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Birth Outcomes in HIV-1-Infected Women Receiving Highly Active Antiretroviral Therapy (HAART) Prior to Conception versus During Pregnancy in Yaoundé, Cameroon

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Abstract

Objective: To assess the impact of antiretroviral on birth outcome according to the timing of antiretroviral initiation in relation to pregnancy in human immunodeficiency virus (HIV) infected pregnant women.

Methods: Cross sectional study, observational, in a single referral site, the Centre Hospitalier d'ESSOS of Yaoundé from 2008 to 2013. Babies born to HIV positive mothers under HAART prior to conception were compared with those initiating treatment during pregnancy. Main measurement: rate of preterm birth (PTB) defined as gestational age<37 weeks at birth and low birth weight (LBW)<2500 g.

Results: We included 617 newborn babies. Almost 96% of their mothers were taking antiretroviral drugs free of protease inhibitor. Overall rate of LBW was at 11.6% and PTB at 9.7 %. In bivariate analysis, PTB were similarly rated in preconception HAART(8.1%) versus during pregnancy (10.1%), odd ratio (1.22: 0.6-2.5, p=0.90); in ART started during pregnancy, the PTB frequency was analogous, irrespective of the moment of antiretroviral therapy (ART) started before 28 weeks (10.9%), or after (9%), p=0.9. In addition, LBW rates were registered at 11.7% prior to pregnancy versus 11.6% after conception (p=0.9). The ART started during pregnancy <28 weeks pregnancy was almost twice associated to a higher risk of LBW odd ratio (1.87: 1.02-3.44, p<0.05).

Conclusion: ART prior to conception mainly free of protease inhibitor does not increase the risk of PTB or LBW in Yaoundé, Cameroon.

Keywords: HIV-1; Antiretroviral therapy; Pregnancy; LBW; PTB; Monotherapy; Nutritional status

Introduction

Mother-to-child transmission (MTCT) of HIV can occur during pregnancy, delivery or the breastfeeding period; without any medical care, the transmission rate ranges from 30 to 45%. During the recent years, this rate has been significantly and increasingly curtailed thanks to the use of combined antiretroviral therapy (ART) with the use of more and more effective regimen [1,2], leading to a residual transmission rate of HIV below 2% even during breastfeeding in countries with limited resources. More still, this transmission rate can be slashed at a lowest level for women under ART before conception and therefore justify the moving towards generalization of highly active antiretroviral therapy (HAART) during pregnancy [3,4]. The safety of those treatments during pregnancy is controversial; numerous studies have been conducted assessing the impact of those protocols on birth outcomes namely preterm delivery and low birth weight, with conflicting results depending on the ART protocol, the timing of the treatment and other associated factors [5-8]. In western countries, the antiretroviral therapy started prior to conception or the usage of protease inhibitors has been indexed. In Africa unfortunately, only a few reports are available on the topic, especially considering those benefiting of highly active antiretroviral therapy (HAART), in relation to the timing of treatment commencement, prior pregnancy or after [9,10]. Since 2006, the Cameroon national guidelines recommended the use of combined ART for women with severe immunodeficiency, while women with a conserved immune status were eligible to immunotherapy by Zidovudine (option A); later on in 2013, the country went in for B^+ option as recommended by the World Health Organization (WHO), since option A had faced many operational bottlenecks. In this context, due to a growing number of women getting pregnant under combined ART, we set up a study in order to assess the impact of ART on both birth weight and term at birth according to the timeline of ART started prior to conception or during pregnancy.

Methods

Study design

This was a cross sectional study nested within an observational cohort of mothers and babies pairs. The characteristic of this cohort was described elsewhere [11].

Study site

The study site was the Centre Hospitalier d'ESSOS, a teaching hospital recorded as a referral centre for antiretroviral treatment in Yaoundé and located in the area of Djoungolo.

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Study population

We considered to include infants born from HIV positive women under ART, prior to conception (N=136) versus during pregnancy (N= 481). Inclusion criteria were as follows: having been exposed to ART before birth, availability of outcomes data. The study population was extracted from our Prevention MTCT (PMTCT) registry, targeting babies born between April 2008 and December 2013. Newborn babies born from mothers exposed to monotherapy by Zidovudine were excluded from this study.

Ethical consideration

This study received the approval of ethical institutional review board of the Centre Hospitalier d'ESSOS. Informed consent was obtained from all the respondents and confidentiality ensured in all process.

Data collection and procedures

HIV exposed newborn babies were registered at birth and their weight and length were recorded in the PMTCT registry. Gestational age was established from the first day of the last period to birth delivery. Infants' data at birth completed maternal data which included age, parity, CD4 cell count, protocol regimen and timing of the commencement of the treatment. After exclusion of multiples births, newborn babies were classified in two groups according to the onset of the maternal treatment.

Antiretroviral treatment guidelines

At our centre, in conformity with national guidelines, pregnant women eligible for HAART were initiated under first-line therapy consisting of Zidovudine, Lamuvidine and Nevirapine (assuming CD4 cell count below 250/mm^3); Nevirapine was switched with Efavirenz (EFV)whenever the level of CD4 cell count was ≥250/mm^3. Efavirenz was avoided during the first trimester for all pregnant women requiring HAART. It was recommended to maintain the ART treatment protocol for women conceiving under HAART, under the restriction of avoiding EFV; as a result, women presenting in the first trimester of pregnancy who were receiving efavirenz-containing regimens were changed to NVP or to lopinavir/ritonavir according to their level of CD4 cell count.

Data analysis

Data routinely collected were transferred into an Excel database sheet 2 and analyzed with the R software version 3.0. Descriptive data included maternal demographic characteristics and obstetric history, ART used including timing of treatment and CD4 cell count. The infant birth outcomes analyzed were low birth weight (<2500 g) and preterm delivery (gestational age <37 weeks). Associations between independent variable (moment of ART commencement) and preterm birth or low birth weight were examined using the chi-squared test, using the chi-squared test for qualitative data and Student's *t*-test for quantitative variables. Factors associated with LBW or PTB having a *p*-value below than 0.5 were anticipated to enter into a logistic regression model to identify which factors were independently associated with LBW or PTB.

Results

Population study

A total of 617 mother–child pairs delivering between 2008 and 2013, were included in this analysis. The characteristics of the mother–child pairs by timing of ART exposure (prior conception versus after conception) are shown in Table 1. The majority (481 of 617; 78%) of women on treatment were enrolled for ART treatment during pregnancy while the remaining 136 (22%) were on treatment prior to conception. The median duration of ART treatment was 39 weeks [interquartile range (IQR) 38-40 weeks] for those becoming pregnant under treatment versus 14 weeks gestation [interquartile range (IQR) 10-19 weeks] for those initiating treatment during pregnancy. There were some statistically significant differences between treatment groups; as, women receiving during pregnancy HAART had a poorer immunological status than women becoming pregnant under treatment, in addition, the latest were more likely to be multiparous than those initiating HAART after conception (Table 1).

Protocols of women already on ART at the time of conception

136/617 women (22%) conceived while on ART. Among them, 68% (N=92) were under Zidovudine-Lamivudine-Nevirapine, 14% (N=19) on Zidovudine-Lamuvidine-Efavirenz, 10% (N=14) on Tenofovir-Lamivudine-Nevirapine, 4% (N=5) were taking Tenofovir-Lamivudine-Efavirenz; overall 130/136 were on NNRTI-based HAART and the remaining six (4%) on Protease Inhibitor-based HAART.

Protocols of women who started ART during pregnancy

A total of 481 women were on ART during pregnancy. Among them, 64% (N=307) were ingesting Zidovudine-Lamivudine-Nevirapine, 26% (N=123) were put on Zidovudine-Lamuvidine-Efavirenz, 4% (N=19) on Tenofovir-Lamivudine-Nevirapine, 2% (N=12) were taking Tenofovir-Lamivudine-Efavirenz; overall 461/481 were on NNRTI-based HAART and the remaining twenty (4%) on Protease Inhibitor-based HAART.

Gestational age at delivery and preterm birth rate

The rate of premature infants was low (Table 2) at 9, 7%. This rate remained at 8.1% when ART started before conception versus 10.1% after conception; this percentage ranges from 10.9% at ART started during the first 28 weeks of pregnancy to 9% in later ART started, (p-value=0.9). In addition, only 4 newborn babies (0, 6%) were severely premature infants (<32 weeks).

Low birth weight rate

As indicated in Table 3, the overall rate of LBW was 11.6%. In bivariate analysis, the 11.7% of LBW from women under ART prior to

Variables	ART prior to pregnancy			ART during pregnancy			P value (t student)
	Mean	Median	IQR	Mean	Median	IQR	
Maternal age	28.03	28	24 - 33	27.24	27	23 - 31	0.17
Parity	1.82	2	1 - 3	1,35	1	1 - 2	**0.002**
Lymphocyte CD4cell count	439	400	330.5 - 531.2	322.27	302	202 - 416	**<0.001**
Birth weight	3118.25	3100	2750 - 3500	3113,34	3150	2800- 3500	0.92
Term at delivery	38.95	39	38 - 40	39.03	39	38 - 40	0.65

Table 1: Maternal characteristics, birth weight and term birth of babies born to HIV infected mothers under highly active antiretroviral therapy in Yaoundé.

Timing of commencement of HAART	Term N	Preterm birth N(%)	OR	p-value
Overall (N=617)	557	60(9.7)		
Prior to pregnancy (N=136)	125	11(8.1)	1	
During pregnancy (N=481)	432	49(10.1)	1.22(0.6-2.5)	0.9
▪ During pregnancy before 28 weeks(N=283)	252	31(10.9)	1.3 (0.6-2.8)	0.9
▪ During pregnancy after 28 weeks (N=198)	180	18(9)	1.01(0.5-2.4)	0.9

Table 2: Preterm birth and timing of Highly Antiretroviral Therapy in Yaounde, Cameroon.

Timing of commencement of HAART	Normal Weight	Low Birth weight N(%)	OR	p-value
Overall (N=617)	545	72(11.6)		
Prior to pregnancy (N=136)	120	16(11.7)	1	
During pregnancy (N=481)	425	56(11.6)	0.99(0.5-1.8)	0.9
▪ During pregnancy<28 weeks(N=283)	243	40(14.1)	1.23 (0.6-2.29)	0.9
▪ During pregnancy ≥ 28 weeks (N=198)	182	16(8)	0.6(0.3-1.4)	0.9

Table 3: Low birth weight and timing of Highly Antiretroviral Therapy in Yaoundé, Cameroon.

pregnancy was not significantly different from 11.6% for ART started during pregnancy. However, we recorded almost twice more LBW for babies having been exposed to ART during the first 28 weeks of pregnancy (14.1%) versus (8%) after, odd ratio (1.87: 1.02-3.44, p<0.05).

Discussion

In this Cameroonian cohort of HIV-infected pregnant women and their children, the use of HAART mostly free of PI initiated before or during pregnancy did not increase the risk of premature delivery, neither the rate of low birth weight, irrespective of the timing of treatment start. However, we found a slightly increase of lower birth weight in women starting treatment during the 28 weeks of pregnancy comparing to later. Overall, the rate of LBW or PTB was quite lower than previous reports in Africa. In Ethiopia the rate of LBW was recorded above 30% in women under HAART during pregnancy, reaching almost 50% in those on ART prior to pregnancy added to a rate of PTB above 20% [12]. In Botswana, HAART started prior to conception or during pregnancy was significantly associated to PTB, in almost 10% rate ingestion of PI, other worse outcomes including stillbirths [13]. Out of Africa, worrying levels of both PTB and LBW reaching 20% or above have been posted from India [14], Germany and Austria [15]. Earlier, some reports have focused on the side effects of HAART prior to conception on birth outcomes [16]. Finally, our findings are matching the observational results earlier reported in the dream cohort covering many settings in Africa [17], which are favoring the widely use of HAART to improve the maternal immunologic profile resulting on a better newborn scale at birth. Altogether, the favorable outcome of this observational study can be attributed to the immunological profile of the mothers which is sparsely compromised as well as the restricted use of protease inhibitors incriminated in some studies [18]. Though limited, the results of this analysis defend the harmless of HAART prior to pregnancy versus after as previously reported, assuming a low use of protease inhibitors and therefore is supportive to the recent recommendations to generalize combined antiretroviral therapy during pregnancy by using a preferable first line of ART free of PI in low resources settings [19]. At last, we acknowledge the limitation of this cross sectional study as our data did not record neither the nutritional status of our mother, nor the hypertension, both factors known to affect the favorable outcomes of pregnancy; we therefore recommend a prospective follow-up of HIV mother's baby pairs to further explore birth outcomes after antenatal exposure to ART in the context of B^+ option [20].

Conclusion

Combined ART started prior conception versus during pregnancy does not seem to increase the risk of PTB or LBW in Yaoundé. Further studies are required locally to confirm this tendency.

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Author's Contributions

All authors contributed equally.

References

1. Rollins N, Mahy M, Becquet R, Kuhn L, Creek T, et al. (2012) Estimates of peripartum and postnatal mother-to-child transmission probabilities of HIV for use in Spectrum and other population-based models. Sex Transm Infect 88 Suppl 2: i44-51.
2. World Health Organization (2010) Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. Recommendations for a public health approach. Geneva.
3. Hirnschall G, Harries AD, Easterbrook PJ, Doherty MC, Ball A (2013) The next generation of the World Health Organization's global antiretroviral guidance. J Int AIDS Soc 16: 18757.
4. Recommendations for use of antiretroviral drugs during pregnancy (2009) Ministry of Public health Cameroon, Yaoundé.
5. Thorne C, Patel D, Newell ML (2004) Increased risk of adverse pregnancy outcomes in HIV-infected women treated with highly active antiretroviral therapy in Europe. AIDS 18: 2337-2339.
6. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA (2007) Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. AIDS 21: 1019-1026.
7. Goldstein PJ, Smit R, Stevens M, Sever JL (2000) Association between HIV in pregnancy and antiretroviral therapy, including protease inhibitors and low birth weight infants. Infectious diseases in obstetrics and gynecology 8: 94-98.
8. Kourtis AP (2010) Antiretroviral drug use during pregnancy and risk of premature delivery: is there a connection? J Infect Dis 201: 978-980.
9. Ndirangu J, Newell ML, Bland RM, Thorne C (2012) Maternal HIV infection associated with small-for-gestational age infants but not preterm births: evidence from rural South Africa. Hum Reprod 27: 1846-1856.
10. Ekouevi DK, Coffie PA, Becquet R, Tonwe-Gold B, Horo A, et al. (2008) Antiretroviral therapy in pregnant women with advanced HIV disease and pregnancy outcomes in Abidjan, Côte d'Ivoire. AIDS 22: 1815-1820.
11. Njom Nlend AE, Same Ekobo C, Bitoungui M, Ekani B, Tchokoteu P, et al. (2012) Early Outcomes of HIV Exposed Children in the First District-wide Programme using Extended Regimens for the Prevention of Mother-to-Child Transmission of HIV, in Yaounde, Cameroon. Journal of tropical pediatrics 58: 297-302.

12. Kebede B, Andargie G, Gebeyehu A (2013) Birth outcome and correlates of low birth weight and preterm delivery among infants born to HIV-infected women in public hospitals of Northwest Ethiopia. Health 5: 25.

13. Chen JY, Ribaudo HJ, Souda S, Parekh N, Ogwu A, et al. (2012) Highly active antiretroviral therapy and adverse birth outcomes among HIV-infected women in Botswana. J Infect Dis 206: 1695-1705.

14. Darak S, Darak T, Kulkarni S, Kulkarni V, Parchure R, et al. (2013) Effect of Highly Active Antiretroviral Treatment (HAART) During Pregnancy on Pregnancy Outcomes: Experiences from a PMTCT Program in Western India. AIDS patient care and STDs 27: 163-170.

15. Grosch-Woerner I, Puch K, Maier RF, Niehues T, Notheis G, et al. (2008) Increased rate of prematurity associated with antenatal antiretroviral therapy in a German/Austrian cohort of HIV-1-infected women. HIV Med 9: 6-13.

16. Machado ES, Hofer CB, Costa TT, Nogueira SA, Oliveira RH, et al. (2009) Pregnancy outcome in women infected with HIV-1 receiving combination antiretroviral therapy before versus after conception. Sexually transmitted infections 85: 82-87.

17. Marazzi MC, Palombi L, Nielsen-Saines K, Haswell J, Zimba I, et al. (2011) Extended antenatal use of triple antiretroviral therapy for prevention of mother-to-child transmission of HIV-1 correlates with favorable pregnancy outcomes AIDS 25: 1611-1618.

18. Cotter AM, Garcia AG, Duthely ML, Luke B, O'Sullivan MJ (2006) Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth? J Infect Dis 193: 1195-1201.

19. Ahmed S, Kim MH, Abrams EJ (2013) Risks and benefits of lifelong antiretroviral treatment for pregnant and breastfeeding women: a review of the evidence for the Option B+ approach. Curr Opin HIV AIDS 8: 474-489.

20. Watts DH, Mofenson LM (2012) Antiretrovirals in pregnancy: a note of caution. J Infect Dis 206: 1639-1641.