JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Letter to the Editor

Lack of new HBV infections over 2 years of follow-up in HIV-positive women receiving ART up to 6 or 24 months after delivery

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Key words: Hepatitis B virus; human immunodeficiency virus; antiretroviral therapy; pregnancy; sub-Saharan Africa.

J Infect Dev Ctries 2018; 12(5):394-396. doi:10.3855/jidc.9915

(Received 07 November 2017 – Accepted 15 January 2018)

Dear Editor,

Hepatitis B virus (HBV) infections are endemic in most sub-Saharan countries. Although it is traditionally thought that HBV infection is acquired during childhood in Africa [1, 2] evidence shows that there is an ongoing sexual transmission of this disease among human immunodeficiency virus (HIV) infected adults [3,4]. In a study conducted in Uganda, prevalent HBV infection was found to increase with age and was associated to sexually transmitted infections [5].

Previous studies have reported HBV prevalence in the HIV-positive population of pregnant women in Malawi between 5 and 13 % [6-8]. Since acute HBV infection is associated with high levels of HBV-DNA, and therefore with an increased risk of transmission to the infants, it is important to determine the rate of new infections in this population.

The aim of this study was to assess the rate of new infections over a follow-up of 2 years in a cohort of HIV-infected women screened for HBV during pregnancy and testing HBsAg negative.

Women enrolled in the Safe Milk for African Children (SMAC) [9] observational study, conducted in Malawi between 2008 and 2011 to evaluate safety of antiretroviral administration during pregnancy and breastfeeding, were studied.

The study was conducted within the structures of the Drug Resource Enhancement against AIDS and Malnutrition (DREAM) Program implemented by the Italian non-governmental organization named Community of Saint Egidio, and was approved by the National Health Sciences Committee of Malawi. Written informed consent was obtained by all participating subjects.

In the study, treatment-naive HIV-infected pregnant women, received, in the presence of a CD4+ cell count < 350 cells/mm^3, a combination of stavudine (30 mg twice daily), lamivudine (150 mg twice daily) and nevirapine (200 mg twice daily) and continued it indefinitely or, in case of a CD4+ count > 350/mm^3, zidovudine (300 mg twice daily), lamivudine and nevirapine from week 26 of gestational age until 6 months postpartum. All mothers exclusively breastfed until six months.

Haematochemical and viro-immunological analyses were performed at the local DREAM laboratories in Malawi. Alanine aminotransferase (ALT) levels were monitored in these women every 3 months. Prevalence of HBsAg positivity was 8.7% in this cohort at baseline (week 26 of gestation) [7].

The present study included those patients who had tested negative for HBsAg at baseline and who had complete data of follow-up until 24 months after delivery. The presence of HBsAg was determined by the Enzygnost HBsAg 6.0 kit (Siemens Healthcare, Tarrytown, NY, USA). Samples which tested positive with this first assay were confirmed using the Enzygnost HBsAg Confirmatory Test (Siemens

Healthcare, Tarrytown, NY, USA), which is based on neutralization prior to testing with Enzygnost HBsAg 6.0. Only samples confirmed during the second assay were considered HBsAg-positive. HIV-RNA was quantified in plasma using the Versant kPCR 1.0 assay (Siemens Healthcare, Tarrytown, NY, USA) with the detection limit of 37 copies/mL (1.57 log10/mL).

Characteristics of the 125 women included in the study are reported in Table 1. Mean follow-up time was 788 days (range 702-936). At month 6, when all patients were on treatment, the percentage of patients with HIV-RNA < 400 copies/mL was 91.1% (102/112). At month 12 and 24, among 67 patients on continuous therapy, the percentage of patients with HIV-RNA < 400 copies/mL was 82.5% (47 out of 57 available samples) and 83.1% (54 out of 65 available samples), respectively, indicating good adherence to ART in these women.

None of these women was HBsAg-confirmed positive (6 were border-line positive with the first assay) when tested 24 months after delivery. Medians and interquartile range (IQR) for ALT levels were always within the normal range over the 2 years of follow-up. Only 4 patients had a grade ≥ 3 episode of ALT elevation.

Antiretroviral therapy containing anti-HBV drugs such as tenofovir and lamivudine, may interfere with replication of HBV, and indeed it has been shown that HBV incidence is reduced with HBV active antiretroviral therapy (ART): in an HIV-positive population (71% females) incidence was 1.17/100 person-years, 0.49/100 person-years with ART use and 2.25/100 person-years in the absence of ART [5]. Therefore, we cannot exclude that lamivudine-containing ART may have played a role in the lack of HBV acquisition for all women in the study up to 6 months after delivery and indefinitely for half of them.

With the implementation of Option B-plus approach [10] all pregnant women will receive indefinitely dually-active anti-HBV therapy (containing tenofovir and lamivudine). Further studies will therefore show the possible impact of this strategy also on HBV infection acquisition.

In conclusion, although these findings were obtained from a relatively limited number of subjects, it may be suggested that HBV infection acquisition is not common in HIV-positive postpartum women receiving ART up to 6 or 24 months after delivery; this represents a reassuring finding and might support the idea that performing once an HBV screening on pregnant women in low-income countries, could provide significant information on these patients and also be an affordable option.

Acknowledgements

The authors wish to thank Alessandra Mattei for administrative work. This work was supported by the Istituto Superiore di Sanità, Rome, Italy, under Grant N. 528c/28c7.

Table 1. Patients' characteristics.

Characteristic	All -- N (%)
Mothers	125 (100)
Age, *median (IQR)*°	27 (24-31)
Presence of ≥1indicators of a higher socio-economic status*	
Yes	81 (63.8)
No	44 (34.6)
WHO# Stage	
I	94 (74.0)
≥ II	29 (22.9)
Week of gestation at screening, *median (IQR)*	26 (24-30)
ART§ duration during pregnancy (days), *median (IQR)*	63 (41.0-90.5)
Baseline hemoglobin, *median (IQR)*	10 (9-11)
Baseline ALT (IU/mL), *median (IQR)*	12.7 (10.6-17.9)
Baseline CD4+ cell count, *cells/mm^3 median (IQR)*	336 (216-494)
Baseline HIV-RNA load, *log_{10} copies/mL, median (IQR)*	4.1 (3.4-4.6)
Baseline weight (kg), *median (IQR)*	58.0 (52.1-65.7)
Median ALT value at different time points *(IQR)* (IU/mL)	
Month 1	24.9 (17.7-36.0)
Month 6	22.1 (16.9-31.0)
Month 12	21.3 (13.4-31.8)
Month 18	19.7 (13.0-37.6)
Month 24	22.3 (13.6-31.0)

° Interquartile Range; *Either electricity at home, employment or a level of education above primary; # World Health Organization; § Antiretroviral Therapy.

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Conflict of interests: No conflict of interests is declared.