Prevalence, Risk Factors, and Outcomes for Occult Hepatitis B Virus Infection Among HIV-Infected Patients

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Background: Occult hepatitis B virus (HBV) is defined by the presence of HBV DNA in individuals with HBV core antibodies (anti-HBc) but without HBV surface antigen (HBsAg). The prevalence of occult HBV in HIV-infected patients remains controversial, and the risk factors and clinical significance are unknown.

Objectives: To determine the prevalence, risk factors, and clinical significance of occult HBV among HIV-infected patients. Hypothesized risk factors include chronic hepatitis C virus (HCV), CD4 count <200 cells/mm^3, HIV RNA level >1000 copies/mL, and lack of use of anti-HBV antiretrovirals.

Methods: We examined randomly selected HBsAg$^-$/anti-HBc$^+$ HIV-infected patients in the Penn Center for AIDS Research Adult/Adolescent Database and Specimen Repository. HBV DNA was qualitatively detected using a transcription-mediated amplification assay. Risk factors and transaminases were ascertained at the time sera were collected.

Results: A total of 699 HBsAg$^-$/anti-HBc$^+$ HIV-infected patients were identified. Of 179 randomly selected subjects, 17 (10%; 95% confidence interval [CI]: 5% to 14%) had occult HBV. Differences in the prevalence of HBV surface antibody (anti-HBs) between those with (7 [41%]) and without (94 [58%]) occult HBV were not statistically significant ($P = 0.3$). An HIV RNA level >1000 copies/mL (adjusted odds ratio [OR] = 4.88, 95% CI: 1.01 to 30.26) and the absence of chronic HCV (adjusted OR = 0.26, 95% CI: 0.05 to 0.95) were associated with occult HBV. Occult HBV did not increase the risk of transaminitis (adjusted OR = 0.42, 95% CI: 0.12 to 1.45).

Conclusions: Occult HBV occurred in a sizable proportion of HIV-infected patients and was associated with detectable HIV and the absence of chronic HCV. It did not increase the risk of transaminitis. The presence of anti-HBs does not rule out occult HBV. Future studies should examine the long-term clinical implications of occult HBV in HIV-infected patients.

Key Words: HIV, HIV/hepatitis B virus coinfection, occult hepatitis B virus

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Exposure to hepatitis B virus (HBV) infection is common among HIV-infected patients because of shared routes of transmission,[1] and serologic markers of prior or active HBV infection are identified in up to 68% of HIV patients.[2] In the absence of HBV surface antigen (HBsAg), the presence of HBV core IgG antibody (anti-HBc) and HBV surface antibody (anti-HBs) usually indicates past resolved infection. The presence of isolated anti-HBc is often interpreted as evidence of remote HBV infection with subsequent loss of anti-HBs but may also represent a false-positive result. These patients are generally not considered to have detectable HBV DNA or to be at risk for complications from chronic HBV, including hepatic fibrosis, cirrhosis, and hepatocellular carcinoma.[3]

Sensitive molecular assays have detected HBV DNA in a subset of patients who have presumably recovered from acute HBV infection, however. This has resulted in the clinical entity known as occult HBV infection, defined as the presence of HBV DNA in the serum and/or liver tissue in the absence of HBsAg.[4–6] Few studies have examined the prevalence of occult HBV in HIV, and no studies have evaluated risk factors for occult HBV among HIV-infected patients. In addition, the clinical impact of occult HBV on hepatic transaminitis and fibrosis remains unclear in HIV.

To address these questions, we first determined the prevalence of occult HBV among a random sample of HBsAg$^-$/anti-HBc$^+$ HIV-infected subjects followed in the

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Penn Center for AIDS Research (CFAR) prospective HIV cohort study. Second, we examined risk factors for occult HBV among these subjects. Finally, we determined whether occult HBV was associated with transaminitis and significant hepatic fibrosis as determined by the aspartate aminotransferase (AST)–to-platelet ratio index (APRI), a noninvasive measure of significant liver fibrosis in patients with chronic HBV and hepatitis C virus (HCV).[7–10]

METHODS

Study Designs

We used 3 study designs to address our specific aims. First, to determine the prevalence of occult HBV in HIV, we performed a seroprevalence study among $HBsAg^-$/$anti\text{-}HBc^+$ HIV-infected subjects. Second, to determine risk factors for occult HBV, we performed a case-control study. Cases represented all subjects identified with occult HBV, and controls were all subjects without occult HBV. Using this study design, each hypothesized risk factor represented an exposure and occult HBV status represented the outcome. Finally, to examine if occult HBV was associated with transaminitis and significant hepatic fibrosis by APRI score, we collected liver transaminases and platelet values from the same date at which serum samples were evaluated for occult HBV. We then performed a cross-sectional study in which occult HBV represented the exposure and liver transaminases and APRI score were the study outcomes.

Study Subjects

We examined subjects in the Penn CFAR Adult/Adolescent Database and Specimen Repository, initiated in November 1999 to track demographic, clinical, and laboratory data from HIV-infected patients cared for at University of Pennsylvania–affiliated hospitals (Hospital of the University of Pennsylvania [HUP], Penn Presbyterian Medical Center [PPMC], Philadelphia Veterans Affairs Medical Center [PVAMC], Pennsylvania Hospital, and the adolescent HIV clinic at the Children's Hospital of Philadelphia). Subjects in the CFAR Adult/Adolescent Database have laboratory-confirmed HIV, provide informed consent, and complete a standardized questionnaire that collects demographic, medical, psychosocial, and HIV data at enrollment. A serum sample is drawn from each enrolled subject and stored at −70°C in the CFAR Specimen Repository. Subjects complete a follow-up questionnaire and have a serum sample drawn every 6 months. Additional laboratory data, such as HBV and HCV serostatus, may be downloaded into the CFAR Adult/Adolescent Database from hospital laboratory computer systems.

All $HBsAg^-$/$anti\text{-}HBc^+$ subjects enrolled in the CFAR Adult/Adolescent Database at the HUP, PPMC, and PVAMC sites from November 1, 1999 through December 31, 2002 were eligible for inclusion. A simple random sample of 180 subjects was targeted to have 80% power to detect a 20% difference in the prevalence of occult HBV between those with and without each risk factor of interest. This sample size also provided 80% power to detect a 20% difference in transaminitis between subjects with and without occult HBV. We oversampled to account for subjects who might not have serum samples available in the CFAR Specimen Repository.

To avoid misclassification of study subjects by HBV and HCV serostatus, we repeated the HBsAg (Elecsys 2010; Roche Diagnostics, Indianapolis, IN), anti-HBc (HBV Core Antibody Assay; Diagnostic Products Corporation, Los Angeles, CA), and HCV antibody (anti-HCV; Abbott HCV EIA 2.0 or 3.0 enzyme immunoassay; Abbott Laboratories, Abbott Park, IL) tests on the same serum sample in which HBV DNA testing was performed. HBsAg and anti-HBc tests were performed on the serum of all subjects, whereas anti-HCV testing was repeated only for HIV-infected subjects who were previously recorded as $anti\text{-}HCV^-$. All subjects with HCV coinfection had detectable HCV RNA.

Main Outcome Measures

The primary outcome for the determination of the prevalence and risk factors for occult HBV was the presence of HBV DNA as determined by the Gen-Probe HBV modified Ultrio transcription-mediated amplification (TMA) assay (Gen-Probe, San Diego, CA). This qualitative test, based on the same technology as the Procleix HIV-1/HCV (Gen-Probe) and Ultrio (Gen-Probe) assays,[11] requires only 500 μL of serum for processing and has a lower limit of detection of 15 HBV copies/mL.[12] The most recent sample of each eligible subject's banked serum (through December 31, 2002) was obtained from the CFAR Specimen Repository for HBV DNA testing.

The main outcomes for the determination of the clinical significance of occult HBV were (1) transaminitis, defined as alanine aminotransferase (ALT) >40 U/L or AST >30 U/L,[13,14] and (2) significant liver fibrosis as determined by APRI score.

Data Collection

Demographic and clinical data, including age, gender, race/ethnicity, duration of HIV diagnosis, possible mode of HIV acquisition, self-reported alcohol use within the past 30 days, use of highly active antiretroviral therapy (HAART; defined as use of 3 antiretroviral agents), HAART regimen, CD4 T-lymphocyte count, HIV viral load (determined by Versant HIV-1 RNA 3.0 Assay; Bayer Diagnostics, Tarrytown, NY; lower limit of detection of 75 copies/mL), ALT, AST, and platelet count, were collected from the CFAR Adult/Adolescent Database. Antiretroviral use was classified into 3 categories: (1) receipt of HAART that included an anti-HBV antiretroviral, (2) receipt of HAART without an anti-HBV antiretroviral, and (3) no HAART.

Data Analysis

Baseline cohort characteristics were described using proportions for categorical data and medians with interquartile ranges (IQRs) for continuous variables. Differences between subjects by occult HBV status were assessed using χ^2 or Fisher exact tests for categorical data and Wilcoxon rank-sum tests for continuous data.

We used multivariable logistic regression analysis to identify risk factors for occult HBV. Hypothesized risk factors included CD4 count <200 cells/mm^3, HIV RNA level >1000 copies/mL, chronic HCV, and lack of use of an antiretroviral with anti-HBV activity. Potential confounders included age,

gender, race/ethnicity, HAART use, anti-HBs, and active alcohol use. Further model reduction was achieved by eliminating factors that proved to be potential risk factors only infrequently in 1000 bootstrap samples of the data.[15] Robust 95% confidence intervals (CIs) that do not depend on large-sample assumptions were then estimated using bias-corrected bounds from another round of bootstrap resampling.[16]

We examined differences in ALT/AST levels and transaminitis by occult HBV status. Multivariable logistic regression was used to examine the association between occult HBV and transaminitis while controlling for potential confounders. The odds ratio (OR) and 95% CI of transaminitis between subjects with and without occult HBV were determined.

Finally, to assess the association between occult HBV and significant liver fibrosis, we calculated the APRI score: APRI = (AST [/ULN]*100)/platelet count [10^9/L]). The APRI has been validated to identify advanced hepatic fibrosis in HCV-monoinfected,[7,9] HIV/HCV-coinfected,[10] and HBV-monoinfected subjects[8] with a high degree of accuracy. The APRI accurately represents liver fibrosis only when liver disease has reached a severely advanced stage. Significant fibrosis was defined by an APRI score >1.5, and no fibrosis was defined by an APRI score ≤ 0.5.

All data were analyzed using STATA 8.2 (Stata Corporation, College Station, TX). Statistical significance was declared with 2-sided probability values <0.05.

The study was approved by the Institutional Review Boards of the University of Pennsylvania and PVAMC.

RESULTS

Of 1193 HIV-infected patients enrolled in the CFAR Adult/Adolescent Database between November 1, 1999 and December 31, 2002, we identified 699 (59%) $HBsAg^-$/anti-HBc^+ subjects. A total of 222 subjects were randomly selected for the study. Thirty-three subjects did not have a serum sample in the CFAR Specimen Repository and so were excluded. On repeat HBsAg and anti-HBc testing, 3 subjects were $HBsAg^+$ and 7 subjects were anti-HBc^- and were also excluded. All subjects found to be anti-HCV^- remained so on repeated testing. The final sample included 179 subjects.

Table 1 presents the baseline characteristics of these subjects. Subjects were primarily African American (75%) and male (88%), 24% self-reported a history of injection drug use, and 55% had chronic HCV. HAART was prescribed to 73% of subjects, and 59% were receiving an antiretroviral agent with anti-HBV activity.

After testing for HBV DNA, 17 (10%; 95% CI: 5% to 14%) subjects were identified with occult HBV. Subjects with and without occult HBV were similar with regard to age, gender, race, ethnicity, duration of HIV diagnosis, and use of HAART. Individuals with occult HBV less commonly had anti-HBs (7 [41%]) compared with those without (94 [58%]), but this difference was not statistically significant ($P = 0.3$).

On univariable analysis, subjects with occult HBV had lower median CD4 cell counts (273 [IQR: 123–386] cells/mm^3 vs. 366 [IQR: 222–558] cells/mm^3; $P = 0.04$) and higher median HIV RNA levels (23,205 [IQR: 75–53,676] copies/mL vs. 87 [IQR: 75–6199] copies/mL; $P = 0.02$), and were not

TABLE 1. Baseline Subject Characteristics: Total and by Occult HBV Status

Characteristic	All Subjects (n = 179)	HBV DNA^- (n = 162)	HBV DNA^+ (n = 17)	*P*
Median age (y, IQR)	47 (41–53)	47 (41–52)	51 (42–54)	0.3
Male gender (%, no.)	88% (158)	88% (143)	88% (15)	>0.5
Race (%, no.)				0.4*
African American	75% (134)	73% (119)	88% (15)	
White	18% (32)	19% (31)	6% (1)	
Hispanic (%, no.)	4% (8)	4% (8)	0% (0)	0.3
Injection drug use (%, no.)	24% (43)	25% (40)	18% (3)	0.1
Median duration of HIV diagnosis (y, IQR)	10 (5–13)	9 (5–13)	11 (6–14)	0.3
Alcohol use in past 30 days (%, no.)	41% (73)	40% (64)	53% (9)	0.2
No. with HBVs (%, no.)	56% (101)	58% (94)	41% (7)	0.3
Chronic HCV infection (%, no.)	55% (99)	57% (92)	41% (7)	0.2*
CD4 count <200 cells/mm^3 (%, no.)	25% (45)	23% (38)	41% (7)	0.1*
HIV viral load >1000 copies/mL (%, no.)	40% (71)	36% (59)	71% (12)	0.006
HAART use (%, no.)	73% (130)	74% (120)	59% (10)	0.2
Receipt of anti-HBV antiretroviral (%, no.)	59% (104)	62% (99)	29% (5)	0.02*
Anti-HBV antiretroviral use (%, no.)				
Lamivudine	52% (93)	54% (88)	29% (5)	0.07*
Tenofovir	12% (21)	13% (21)	0% (0)	0.2*
Emtricitabine	1% (1)	1% (1)	0% (0)	>0.5*
No. anti-HBV antiretroviral agents (%, no.)				0.04*
0	42% (75)	39% (63)	71% (12)	
1	52% (93)	54% (88)	29% (5)	
2	6% (11)	7% (11)	0% (0)	

**P* values for differences between subjects with and without occult HBV, as determined by Fisher exact test.

TABLE 2. Evaluation of Risk Factors for Occult HBV Infection.

Risk Factor	Adjusted OR (95% CI)*
CD4 count <200 cells/mm^3	1.60 (0.34 to 6.62)
HIV viremia >1000 copies/mL	4.88 (1.01 to 30.26)
Chronic HCV infection	0.26 (0.05 to 0.95)
Anti-HBV antiretroviral use	0.48 (0.07 to 1.97)

*ORs and 95% CIs obtained via bootstrap resampling. Each risk factor was adjusted for the other risk factors as well as for age and use of HAART.

receiving an antiretroviral with anti-HBV activity (5 [29%] vs. 99 [61%]; $P = 0.01$). Occult HBV was associated with an HIV RNA level >1000 copies/mL but not with CD4 cell counts <200 cells/mm^3 or the presence of chronic HCV (see Table 1). A total of 7 (7%) of 99 (95% CI: 2% to 12%) HIV-positive/HCV$^+$ subjects were identified with occult HBV compared with 10 (13%) of 80 (95% CI: 5% to 20%) HIV-positive/HCV$^-$ subjects ($P = 0.1$). Lack of receipt of an antiretroviral with anti-HBV activity was associated with occult HBV, and use of 2 such agents significantly decreased the likelihood of occult HBV.

Table 2 shows results of the multivariable analysis with bootstrap resampling examining risk factors for occult HBV. After controlling for all other hypothesized risk factors as well as age and use of HAART, only an HIV RNA level >1000 copies/mL (adjusted OR = 4.88, 95% CI: 1.01 to 30.26) and chronic HCV (adjusted OR = 0.26, 95% CI: 0.05 to 0.95) remained associated with occult HBV.

Median ALT levels were higher in the HBV DNA$^-$ group, but a greater proportion of these subjects were chronically infected with HCV (Table 3). Fewer subjects with occult HBV had transaminitis compared with those without occult HBV (4 [24%]) vs. 78 [48%]), but this difference was not statistically significant ($P = 0.07$). Univariable logistic regression demonstrated no association between occult HBV and transaminitis (OR = 0.33, 95% CI: 0.10 to 1.06). After controlling for chronic HCV, HAART, and active alcohol use, there was little change in the OR (adjusted OR = 0.42, 95% CI: 0.12 to 1.45). Occult HBV was also not associated with significant fibrosis as determined by APRI score (see Table 3).

DISCUSSION

In this study, we found the prevalence of occult HBV to be 10% among a randomly selected group of HBsAg$^-$/anti-HBc$^+$ HIV-infected patients. Almost half of the subjects with occult HBV had anti-HBs, suggesting that this antibody does not result in complete HBV elimination. In addition, anti-HBV antiretroviral use was evaluated among all subjects, and subjects with occult HBV were typically not receiving these medications. An HIV RNA level >1000 copies/mL and the absence of chronic HCV were identified as risk factors for occult HBV. Finally, occult HBV did not increase the risk of hepatic transaminitis among HIV-infected subjects.

In the absence of HIV, the prevalence of occult HBV has been reported to range from 7% to 60% among HBsAg$^-$/anti-HBc$^+$ patients.[17] Previous studies examining the prevalence of occult HBV in HIV-infected patients have similarly reported

TABLE 3. Evaluation of Clinical Significance of Occult HBV Infection

Characteristic	All Subjects (n = 179)	HBV DNA$^-$ (n = 162)	HBV DNA$^+$ (n = 17)	*P*
Median ALT level (U/L, IQR)	35 (25–55)	38.5 (27–55)	25 (21–34)	0.01
HCV$^-$	29.5 (20.5–40)	31 (20–41)	24.5 (21–28)	0.2
HCV$^+$	47 (31–64)	49 (32–65)	32 (21–46)	0.02
Median AST level (U/L, IQR)	40 (28–60)	40 (29–60)	32 (27–60)	>0.5
HCV$^-$	30 (24–40)	29.5 (24–39)	32 (24–60)	0.4
HCV$^+$	48 (36–79)	48.5 (37.5–79.5)	42 (27–64)	0.2
Transaminitis (%, no.)†	46% (82)	48% (78)	24% (4)	0.07*
HCV$^-$	11% (20)	11% (18)	12% (2)	>0.5*
HCV$^+$	35% (62)	37% (60)	12% (2)	0.1*
ALT >40 U/L (%, no.)	46% (82)	48% (78)	24% (4)	0.07*
HCV$^-$	11% (20)	11% (18)	12% (2)	>0.5*
HCV$^+$	35% (62)	37% (60)	12% (2)	0.1*
AST >30 U/L (%, no.)	47% (85)	48% (77)	47% (8)	>0.5
HCV$^-$	11% (19)	9% (15)	24% (4)	0.09*
HCV$^+$	37% (66)	38% (62)	24% (4)	0.3*
Significant fibrosis (APRI >1.5)	13% (23)	14% (22)	6% (1)	>0.5*
HCV$^-$	3% (5)	2% (4)	6% (1)	0.4*
HCV$^+$	10% (18)	11% (18)	0% (0)	0.2*
No fibrosis (APRI ≤0.5)	54% (96)	53% (86)	59% (10)	>0.5
HCV$^-$	32% (57)	32% (52)	29% (5)	>0.5*
HCV$^+$	22% (39)	21% (34)	29% (5)	>0.5*

**P* values determined by Fisher exact test.
†Transaminitis defined by ALT >40 U/L or AST >30 U/L.

a wide range of prevalences from 0% to 89.5% (Table 4).[2,18–25] These observational studies used different study designs (cross-sectional in 6 studies and longitudinal in 3 studies) and employed a variety of methods with different sensitivities to identify occult HBV. They were often limited by their small sample sizes, did not always report the number of subjects on antiretrovirals with anti-HBV activity, and rarely examined the clinical significance of occult HBV. In contrast, our study is the largest to date to examine occult HBV in HIV-infected patients and evaluated clinically relevant outcomes. Furthermore, we repeated HBV and HCV serologic test results on the same serum sample in which HBV DNA testing was performed to avoid misclassification of hepatitis serostatus. Three subjects were subsequently identified with active HBV, presumably because of activities that put them at risk for HBV infection, and 7 were found to be anti-HBc$^-$, suggesting that the initial anti-HBc results were false positive.

The mechanism for occult HBV remains unclear, but mutations in the S region of the HBV genome that could prevent production of HBsAg, host immune dysfunction allowing low-level HBV DNA levels, and inhibition of HBV replication by chronic HCV coinfection have been proposed.[17] To help shed light on its mechanism, we examined potential risk factors for occult HBV. In particular, detectable HIV RNA was found to increase the risk of occult HBV, suggesting that immune dysfunction or dysregulation independent of CD4 cell count might impair elimination of HBV and allow HBV replication to persist at low levels. Chronic HCV was also found to be protective against occult HBV. Previous data among HIV-uninfected patients have suggested that chronic HCV might downregulate HBV expression and allow HBV replication at extremely low levels, promoting the development of occult HBV.[17] Our results suggest that chronic HCV may act as a more dominant virus in the presence of HIV and downregulate HBV replication enough to suppress HBV replication completely, however, thereby reducing the risk of occult HBV in HIV/HCV-coinfected patients.

A major question about occult HBV is whether such small amounts of HBV DNA are associated with transaminitis and progressive liver damage.[6,26] The clinical impact of occult HBV has been examined primarily among HIV-uninfected chronic HCV patients. Among these patients, occult HBV has been shown to promote hepatic inflammation[27] and increase the risk of advanced fibrosis and cirrhosis.[27–29] Occult HBV has also been found to increase the risk of hepatocellular carcinoma in these individuals, possibly by integration with the host genome and/or synthesis of pro-oncogenic proteins by free intrahepatic HBV genomes.[4,17,30–34]

The clinical significance of occult HBV in HIV has been unclear. Two prior studies among HIV-infected patients found that occult HBV increased the frequency of transaminitis and hepatic flares,[19,25] but a third study found that occult HBV was associated with only minimal hepatocellular inflammation.[23] In this study, occult HBV did not increase the risk of transaminitis, even after adjusting for HAART, chronic HCV, and alcohol use. We also did not find an association between occult HBV and significant liver fibrosis as determined by APRI score. Thus, the likely low levels of HBV DNA in occult HBV might not be sufficient to induce clinically significant inflammation.

The clinical implications of occult HBV in HIV require further examination, however. In particular, longitudinal studies are needed in HIV-infected patients to determine if occult HBV is associated with an increased incidence of transaminitis, more advanced hepatic fibrosis, and hepatocellular carcinoma. Furthermore, because occult HBV has been shown to reduce response rates to interferon-based treatment among HCV-monoinfected subjects,[28,35–37] the effect of occult HBV on response to combination pegylated interferon and ribavirin therapy should be examined among HIV/HCV-coinfected patients. The results of these studies should provide data on the long-term effects of occult HBV in HIV and help to determine the need to test for occult HBV with sensitive HBV DNA assays and subsequently treat with anti-HBV agents.

TABLE 4. Published Studies Examining the Prevalence of Occult HBV in HIV-Infected Patients

Reference	No. Subjects	Prevalence of Occult HBV	HBV Assay
Hofer et al, 1998[19]	57 anti-Hbc+ only	89.5%	Nested PCR of HBV core and surface genes
Piroth et al, 2002[22]	37 anti-Hbc$^+$ only	35%	Qualitative PCR of HBV core and surface gene; results confirmed by Southern blot hybridization
Nunez et al, 2002[21]	85 anti-Hbc$^+$ only	0%	COBAS Amplicor HBV Monitor Assay (Roche Diagnostics)
Santos et al, 2003[2]	41 anti-Hbc$^+$ only	10%	PCR assay to amplify core and pre-S regions of HBV genome
	60 anti-HBc$^+$/anti-HBs$^+$	20%	
Shire et al, 2004[23]	38 anti-Hbc$^+$ only	10.5%	COBAS Amplicor HBV Monitor Assay (Roche Diagnostics)
	91 anti-HBc$^+$/anti-HBs$^+$	0%	
Gandhi et al, 2003[18]	42 anti-Hbc$^+$ only	2.4%	HBV TMA assay (Gen-Probe)
Wagner et al, 2004[24]	48 anti-HBc$^+$ only	29.2%	Nested PCR of S region of HBV genome; quantitative HBV viral load measured hybrid capture ultrasensitive test (Digene)
Neau et al, 2005[20]	160 anti-HBc$^+$ only	0.6%	COBAS Amplicor HBV Monitor Assay (Roche Diagnostics)
Filippini et al, 2006[25]	41 anti-HBc$^-$/anti-HBs$^-$	8.8%	Qualitative PCR of HBV core gene
	31 anti-HBc$^+$/anti-HBs$^-$	35.5%	
	4 anti-HBc$^+$/anti-HBs$^+$	21.4%	

PCR indicates polymerase chain reaction.

Our study had several limitations. We identified only 17 subjects with occult HBV, and this small number limits our statistical power, particularly for determining risk factors for occult HBV. We used bootstrap resampling to obtain robust estimates of the association between hypothesized risk factors and occult HBV, however. Additionally, subjects came from study sites in a predominantly urban setting, potentially limiting the generalizability of our results.

In conclusion, we found a 10% prevalence of occult HBV infection among $HBsAg^{-}$/anti-HBc^{+} HIV-infected subjects. The presence of anti-HBs did not rule out occult HBV. Detectable HIV RNA and the absence of chronic HCV were associated with occult HBV. Occult HBV did not increase the risk of transaminitis. Future studies should examine the long-term clinical implications of occult HBV in HIV-infected patients.

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