CLINICAL PRACTICE ARTICLE

Pregnancy Outcome among HIV Positive Women Receiving Antenatal HAART Versus Untreated Maternal HIV Infection

Onakewhor Joseph, Olagbuji Biodun and Ezeanochie Michael

ABSTRACT

Objective: To evaluate adverse pregnancy outcome in HIV infected women who received highly active antiretroviral therapy (HAART) from early pregnancy compared with untreated-maternal HIV infection.

Study Design: A cohort study.

Place and Duration of Study: Antenatal clinic, University of Benin Teaching Hospital, Nigeria, from January 2008 to June 2009.

Methodology: Two hundred and forty nine HIV infected women who had intrapartum care constituted the study population. Unbooked HIV positive pregnant women, who had not received antiretroviral drugs during the antenatal period but received nevirapine in labour, referred to as untreated-maternal HIV infection, were compared with women who received HAART early in pregnancy. Outcome measures of interest were obstetric complications and perinatal outcome proportion.

Results: Intrauterine growth restriction (IUGR) (20.5% vs. 6.3%, p = 0.003), pre-term birth (25.0% vs. 9.8%, p = 0.005) and caesarean delivery (45.5% vs. 29.8%, p = 0.04) were significantly higher among women with untreated-HIV infection in pregnancy compared with women who received HAART from early pregnancy. Untreated maternal HIV-infection was associated with higher frequency of birth weight less than 2500g, 5-minutes Apgar score less than 7 and admission into neonatal unit (p < 0.05). Women with primary education were significantly higher in the group with untreated maternal HIV infection (27.3% vs. 12.7%, p = 0.003).

Conclusion: Untreated maternal HIV-infection in pregnancy may be associated with adverse pregnancy outcome. HIV positive women with low level of education utilise PMTCT services suboptimally. This information is important for programmes designed to increase access to PMTCT services including HAART from early pregnancy.

Key words: *HIV. Pregnancy. Antiretroviral prophylaxis. Labour. HAART therapy.*

INTRODUCTION

HIV/AIDS infection is an important cause of maternal and perinatal morbidity/mortality in sub Saharan Africa.[1,2] Anaemia, pre-term labour, intrauterine growth restriction (IUGR), foetal deaths, still births and low birth weight are some of the complications associated with HIV in pregnancy.[3-6] There is now a consensus that HIV positive pregnant women should receive appropriate antiretroviral regimen to reduce the burden of the infection. Use of highly active antiretroviral therapy (HAART) from early pregnancy, short course combination antiretroviral therapy (ART) in late pregnancy and single dose nevirapine in labour are among the ART regimen available for HIV positive women during pregnancy.[7-9]

Although the single dose nevirapine in labour is the most widely implemented ART regimen,[10] HAART when started early in pregnancy has been recognised to be more efficacious with associated improvement in infant survival.[11] There is an evidence that the risk of HIV transmission from mother to child is associated with late initiation of therapy during pregnancy.[12] This scientific evidence provided the basis for the new recommendation by the World Health Organisation for earlier and more efficacious antiretroviral prophylaxis options using HAART to reduce the risk of HIV transmission and improve infant survival.[13]

Widespread utilisation of HAART for prophylaxis in pregnancy may be hindered by certain factors in Nigeria and other under-resourced countries such as limited resources and logistics for sustainability. Importantly, other barriers may be client related such as non-utilisation of antenatal care services or the presence of informal/alternative care providers in an environment where there is widespread poverty and ignorance. These may limit the success of universal antenatal HIV testing of all pregnant women since routine antenatal HIV testing is essential to a successful prevention of maternal-to-child transmission (PMTCT) programme. PMTCT services were offered to the women according to the 2005 Nigerian National Guidelines on PMTCT as published by the FMOH with the use antiretroviral drugs for HIV positive women with HAART (Zidovudine,

Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin-City, Edo State, Nigeria.

***Correspondence:** Dr. Olagbuji Biodun, Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, PMB 1111, Benin-City, Edo State, Nigeria. E-mail: nelsonabiodun@yahoo.com*

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Lamivudine and Nevirapine) as a first line regimen, while HIV positive women diagnosed in labour were offered single dose nevirapine. The PMTCT programme consists of routine HIV testing and counselling (with provision to opt-out), post-test counselling and administration of antiretroviral drugs. Also, modified intrapartum care, infant feeding options, treatment of opportunistic infections and administration of antiretroviral therapy to the baby soon after birth are carried out as published in the guideline.[7]

The data from this study will provide relevant information for programme management in an environment where HAART is infrequently used for PMTCT.

The objective of the present study was to evaluate the pregnancy outcome among women with untreated-HIV infection who had single dose nevirapine in labour and those who received HAART early in pregnancy for PMTCT.

METHODOLOGY

It was a cohort study. The prenatal and delivery records of 249 HIV positive women attending antenatal clinic at the University of Benin Teaching Hospital (UBTH), Nigeria, were reviewed between January 2008 to June 2009. The hospital is a referral centre that offers care for HIV infected persons including comprehensive PMTCT services in a programme funded by the Nigerian Federal Ministry of Health (FMoH) and Institute of Human Virology, Nigeria (IHVN). Approval for this study, regarding ethical issues related to human subjects, was given by the Research and Ethics Committee of the hospital. Women with HIV infection in pregnancy who received HAART from early pregnancy for antiretroviral treatment or prophylaxis were compared with untreated-maternal HIV-infected women. Women who did not receive antiretroviral therapy during the antenatal period or HIV positive women diagnosed in labour constituted the group referred to as untreated-maternal HIV infection.

Patients with AIDS, chronic medical disorders predating pregnancy, multiple gestation and short duration of HAART (commencement in the third trimester) were excluded from the study.

During the study period, women with untreated HIV-infection referred in labour from peripheral hospitals following a diagnosis of HIV infection were re-counselled, rescreened and women diagnosed HIV-positive received single dose nevirapine for PMTCT. They were compared with HIV positive women who had antenatal care in our centre and received HAART from early pregnancy (second trimester) following the diagnosis of HIV infection and delivered after 28 weeks of gestation. The data was obtained from a comprehensive obstetric and perinatal hospital database which contained detailed information on every woman delivering at UBTH. The data were coded by the doctors on duty at each delivery and subsequently presented at the daily departmental clinical meetings where they were vetted by the consultants before storage in the database to ensure the completion of reporting.

Outcomes of interest included; the social and demographic characteristics of the women, antenatal complications of pregnancy, labour and the foetal outcome.

Data analysis was conducted using the statistical package for social sciences version 15, (SPSS, Chicago, IL, USA). The differences in proportion were evaluated using chi-square test for categorical variables and the t-test for continuous variables. Statistical significance was set at p-value < 0.05.

RESULTS

Of the 249 women in the study population, 44 women (17.7%) had antenatally untreated-HIV infection, while 205 women (82.3%) received HAART from early pregnancy. Significantly higher number of women with untreated-HIV infection had primary education compared to the women who were on HAART (27.3% vs. 12.7%, p=0.003) (Table I). There was no significant difference between both groups with regards to age groups, mean parity and mean gestational age at delivery.

Table I: Clinical characteristics of the women.

Variable	HAART (n=205) (%)	Nevirapine (n=44) (%)	p-value
Age (years)			
< 35	25 (12.2)	6 (13.6)	0.793
≥ 35	180 (87.8)	38 (86.4)	
Parity (mean±SD)	1.8±2.3	1.2±1.5	0.09
Level of Education			
None	0 (0)	0 (0)	
Primary	26 (12.7)	12 (27.3)	0.003
Secondary	110 (53.7)	27 (61.4)	
Tertiary	69 (33.7)	5 (11.4)	
Gestational age at delivery (mean±SD)	38.1±2.4	37.8±2.8	0.475

The antenatal obstetric complications and mode of delivery between both groups are compared in Table II. Intra-uterine foetal growth restriction (20.5% vs. 6.3%, p=0.003), pre-term birth (25.0% vs. 9.8%, p=0.005) and caesarean delivery (45.5% vs. 29.8%, p=0.04) were significantly higher among the women with untreated-HIV infection (p < 0.05). The occurrence of premature rupture of membranes (PROM) and anaemia at admission in labour were comparable between both groups.

With regards to perinatal outcome (Table III) birth weight less than 2500 g (36.4% vs. 18.5%, p=0.009), 5-minute Apgar score less than 7 (13.6% vs. 5.4%, p=0.048) and

Table II: Antenatal obstetric complications and mode of delivery.

Variable	HAART (n=205) (%)	Nevirapine (n=44) (%)	p-value
Intra-uterine foetal growth restriction	13 (6.3)	9 (20.5)	0.003
Pre-term premature rupture of membranes	28 (13.7)	8 (18.2)	0.431
Pre-term birth	20 (9.8)	11 (25.0)	0.005
Anaemia in labour	61 (29.8)	19 (43.2)	0.084
Delivery by caesarean section	61 (29.8)	20 (45.5)	0.04

Table III: Perinatal outcome.

Variable	HAART (n=205) (%)	Nevirapine (n=44) (%)	p-value
Stillbirth	4 (2.0)	2 (4.5)	0.309
Early neonatal death	1 (0.5)	0 (0)	0.642
5th minute Apgar score < 7	11 (5.4)	6 (13.6)	0.048
Birth weight < 2500 grams	38 (18.5)	16 (36.4)	0.009
Birth weight (mean±SD)	2877 ± 651	2721 ± 679	0.155
Admission into the neonatal unit	20 (9.8)	11 (25.0)	0.005

admission into the neonatal unit (25.0% vs. 9.8%, p=0.005) were significantly higher in women who had single dose nevirapine compared with those who received antenatal HAART (p < 0.05). There was no significant difference between both groups with respect to the other indices of foetal outcome.

DISCUSSION

In this study about 20% of the study population were untreated for maternal HIV-infection in pregnancy (received single dose nevirapine in labour for PMTCT) compared to about 80% that received antenatal HAART commencing early in pregnancy. About one fifth of the study population, who might have benefited from antenatal HAART in conformity with current best practice to suppress the viral load below detectable levels in pregnancy, were unable to access it despite its availability in our centre. A lower level of education and possibly lack of awareness of PMTCT services in the cohort with untreated-HIV infection compared to those who had HAART early in pregnancy, could be reasons for not accessing optimum PMTCT services including HAART. This is similar to a previous study in Tanzania which showed that low maternal education and rural residence were associated with unknown HIV status which was found to be a reason for single dose intra-partum nevirapine in this cohort study.[14] This suggests that provision of the capacity to safely administer HAART in health facilities may not necessarily be the only determinant of HIV infected pregnant women accessing these services as social and cultural determinants may also be contributory factors.

The present findings demonstrated a significant increase in the incidence of intra-uterine growth restriction, pre-term birth and delivery by caesarean section among antenatally HIV- untreated women who had single dose nevirapine in labour compared to women who had HAART from early pregnancy. These findings are similar to those seen in the previous study by Habib *et al.* in which antenatally untreated HIV-infected women had higher rates of adverse pregnancy outcomes than treated HIV-infected women who had antiretroviral therapy in pregnancy.[14] The higher incidence of pre-term births among antenatally untreated HIV-infected women shows that HIV itself may be a risk factor for pre-term birth and not necessarily antiretroviral therapy as the association of HIV and antiretroviral therapy with pre-term delivery remains unclear with conflicting findings from previous studies.[15-19]

The findings show that women with untreated HIV infection had higher incidence of IUGR. The difference in outcome of IUGR among the groups of women in this study affirms the current recommendations of World Health Organization regarding early initiation of antiretroviral therapy for HIV-infected women during pregnancy as it may reduce the incidence of IUGR and decrease the perinatal and infant mortality associated with IUGR.[20] The higher rate of caesarean section in women without early antenatal HAART is not unexpected as caesarean section is a recommended delivery modality for women with untreated HIV-infection in pregnancy. This could also be explained by the occurrence of IUGR and pre-term delivery in this study which are recognised risk factors for intrapartum foetal distress and still births. These reasons may also be responsible for the increase in admission into the neonatal unit among the newborns of women with antenatally untreated-HIV infection.

Although, the retrospective design is a limitation of this study, it remains relevant as a prospective design would hardly be ethical since it is now standard practice to offer antiretroviral treatment to HIV positive women during pregnancy to reduce the risks of mother to child transmission.

These findings support the new WHO recommendation for the use of HAART as the first line regimen for antiretroviral prophylaxis in HIV-infected pregnant women as this is also associated with better pregnancy outcome and improved infant survival. However, with the recent effort to scale up the access to antiretroviral prophylaxis using HAART from early pregnancy for PMTCT, client related factors and other socio-cultural barriers may be impediment to the success of this programme in our environment. Therefore, this information is important for the incorporation of strategies to overcome these barriers in addition to increasing the capacity to safely administer HAART at the peripheral centres.

CONCLUSION

Improved obstetric and perinatal outcomes for HIV positive women are to be expected when HAART is initiated from early pregnancy for PMTCT compared to administering single dose nevirapine in labour.

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