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Isolated Hepatitis B Core Antibody Status is not Associated with Accelerated Liver Disease Progression in HIV/Hepatitis C Co-infected Women

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Background

- Hepatitis B core antibody positivity (isolated anti-HBc) in the absence of hepatitis B surface antigen or surface antibody is a common serologic finding
- The prevalence of isolated anti-HBc is high in HIV disease; in the Women's Interagency HIV Study (WIHS), the prevalence was 15% at the baseline visit.
- The clinical significance of isolated anti-HBc is unclear; it could signify resolved infection with low anti-HBs, a false positive test or active infection in the absence of HBsAg; the likelihood that isolated anti-HBc represents active infection varies by population studied,
- In a cross-sectional study in the WIHS, the prevalence of HBV DNA among women with isolated anti-HBc was 2% but we have not tested for intermittent viremia
- We sought to determine if the presence of isolated anti-HBc changes the trajectory of liver disease progression among HIV/hepatitis C co-infected women

Methods

- WIHS is a multisite observational study of women with HIV-infected and demographically similar HIV-uninfected women from Chicago, San Francisco, Los Angeles, Washington DC and New York City; women are seen semiannually for interview, physical exam and specimen collection.
- The current study is a nested study of HIV/HCV co-infected WIHS women comparing liver disease progression defined by the Enhanced Liver Fibrosis (ELF) serum marker between women with and without isolated anti-HBc
- ELF is a a serum marker that combines direct markers of extracellular matrix remodeling and fibrosis: tissue inhibitor of metalloproteinase-1, hyaluronic acid and propeptide type III collagen,
- ELF was performed on stored serum from every 4th visit (q 2years) forHIV/HCV co-infected women with no or minimal fibrosis by APRI and FIB-4 at the baseline visit.
- HIV-infected women were included in this study if they were HCV RNA positive, HBsAg negative and had at least 3 ELF measurements.
- Distributions of exposure variables at the index visit were compared by isolated core antibody status using Pearson Chi-Square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables (Table 1). Multivariable associations between isolated core antibody status and ELF were assessed using mixed effects linear regression models to account for correlation between repeated measurements on women over time. (Table 2)

Results

- 361 women were included in the study for a total of 2225 ELF determinations and a median duration of follow-up of 9.5 years
- Of 361 women, 138 had isolated anti-HBc, 71 had negative HBV serologies, 13 had anti-HBs alone, consistent with HBV vaccine and 139 had anti-HBs + anti-HBc
- Women with isolated anti-HBc did not differ from comparator women in terms of age, race/ethnicity, CD4, use of HAART or HCV/HBV active drugs, and hazardous drinking. Women with isolated anti-HBc were more likely to have used injection drugs (Table 1)
- There was no difference between the groups in change in ELF over time (unadjusted p=0.274, Figure) or in a model adjusted for age, race, CD4, HAART use, IDU, HCV therapy and alcohol (p=0.187). There was no difference in mean ELF over time in a similarly adjusted model (p=0.918, Table 2).

Table 1: Patient Characteristics by Isolated Hepatitis B Core Antibody Status

	Isolated Anti-HBc, n (%) or Median (IQR)	Non-isolated Anti-HBc, n (%) or Median (IQR)	p-value†
Total women, n	138	223	--
Total study visits, median (IQR)	6 (5-7)	6 (5-7)	0.508
Total follow-up time in years, median (IQR)	9.87 (7.24-11.62)	9.43 (7.31-11.47)	0.426
Year of index visit, median (IQR)	1996 (1995-1997)	1996 (1995-1997)	0.773
ELF at index visit, median (IQR)	9.07 (8.46-9.71)	9.10 (8.47-9.74)	0.801
Age at index visit, median (IQR)	40 (36-44)	40 (36-43)	0.742
Race/Ethnicity			0.910
White	20 (14.5)	36 (16.1)	
Black	86 (62.3)	138 (61.9)	
Hispanic	29 (21.0)	46 (20.6)	
Other race	3 (2.2)	3 (1.4)	
CD4 count at index visit, median (IQR)	362 (226-577)	357 (226.5-529)	0.487
CD4 count, all visits (n=2201), median (IQR)	381 (224-586.5)	372 (217-562)	0.800
HAART use, all visits[a] (n=2223)	384 (45.1)	737 (53.8)	0.019
Used Lamivudine[a] (n=2174)	366 (44.2)	627 (46.6)	0.518
Used Emtricidibine[a] (n=2223)	39 (4.6)	71 (5.2)	0.589
Used Tenofovir[a] (n=2223)	93 (10.9)	176 (12.8)	0.304
Any treatment for Hepatitis C during study	14 (10.1)	13 (5.8)	0.130
Hazardous alcohol use, all visits[a,b] (n=2185)	141 (16.9)	223 (16.5)	0.894
IDU, ever (at index visit)	134 (97.1)	183 (82.1)	<0.001
IDU, recent use, all visits[a] (n=2193)	88 (10.5)	118 (8.7)	0.408

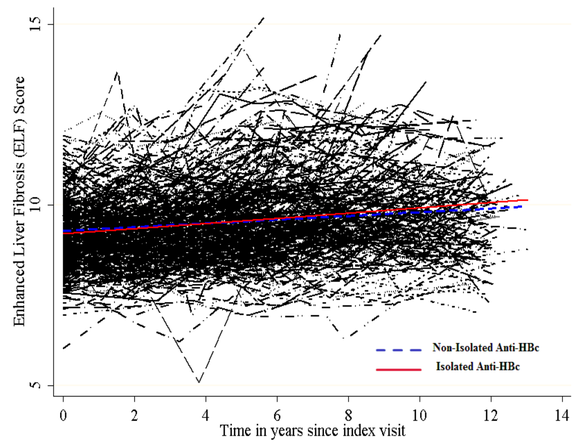
a. Time frame for exposure is since last WIHS visit
b. Hazardous alcohol use was defined as > 7 drinks per week or > 3 drinks on any occasion since the last WIHS visit.

Table 2: Results from Mixed Effects Linear Regression Models: Factors Associated with Liver Disease Progression as Measured by Enhanced Liver Fibrosis (ELF) Score

	Estimate**	95% CI	p-value
Isolated Anti-HBc	0.01	-0.18, 0.20	0.918
Age in years	0.04	0.03, 0.06	<0.001
Race/Ethnicity [Reference=White]			
Black	0.01	-0.25, 0.26	0.963
Hispanic	0.25	-0.05, 0.55	0.108
Other race	-0.19	-0.93, 0.55	0.614
CD4 <200	0.41	0.31, 0.52	<0.001
On HAART	-0.15	-0.24, -0.06	<0.001
Hepatitis C treatment	0.01	-0.27, 0.29	0.941
Hazardous alcohol use	-0.03	-0.13, 0.08	0.640
IDU ever	0.18	-0.11, 0.46	0.225
Time in years	0.06	0.04, 0.08	<0.001

**Estimate reflects mean ELF compared to the reference category.

Liver Disease Progression in HIV/HCV–infected women with and without isolated anti-HBc:
Enhanced Liver Fibrosis Markers over Time



Unadjusted p= 0.274
Not pictured: p=0.187. for group x time interaction in model with age, race, CD4 <200, HAART use, HCV therapy, hazardous alcohol use and IDU

Conclusions

- Over 9.5 years of follow-up, HIV/HCV co-infected women with isolated anti-HBc did not have accelerated liver disease progression compared to women with HBV serologies consistent with resolved infection, vaccination and no exposure to HBV.
- Predictors of liver disease progression were, as expected, greater age, lower CD4 count and non-use of potent ART
- These findings suggest that occult HBV does not contribute substantially to liver disease progression in women with isolated anti-HBc in the WIHS. We suggest that this is because occult HBV is rare and that isolated anti-HBc more often reflects resolved infection or false positive serology in this population.