Hepatitis B Virus Mother-to-Child-Transmission among HIV-Infected, Pregnant Women in Kenya

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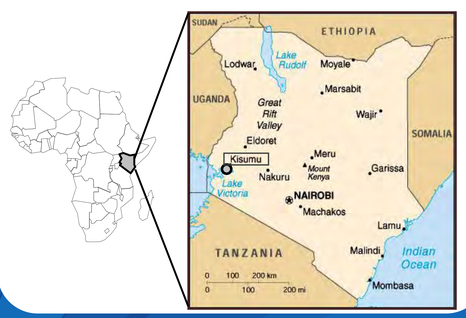
ABSTRACT

- **BACKGROUND**: Like HIV, hepatitis B virus (HBV) can be transmitted from mother to child. Our objective was to assess the prevalence of HBV co-infection and the HBV vertical transmission rate among HIV-infected mothers receiving triple-antiretroviral (ARV) regimens.
- **METHODS**: The Kisumu Breastfeeding Study (2003-2009) was a prospective clinical trial of triple-ARV regimens to prevent mother to child HIV transmission (MTCT) in Kenyan women. Women received ARV regimens containing 3TC from 34 weeks' gestation through 6 months of postpartum breastfeeding. Infant HBV vaccination starts at six weeks of life in Kenya. We retrospectively performed maternal HBV serology testing, including surface antigen (HBsAg), surface antibody (HBsAb), core antibody (HBcAb), and e antigen (HBeAg), in serum at enrollment (pre-ARV) and at six months postpartum. Maternal active HBV co-infection was defined as having detectable HBsAg. We tested infants of mothers with detectable HBsAg or an isolated HBcAb (HBsAg-/HBcAb+/HBsAb-) for HBcAb at two years of life. Infant HBV infection was defined as having detectable HBcAb.
- **RESULTS**: Among 439 HIV-infected women initiating lamivudine-containing ARVs, 25 (5.7%) had active HBV co-infection, including 9 (38%) women with detectable HBeAg. Among infants with available specimens, there were 0/17 HBV MTCT in infants of mothers with active HBV (0%, 95% CI = 0%–16%) and 0/46 HBV MTCT in infants of mothers with isolated HBcAb (0%, 95% confidence interval [CI] = 0%–6%). HBV co-infected mothers did not significantly differ in CD4 count, alanine aminotransferase (ALT) levels, or rates of liver toxicity on ARVs compared with those without HBV co-infection (Table).
- **CONCLUSIONS**: The prevalence of active HBV co-infection among our cohort of HIV-infected pregnant women (5.7%) was almost double the reported Kenyan prevalence (3%). Among HIV/HBV co-infected women receiving lamivudine containing triple-ARV regimens, there were no cases of HBV MTCT suggesting that vertical transmission of HBV is uncommon in this setting.

BACKGROUND

- Among HIV-infected people, hepatitis B virus (HBV) co-infection results in an increased risk of progression to cirrhosis and an increased rate of mortality[1,2].
- HBV can also be transmitted from mother to child in-utero and during the intrapartum period.
- There are limited data that anti-HBV prophylaxis with lamivudine during the final few weeks of pregnancy may be protective against intra-uterine and intrapartum transmission of HBV to the infant though it is not 100% effective[3,4].
- Lamivudine (3TC) is a component of many first-line antiretroviral therapy (ART) regimens[5] and has anti-HBV activity.
- Lamivudine as single-drug anti-HBV therapy is not recommended as resistance can develop in up to 70% to 90%[6].
- HBV-co-infection is frequently undiagnosed, however, which can result in an ART regimen with lamivudine as the only drug with anti-HBV activity.
- To evaluate the impact of HBV co-infection among HIV-infected pregnant women in Kenya, we assessed the prevalence of HBV co-infection and the HBV vertical transmission rate among HIV-infected mothers receiving triple-antiretroviral (ARV) regimens that included lamivudine as the only drug with anti-HBV activity.

Kenya



STUDY METHODS

- The Kisumu Breastfeeding Study (KiBS; 2003-2009) was a prospective clinical trial of triple-ARV regimens to prevent mother to child HIV transmission (MTCT) in Kenyan women[7].
- Women received ARV regimens containing lamivudine from 34 weeks' gestation through 6 months of postpartum breastfeeding.
- Retrospective testing for maternal HBV serology at baseline (pre-ARV) and at 6 months postpartum included: surface antigen (HBsAg), surface antibody (HBsAb), core antibody (HBcAb), and e antigen (HBeAg).
- Active maternal HBV co-infection was defined as detectable HBsAg.
- Infants of mothers with detectable HBsAg or isolated HBcAb (HBsAb and HBsAg both negative) were tested for HBcAb at two years of life.
- Infant HBV infection was defined as having detectable HBcAb by two years of life.
- HBV serology tests (Murex Biotech Ltd, Danford, UK) were performed at the KEMRI clinical laboratory in Kisumu, Kenya.
- Categorical data was compared using Fisher's Exact test. Continuous variables were compared with the Mann-Whitney U test.

RESULTS

Figure 1: Baseline (pre-ARV) HBV serology results, KiBS Study, Kisumu, Kenya

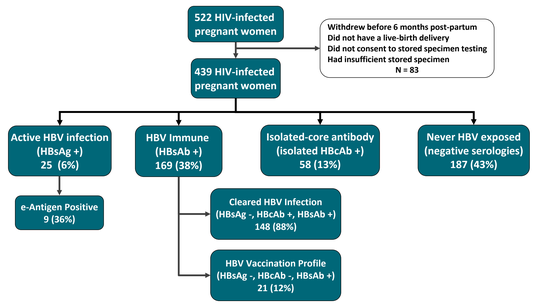


Figure 2: Change in serology after 6 months ART among HBV co-infected women

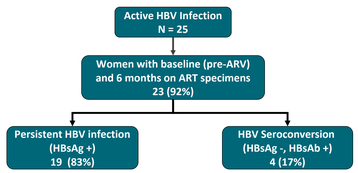
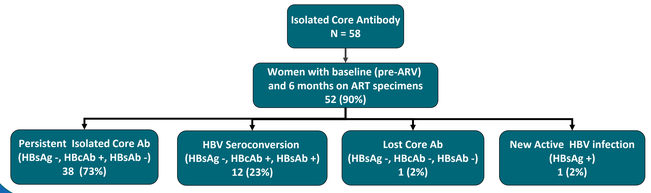


Figure 3: Change in serology after 6 months ART with isolated HBcAb

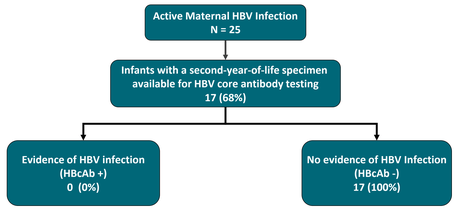


RESULTS CONTINUED

Table 1: Clinical and laboratory features of HIV-infected mothers and their infants by HBV infection status

	HBV Co-infection N = 25	No HBV Co-infection N = 414	P-value*
Age (median; interquartile range (IQR)	22 (21–25)	24 (21–27)	0.10
CD4, initial [cells/mm^3] (median; IQR)	435 (152–815)	401 (279–546)	0.77
CD4, six months postpartum (median; IQR)	634 (433–864)	661 (464–856)	0.50
ALT, initial [U/mL] (median; IQR)	10 (8–15)	10 (7–13)	0.42
ALT, peak [U/mL] (median; range)	31 (13–101)	27 (1–824)	0.39
Severe Hepatotoxicity [ALT >200 U/mL] (n; %)	0	12 (3%)	1.00
Rash-Associated Hepatotoxicity [ALT >100 U/mL with rash] (n; %)	0	8 (2%)	1.00
Maternal Death (n; %)	0	9 (2%)	1.00
Infant ALT, birth [U/mL] (median; IQR)	15 (11–17)	14 (11–20)	0.57
Infant HIV Transmission (n; %)	1 (4%)	18 (4%)	1.00
Infant Death (n; %)	2 (8%)	41 (10%)	1.00

Figure 4: Paired infant serology results among HBV co-infected women and their infants, KiBS Study, Kisumu, Kenya



- The prevalence of active HBV infection among HIV-infected pregnant women was 5.7% (25/439) and 36% (9/25) of actively infected pregnant women were HBeAg positive.
- 53% (231/439) of HIV-infected pregnant women demonstrated serologic evidence of either active or past HBV infection.
- HBV MTCT was 0% (95% CI: 0%–16%) in infants of mothers with active HBV.
- HBV MTCT was 0% (95% CI: 0%–6%) in infants of mothers with isolated HBcAb (n=58).
- HBV/HIV co-infected mothers did not significantly differ in rates of liver toxicity; in fact, 0% (95% CI: 0%–11%) of HBV co-infected mothers developed liver toxicity.
- HBV/HIV co-infected mothers did not significantly differ in CD4 count at baseline or after 6 months of ART or in baseline or peak alanine aminotransferase (ALT) levels.

DISCUSSION, LIMITATIONS & FUTURE DIRECTIONS

- Prevalence of HBV infection was higher (5.7%) than expected in our cohort of HIV-infected pregnant women—nearly double the national average (3%).
- There were no cases of HBV MTCT, suggesting that vertical transmission of HBV is uncommon in this setting despite an ART regimen with lamivudine as the only drug with anti-HBV activity.
- Our small sample size limits conclusions but there are plans to combine with these standardized, quantifiable outcomes (e.g., HBV MTCT) with other similar clinical trials.
- Short-term clinical outcomes, including CD4 cell count reconstitution and liver toxicity, were comparable among HBV co-infected and non-co-infected women.
- HBV DNA testing is planned to confirm absence of HBV MTCT and to evaluate maternal HBV viral loads.

ACKNOWLEDGEMENTS

- KiBS Study Participants
- Kenya Medical Research Institute (KEMRI)/CDC Public Health Research Collaboration
- Ministry of Health Kenya
- GlaxoSmithKline
- IMPAACT Network

KEMRI/CDC
Research And Public Health Collaboration

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