

## Abstract

**Background:** Hepatitis B virus (HBV) co-infection is common in HIV infected persons especially in countries with high HBV endemicity such as Nigeria. As antiretroviral therapy (ART) is introduced into such countries, it is imperative to understand how HBV affects HIV and ART-related outcomes. We hypothesized that HBV would increase the risk for ART-related hepatotoxicity and decrease the ability for a successful virological response to ART.

**Methods:** We tested our hypothesis in HIV infected persons participating in the PEPFAR program in Nigeria who initiated ART with stavudine, lamivudine and zidovudine and who were negative for HCV antibody. We compared subjects who were co-infected with HBV (HBsAg+) to those who were HIV mono-infected (HBsAg-) with regards to HIV parameters and ALT at baseline and after months 3 and 6 of ART. Hepatotoxicity was defined as ALT > 5x the ULN (41 IU/ml) or >3.5x baseline ALT if ALT was above ULN at baseline. Nonparametric tests were used to compare groups.

**Results:** Of the 1968 subjects tested, 229 (11.6%) were co-infected with HBV (HIV/HBV), 1170 were mono-infected with HIV (HIV), and the remainder, who were excluded from this study, were HIV/HCV or HIV/HBV/HCV infected. The mean age was 35 years in those who were HIV/HBV and those who were HIV. Median CD4 count (cells/mm<sup>3</sup>) at baseline was lower in the HIV/HBV group (99) compared to the HIV group (132) ( $P < 0.0001$ ). The baseline HIV RNA was significantly higher in the HIV/HBV group (91529 cp/ml vs. 53278 cp/ml,  $P = 0.0001$ ). Despite these differences, the percent of patients with a HIV VL < 200 cp/ml at months 3 or 6 was similar. CD4 counts increased to 220 vs. 247 in HIV/HBV vs. HIV groups, respectively ( $P = 0.02$ ), but the number with a CD4 increase > 50 was not different (73% and 70%). For patients with baseline and month 6 ALT, mean baseline ALT was higher in HIV/HBV group (42.9 vs. 31.7,  $P = 0.001$ ). At month 6, the same ALT difference remained and the cumulative hepatotoxicity was higher in the HIV/HBV group (4.3%) compared to the HIV group (0.4%,  $P = 0.007$ ).

**Conclusions:** HBV co-infection is high in HIV-infected persons in Nigeria. Although baseline CD4 counts were lower and both baseline HIV RNA and hepatotoxicity rates were higher in HBV co-infection, the immune reconstitution and virological response to ART was not impaired in the first six months. Further follow-up is needed to determine longer term effects of HBV on ART response in this cohort.

## Introduction and Hypothesis

### PEPFAR

- Provides drugs and clinical care to six sites
- Initial ARV regimen in "Branded" program (received Branded medications): Zerit®, Efavir®, Viramune®
- Laboratories: At baseline and every 6 months. Hepatitis B surface antigen (HBsAg) only at baseline.

### Hepatitis B virus (HBV) in Nigeria

- Prevalence in Nigerian blood donors 11-21% (Oronsaye et al, *Trop Doct* 2004, Otegbayo et al, *Trop Gastro* 2003)
- Prevalence in HIV-infected Nigerians 11-75%
- HBV increases risk for ARV-related hepatotoxicity in Western countries but unknown in Nigeria
- Effect of chronic hepatitis B on ART response not clear and never studied in Africa

### Hypothesis

Chronic hepatitis B impacts the risk for hepatotoxicity and the effectiveness of HAART in Nigeria

## Methods

### Study subjects

- Participants in Branded PEPFAR in site in Jos, Nigeria
- Initiated HAAART

### HCV antibody negative

### Laboratory testing

- HBsAg at baseline
- CD4 count, HIV RNA, ALT at baseline, 3 and 6 months

### Outcomes

- HIV RNA- baseline and < 200 copies/ml at 3 and 6 months
- CD4 cell count- baseline and 6 months, > 50 cell/mm<sup>3</sup> at 6 months
- Hepatotoxicity- ALT > 5x ULN or > 3.5 baseline if abnormal at baseline

### Analysis: Stata, version 9

- Continuous variables were compared with the Wilcoxon rank-sum test or Kruskal-Wallis test.
- Categorical variables were compared with the Chi square test or Fisher's exact test as appropriate.

## Study cohort

Figure 1: Flow chart of participants included in this study

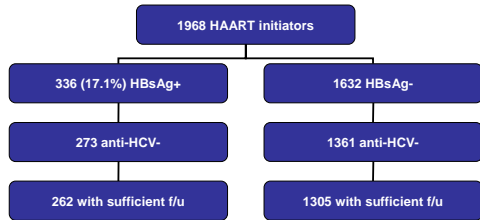


Table 1: Demographics

	HIV/HBV N=262	HIV/HBeAg+ N=53	HIV/HBeAg- N=94	HIV+ only N=1305
Mean age, years	34.7	35	33	35.6
Male gender, %	63	66	64	66
Unmarried, %	19	17	29	26

## Results

### HIV RNA

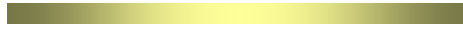
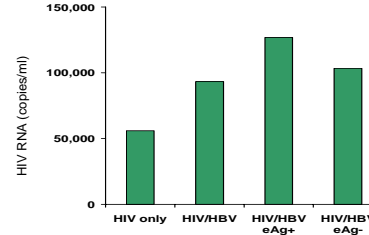


Figure 2: Median baseline HIV RNA levels stratified by HIV and HBV status

### CD4 cell count



Figure 3: Median baseline CD4 cell count stratified by HIV and HBV status



HIV-HBV co-infected individuals had significantly higher baseline HIV RNA ( $P = 0.0001$ ) and lower CD4+ cell counts ( $P = 0.0005$ ) than those only infected with HIV. These associations were most prominent in those who were HBeAg+.

Table 2: HIV RNA < 200 copies/ml at 3 and 6 months

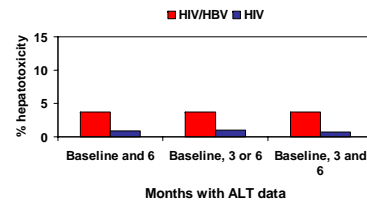
	HIV/HBV	HIV/HBeAg+	HIV/HBeAg-	HIV
3 months (%)	65	67	60	68
6 months (%)	74	76	75	76

Table 3: CD4 cell count at 6 months

	HIV/HBV	HIV	P
Median (cells/mm <sup>3</sup> )	222	247	0.01
↑ > 50 cells/mm <sup>3</sup> (%)	75	73	NS

## Hepatotoxicity

Figure 4: Prevalence of hepatotoxicity stratified by HBV status



## Conclusions

- Hepatitis B co-infection is common in Jos, Nigeria
- Hepatitis B co-infected who are eAg+ have lowest CD4 counts and highest HIV RNA levels at baseline
- Hepatitis B co-infection in first 6 months does not limit HAAART response
- Hepatotoxicity rates are low even in HIV-HBV co-infected patients

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