18.2% | 27, 81.8% | |

Table 6 Predictors Of LBW And Preterm Delivery

| Predictors of LBW | | | | |
|---------------------------------------|--------|---------|--------------|--------|
| Educational level | signif | exp (β) | 95% CI lower | upper |
| Tertiary | 0.638 | - | - | - |
| Secondary | 0.155 | 2.844 | 0.672 | 12.32 |
| Primary | 0.232 | 2.314 | 0.584 | 0.168 |
| None | 0.482 | 1.810 | 0.346 | 9.481 |
| Others | 0.442 | 2.195 | 0.296 | 16.285 |
| Maternal age at delivery | 0.002 | 0.904 | 0.848 | 0.966 |
| Gest. Age at delivery | 0.170 | 1.041 | 0.983 | 1.102 |
| Mode delivery | | | | |
| Vaginal delivery | 0.24 | - | - | - |
| ELCS | 0.784 | 1.095 | 0.573 | 2.091 |
| EMCS | 0.102 | 1.954 | 0.875 | 4.367 |
| Drug type | | | | |
| NonNNRTI | 0.176 | - | - | - |
| M/D | 0.039 | 3.042 | 1.055 | 8.768 |
| PI | 0.054 | 3.795 | 0.976 | 14.765 |
| Predictors of preterm delivery | | | | |
| Educational level | signif | exp (β) | 95% CI lower | upper |
| Tertiary | 0.305 | - | - | - |
| Secondary | 0.619 | 1.401 | 0.371 | 5.294 |
| Primary | 0.569 | 1.456 | 0.399 | 5.308 |
| None | 0.359 | 0.492 | 0.108 | 2.242 |
| Others | 0.463 | 2.020 | 0.308 | 13.231 |
| Maternal age at delivery | 0.015 | 0.935 | 0.886 | 0.987 |
| Mode delivery | | | | |
| Vaginal delivery | 0.427 | - | - | - |
| ELCS | 0.347 | 1.311 | 0.746 | 2.305 |
| EMCS | 0.222 | 1.491 | 0.785 | 2.831 |
| Drug type | | | | |
| NonNNRTI | 0.834 | - | - | - |
| M/D | 0.563 | 0.725 | 0.244 | 2.156 |
| PI | 0.646 | 0.739 | 0.204 | 2.681 |

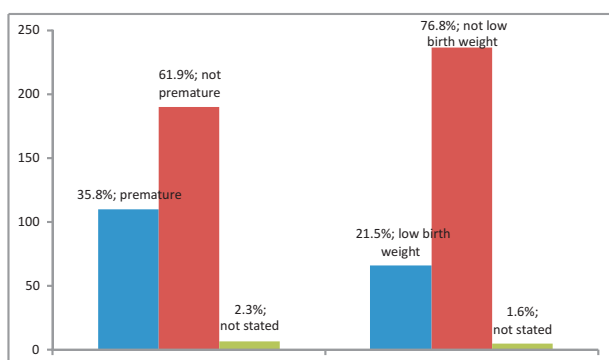


Figure 1; proportion of adverse obstetric outcome - prematurity and low birth weight

REFERENCES

- Ezechi OC, David AN, Gab-Okafor CV, et al. Incidence of and socio-biologic risk factors for spontaneous preterm birth in HIV positive Nigerian women. *BMC Pregnancy Childbirth* 2012; **12**: 93.
- Charurat M, Datong P, Matawal B, Ajene A, Blattner W, Abimiku A. Timing and determinants of mother-to-child transmission of HIV in Nigeria. *Int J Gynaecol Obstet* 2009; **106**(1): 8-13.
- NACA. Update on the HIV/AIDS epidemic and response in Nigeria. National Agency for Control of AIDS. Abuja Nigeria; 2011. . 2011.
- Afe JA AN, Emokpa A, Fagorala T, Disu AE, Abidoye GO, Ganikale I, Audu RA. Outcome of PMTCT services and factors affecting vertical transmission of HIV infection in Lagos, Nigeria *HIV & AIDS review* 2011; **10**(1): 14-8.
- Chamiso D. Pregnancy outcome in HIV-1 positive women in Gandhi Memorial Hospital Addis Ababa, Ethiopia. *East Afr Med J* 1996; **73**(12): 805-9.
- Dinsmoor MJ. HIV infection and pregnancy. *Clin Perinatol* 1994; **21**(1): 85-94.
- Kumar RM, Uduman SA, Khurranna AK. Impact of maternal HIV-1 infection on perinatal outcome. *Int J Gynaecol Obstet* 1995; **49**(2): 137-43.
- Onah HE, Obi SN, Agbata TA, Oguanuo TC. Pregnancy outcome in HIV-positive women in Enugu, Nigeria. *J Obstet Gynaecol* 2007; **27**(3): 271-4.
- ECS. European Collaborative Study; Swiss Mother and Child HIV Cohort Study. Combination antiretroviral therapy and duration of pregnancy. *AIDS* 2000; **14**(18): 2913-20.
- ECS. European Collaborative Study: Exposure to antiretroviral therapy in utero or early life: the health of uninfected children born to HIV-infected women. *J Acquir Immune Defic Syndr* 2003; **32**(4): 380-7.
- Thorne C, Patel D, Newell ML. Increased risk of adverse pregnancy outcomes in HIV-infected women treated with highly active antiretroviral therapy in Europe. *AIDS* 2004; **18**(17): 2337-9.
- Tuomala RE, Watts DH, Li D, et al. Improved obstetric outcomes and few maternal toxicities are associated with antiretroviral therapy, including highly active antiretroviral therapy during pregnancy. *J Acquir Immune Defic Syndr* 2005; **38**(4): 449-73.
- Tuomala RE, Shapiro DE, Mofenson LM, et al. Antiretroviral therapy during pregnancy and the risk of an adverse outcome. *N Engl J Med* 2002; **346**(24): 1863-70.
- Read JS, Burchett S, Shapiro RE, et al. Low birth weight and preterm birth among infants of HIV- infected mothers according to maternal receipt of antiretroviral drug(s) during pregnancy: PACTG 367. 41st Annual Meeting of the Infectious Diseases Society of America. San Diego, October 2003 [abstract 677]. 2003.
- van der Merwe K, Hoffman R, Black V,

- Chersich M, Coovadia A, Rees H. Birth outcomes in South African women receiving highly active antiretroviral therapy: a retrospective observational study. *J Int AIDS Soc* 2011; **14**: 42.
16. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. *AIDS* 2007; **21**(8): 1019-26.
17. Taguebue J MF, Zingg W, Mve Koh V, Atchoumi A, Gervais A, E T. Risk Factors for Prematurity among Neonates from HIV Positive Mothers in Cameroon. *World Journal of AIDS* 2011; **1**: 1-7.
18. Mokuolu OA, Suleiman B, Adesiyun O, Adeniyi A. Prevalence and determinants of pre-term deliveries in the University of Ilorin Teaching Hospital, Ilorin, Nigeria. *Pediatr Rep* 2010; **2**(1): e3.
19. Steer P. The epidemiology of preterm labour. *BJOG* 2005; **112 Suppl 1**: 1-3.
20. Hoyert DL, Mathews TJ, Menacker F, Strobino DM, Guyer B. Annual summary of vital statistics: 2004. *Pediatrics* 2006; **117**(1): 168-83.
21. Bibby E, Stewart A. The epidemiology of preterm birth. *Neuro Endocrinol Lett* 2004; **25 Suppl 1**: 43-7.
22. Romero R, Sirtori M, Oyarzun E, et al. Infection and labor. V. Prevalence, microbiology, and clinical significance of intraamniotic infection in women with preterm labor and intact membranes. *Am J Obstet Gynecol* 1989; **161**(3): 817-24.
23. Ezechi OC, Gab-Okafor CV, Oladele DA, et al. Pregnancy, obstetric and neonatal outcomes in HIV positive Nigerian women. *Afr J Reprod Health* 2013; **17**(3): 160-8.
24. Szyld EG, Warley EM, Freimanis L, et al. Maternal antiretroviral drugs during pregnancy and infant low birth weight and preterm birth. *AIDS* 2006; **20**(18): 2345-53.
25. Yogev Y, Melamed N, Bardin R, Tenenbaum-Gavish K, Ben-Shitrit G, Ben-Haroush A. Pregnancy outcome at extremely advanced maternal age. *Am J Obstet Gynecol* 2010; **203**(6): 558 e1-7.
26. Simchen MJ, Yinon Y, Moran O, Schiff E, Sivan E. Pregnancy outcome after age 50. *Obstet Gynecol* 2006; **108**(5): 1084-8.
27. Callaway LK, Lust K, McIntyre HD. Pregnancy outcomes in women of very advanced maternal age. *Aust N Z J Obstet Gynaecol* 2005; **45**(1): 12-6.
28. Jacobsson B, Ladfors L, Milsom I. Advanced maternal age and adverse perinatal outcome. *Obstet Gynecol* 2004; **104**(4): 727-33.
29. Salihu HM, Shumpert MN, Slay M, Kirby RS, Alexander GR. Childbearing beyond maternal age 50 and fetal outcomes in the United States. *Obstet Gynecol* 2003; **102**(5 Pt 1): 1006-14.
30. Tucker J, McGuire W. Epidemiology of preterm birth. *BMJ* 2004; **329**(7467): 675-8.
31. Frank R, Pelcastre B, Salgado de Snyder VN, Frisbie WP, Potter JE, Bronfman-Pertzovsky MN. Low birth weight in Mexico: new evidence from a multi-site postpartum hospital survey. *Salud Publica Mex* 2004; **46**(1): 23-31.
32. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med* 2008; **359**(1): 61-73.
33. Ahmadu BU, Mustapha B, Bappariya JI, Alfred N, Joel Z. The effects of weathering demonstrated by maternal age on low birth weight outcome in babies. *Ethiop J Health*

- Sci 2013; **23**(1): 27-31.
34. Yu L, Li WY, Chen RY, et al. Pregnancy outcomes and risk factors for low birth weight and preterm delivery among HIV-infected pregnant women in Guangxi, China. *Chin Med J (Engl)* 2012; **125**(3): 403-9.
35. Kourtis AP, Schmid CH, Jamieson DJ, Lau J. Use of antiretroviral therapy in pregnant HIV-infected women and the risk of premature delivery: a meta-analysis. *AIDS* 2007; **21**(5): 607-15.
36. Haeri S, Shauer M, Dale M, et al. Obstetric and newborn infant outcomes in human immunodeficiency virus-infected women who receive highly active antiretroviral therapy. *Am J Obstet Gynecol* 2009; **201**(3): 315 e1-5.
37. Fiore S, Newell ML, Trabattoni D, et al. Antiretroviral therapy-associated modulation of Th1 and Th2 immune responses in HIV-infected pregnant women. *J Reprod Immunol* 2006; **70**(1-2): 143-50.
38. Okolo. Overview of Neonatal Mortality-Global Perspectives. PANCORF (Conference of Paediatric Association of Nigeria). S1-S43 2009.
39. Ugboma HA, Onyearugha CN. Low birthweight delivery: prevalence and associated factors as seen at a tertiary health facility. *Niger J Clin Pract* 2013; **16**(2): 184-7.
40. Holzman C, Eyster J, Kleyn M, et al. Maternal weathering and risk of preterm delivery. *Am J Public Health* 2009; **99**(10): 1864-71.
41. Kogan MD. Social causes of low birth weight. *JR Soc Med* 1995; **88**(11): 611-5.
42. Torres-Arreola LP, Constantino-Casas P, Flores-Hernandez S, Villa-Barragan JP, Rendon-Macias E. Socioeconomic factors and low birth weight in Mexico. *BMC Public Health* 2005; **5**: 20.
43. Wimalasundera RC, Larbalestier N, Smith JH, et al. Pre-eclampsia, antiretroviral therapy, and immune reconstitution. *Lancet* 2002; **360**(9340): 1152-4.
44. ECS. Pregnancy-related changes in the longer-term management of HIV-infected women in Europe. *Eur J Obstet Gynecol Reprod Biol* 2003; **111**(1): 3-8.
45. Suy A, Martinez E, Coll O, et al. Increased risk of pre-eclampsia and fetal death in HIV-infected pregnant women receiving highly active antiretroviral therapy. *AIDS* 2006; **20**(1): 59-66.
46. Xiao R, Sorensen TK, Williams MA, Luthy DA. Influence of pre-eclampsia on fetal growth. *J Matern Fetal Neonatal Med* 2003; **13**(3): 157-62.
47. Vatten LJ, Skjaerven R. Is pre-eclampsia more than one disease? *BJOG* 2004; **111**(4): 298-302.
48. Tovo PA, Newell ML, Mandelbrot L, Semprini AE, Giaquinto C. Recommendations for the management of HIV infected women and their infants - A European Consensus. *Luxembourg: European Commission*; 1999: 1-37.
49. USPHSTF. US Public Health Service Task Force. Recommendations for the use of antiretroviral drugs in pregnant women for maternal health and reducing perinatal HIV-1 transmission in the United States. *MMWR* 2000; **47**: 1-31.