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CCEB

NO INCREASED INCIDENCE OF TRANSAMINITIS IN HIV PATIENTS WITH OCCULT HEPATITIS B

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ABSTRACT

Background: Occult hepatitis B virus (HBV) infection is defined as the presence of HBV DNA in the serum and/or liver tissue in the absence of HBV surface antigen (HBsAg). The clinical significance of occult HBV is unclear in HIV. We examined whether HIV patients with occult HBV had a greater incidence of transaminitis over time than those without occult HBV.

Methods: We performed a cohort study among a random sample of HBsAg–/HBV core antibody positive (anti-HBc+) HIV patients in the Penn CFAR Database and Specimen Repository. Exposure status was defined by HBV viremia, qualitatively evaluated using a transcription-mediated amplification assay (lower limit of detection: 15 HBV copies/mL). The primary outcome was transaminitis, defined as either ALT >40 U/L or AST >30 U/L. The first ALT and AST within each half-year of a subject's follow-up were selected. Among subjects without baseline transaminitis, incidence rate ratios (IRRs) of transaminitis between subjects with and without occult HBV were calculated. Poisson regression was used to control for confounders.

Results: Among 97 HBsAg–/anti-HBc+ subjects without baseline transaminitis, 13 (13%) had occult HBV. These subjects were older, more frequently had detectable HIV viremia, and less commonly received anti-HBV antiretroviral therapy than those without occult HBV. The median duration of follow-up from HBV DNA testing was 25.2 months (IQR, 17.1-30.4 months). Transaminitis occurred at least once in 11 (85%; 95% CI, 55-98%) occult HBV subjects compared to 66 subjects without occult HBV (79%; 95% CI, 68-87%; p>0.5). The incidence of transaminitis among subjects with occult HBV (50 events/100 person-years) was not significantly different from the incidence among those without occult HBV (38 events/100 person-years; IRR=1.32 [95% CI, 0.63-2.53]; p>0.5). The IRR changed little after adjusting for self-reported alcohol use, HAART, and chronic hepatitis C virus (HCV) infection (IRR=1.36; 95% CI, 0.72-2.59).

Conclusions: The incidence of transaminitis over a 2-year period was not significantly increased with occult HBV, even after adjusting for alcohol use, HAART, and chronic HCV, suggesting that it has little short-term clinical impact in HIV. Additional studies should examine whether occult HBV is associated with hepatic fibrosis and hepatocellular carcinoma in HIV patients.

BACKGROUND AND STUDY AIM

- A major question about occult HBV is whether the low levels of HBV DNA in occult HBV can induce inflammation and liver damage.
- To date, the effect of occult HBV on the incidence of hepatic transaminitis among HIV-infected patients has not been determined.
  - These data will help determine the importance of detecting and treating occult HBV in HIV.
- **Specific Aim**: To determine whether HIV patients with occult HBV have an increased incidence of transaminitis over time.
  - Hypothesis: HIV patients with occult HBV have an ↑ incidence of transaminitis over time compared to HIV patients without occult HBV

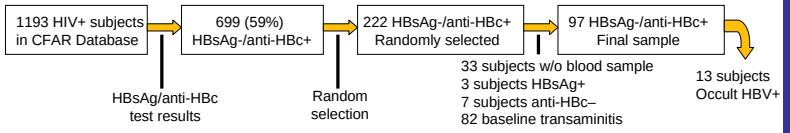
METHODS: STUDY SUBJECTS, EXPOSURES/OUTCOMES

- Study design: Cohort study
- Subjects were included from the **Penn CFAR Database and Specimen Repository**:
  - HIV-infected subjects complete a standardized questionnaire that collects demographic, clinical, and psychosocial data at enrollment and every 6 months
  - Blood sample drawn from each subject at enrollment and every 6 months
- Eligibility criteria: HBsAg–/anti-HBc+ subjects enrolled in CFAR Database between 11/1/99 and 12/31/02
- Identification: Most recent HBsAg and anti-HBc results prior to enrollment
- Selection: Simple random sample
- **Exposure**: HBV viremia
  - Detected using a qualitative HBV transcription-mediated amplification assay (Gen-Probe Incorporated)
  - Lower limit of detection: 15 HBV copies/mL
- **Study outcome**: Transaminitis, defined as either ALT >40 U/L or AST >30 U/L

METHODS: DATA COLLECTION AND ANALYSIS

- Serologic and HBV DNA testing:
  - Performed on selected subject's most recent serum sample in CFAR Specimen Repository through 12/31/02
  - HBsAg and anti-HBc repeated for all subjects; Anti-HCV repeated for anti-HCV– subjects only
- Baseline demographic and clinical data, including age, sex, race/ethnicity, duration of HIV diagnosis, possible mode of HIV acquisition, self-reported alcohol use within the past 30 days, use of HAART, HAART regimen, CD4 count, HIV viral load, ALT, and AST, were extracted from the CFAR Database from the date a subject's serum specimen was collected
- Longitudinal data: First ALT and AST within each half-year of a subject's follow-up were selected
- Among subjects without baseline transaminitis, incidence rate ratios (IRRs) and 95% confidence intervals (CIs) of transaminitis between subjects with and without occult HBV were calculated.
- Poisson regression used to control for self-reported alcohol consumption, HAART use, and chronic HCV

RESULTS: SUBJECT SELECTION



RESULTS: SUBJECT CHARACTERISTICS

Characteristic	HBV DNA- (N=84)	HBV DNA+ (N=13)	P-value
Median age (yr, IQR)	45 (39-51)	51 (42-54)	0.08
Male sex (%, no.)	85% (71)	85% (11)	>0.5
Race (%, no.)			0.3
African-American	67% (56)	85%(11)	
White	33% (28)	15% (2)	
Alcohol use within last 30 days (%, no.)	42% (35)	62% (8)	0.2
Anti-HBs (%, no.)	63% (53)	46% (6)	0.4
Chronic HCV (%, no.)	38% (32)	38% (5)	>0.5
HIV RNA >75 copies/mL (%, no.)	43% (36)	77% (10)	0.03
CD4 count <200 cells/mm³ (%, no.)	24% (20)	38% (5)	0.3
On HAART (%, no.)	71% (60)	54% (7)	0.2
Receipt of anti-HBV ARV (%, no.)	61% (51)	31% (4)	0.06
Anti-HBV ARV usage (%, no.)			
Lamivudine	55% (46)	31% (4)	0.1
Tenofovir	11% (9)	0% (0)	>0.5
Emtricitabine	1% (1)	0% (0)	>0.5
Follow-up (mo, IQR)	25.4 (18.4-33.1)	17.2 (5.0-33.2)	0.3

RESULTS: INCIDENCE OF HEPATIC TRANSAMINITIS

- Transaminitis occurred at least once in 11 (85%; 95% CI, 55-98%) occult HBV subjects compared to 66 subjects without occult HBV (79%; 95% CI, 68-87%; p>0.5).
- Incidence rate of transaminitis with occult HBV (50 events/100 person-years) not different from those without occult HBV (38 events/100 person-years; IRR=1.32 [95% CI, 0.63-2.53]).
- There was little change in the IRR after adjusting for alcohol, HAART use, and chronic HCV (IRR=1.36; 95% CI, 0.72-2.59).

CONCLUSIONS

- Among HIV patients, occult HBV was not associated with an increased incidence of transaminitis over a median 2-year follow-up period.
- Low levels of HBV DNA in occult HBV might not be sufficient to induce inflammation.
- Additional longitudinal studies are needed in HIV patients to determine whether occult HBV is associated with hepatic fibrosis and hepatocellular carcinoma.