Poster 695

Isolated Hepatitis B Core Antibody is Associated with Advanced Hepatic Fibrosis

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Supported by NIAID and NIAAA

Background

- Isolated HBcAb+, defined as the presence of anti-HBc in the absence of HbsAg and anti-HBs, occurs in 3.5-15.8% of healthy blood donors, 20.4-50.3% of patients with HCV, and in up to 89% of HIV-infected patients.
- The relationship between isolated hepatitis B virus (HBV) core antibody (Isolated HBcAb) and liver disease in HIV infected patients is unclear.

Objectives

1) Characterize the prevalence of isolated HBcAb among HIV-infected (HIV+) patients in the Veterans Aging Cohort Study (VACS).

2) Determine if isolated HBcAb was associated with advanced hepatic fibrosis in HIV+ patients in the presence and absence of concomitant chronic HCV infection.

Methods

Cross-sectional study among HIV+ in VACS Virtual Cohort, with laboratory data to determine chronic HCV status and 5 serological patterns of HBV antibodies:

1) Isolated HBcAb,

2) resolved HBV infection (HBcAb+/HBsAb+),

3) no evidence of HBV infection or vaccination (non-immune HBV),

4) HbsAb+ only

5) active HBV infection (HBsAg+).

Main outcome: advanced hepatic fibrosis

- FIB-4 >3.25 and APRI >2.0.
- Laboratory data obtained within +/- 1 year of earliest complete serological data

Analysis: Predictors of advanced fibrosis (age, race/ethnicity, CD4 count, log VL, diabetes, body mass index, alcohol, drug use, smoking) evaluated with logistic regression to determine adjusted odds ratios (OR).

Patients

Among 22379 HIV infected veterans, 8741 with and 13638 without detectable plasma HCV RNA, had complete hepatitis B serologic data for analysis. Of the patients with and without detectable HCV RNA, 7290 and 12196, respectively, had complete data allowing for calculation of baseline FIB 4 and APRI.

Results

Table 1a
Baseline characteristics of HIV/HCV Coinfected Patients

	Isolated HBcAb	Resolved HBV	Non-Immune HBV	HBsAb+ only	HBsAg+	Total
N (full data)	2707	2345	1294	452	492	7290
Age (Median, IQ)	49 (44-53)	48 (43-53)	47* (42-52)	47* (42-52)	46* (40-50)	48 (43-53)
Sex: n (%)						
Male	99.0	98.5	96.8	96.2	99.4	98.3
Female	1.0	1.5	3.2	3.8	0.6	1.7
Ethnicity: n (%)						
White	19.8	31.7*	32.8*	32.3*	35.4	27.8
Black	67.1	53.4	56.8	56.2	53.1	59.2
Hispanic	10.8	11.8	8.2	8.2	7.9	10.3
Unknown/other	2.4	3.1	2.5	3.3	3.7	2.8
CD4 (cells/µL) (%)						
CD4<200	33.1	32.4	31.1	25.0*	42.1*	32.6
CD4 200-500	43.0	41.1	44.2	46.5	36.8	42.4
CD4>500	23.8	26.5	24.7	28.5	21.1	25.0
Log HIV-1 VL (Median, IQ)	3.40 (2.60-4.61)	3.28 (2.6-4.6)	3.74* (2.60-4.76)	3.68 (2.6-4.70)	3.57 (2.60-4.62)	3.45 2.60-4.64)
Undetectable	38.2%	40.0%	35.0%	37.4%	36.4%	38.0%
Habits						
Tobacco (current/past)	74.2/14.1	68.2/15.5*	69.4/13.2*	63.1/15.4*	66.0/13.8*	70.2/14.5
ETOH Abuse	40.9	36.3*	34.1*	33.2*	31.5*	37.1
IVDU	49.1	44.2*	36.1*	35.6*	34.6*	43.4

* P < 0.01, indicated group compared with isolated HBcAb patients

Table 1b
Baseline characteristics of HIV Patients Without HCV Infection

	Isolated HBcAb	Resolved HBV	Non-Immune HBV	HBsAb+ only	HBsAg+	Total
N	1504	4283	4089	1471	849	12196
Age (Median, IQ)	47 (44-54)	48 (40-55)	46* (39-54)	41* (32-50)	44* (38-52)	46 (39-54)
Sex: n (%)						
Male	98.7	98.6	95.1	96.0	98.8	97.1
Female	1.3	1.4	4.9	4.0	1.2	2.9
Ethnicity: n (%)						
White	33.2	47.0*	37.4*	43.0*	37.7*	41.0
Black	53.8	41.7	49.0	42.8	52.6	46.5
Hispanic	8.0	6.6	8.0	7.8	4.5	7.2
Unknown/other	5.0	4.7	5.6	6.4	5.2	5.3
CD4 (cells/µL) (%)						
CD4<200	37.3	28.4*	33.4*	23.2*	38.3	31.2
CD4 200-500	39.6	40.6	40.0	40.9	39.8	40.1
CD4>500	23.1	31.0	27.0	35.9	21.9	28.7
Log HIV-1 VL (Median, IQ)	3.70 (2.60-4.85)	3.08* (1.90-4.56)	3.48* (2.42-4.76)	3.15* (1.88-4.61)	3.67 (2.60-4.83)	3.35 (2.17-4.69)
Undetectable	35.2%	44.9%	39.3%	44.6%	38.0%	41.3%
Habits (%)						
Tobacco (current/past)	59.8/14.6	48.4/17.9*	53.4/16.6*	45.4/13.8*	57.2/11.6*	51.6/16.1
ETOH Abuse	19.6	14.4*	17.7*	14.1*	16.6	16.3
IVDU	23.0	15.3*	17.1*	13.8*	17.3*	16.8

* P < 0.01, indicated group compared with isolated HBcAb patients

Results

Table 2
Clinical Characteristics Associated with Liver Disease

	Isolated HBcAb	Resolved HBV	Non-Immune HBV	HBsAb+ only	HBsAg+	Total
HIV/HCV						
N	2707	2345	1294	452	492	7290
AST	50	42*	41*	41*	50	45
ALT	47	42*	43*	40*	50	44
Platelet (*1000/µL)	191	196*	205*	202*	180*	195
Absolute FIB4	1.90	1.63*	1.49*	1.59*	1.82	1.72
Absolute APRI	0.66	0.55*	0.51*	0.51*	0.71	0.59
FIB 4 >3.25	23%	18%*	18%*	13%*	27%	20%
APRI >2	14%	11%*	13%	8%*	21%*	13%
Platelets <140,000	22%	19%	18%*	18%	28%*	21%
HIV Alone						
N	1504	4283	4089	1471	849	12196
AST	29	28	28*	26*	42*	28
ALT	28	29	27	27	41*	29
Platelet (*1000/µL)	214	218	221*	227*	180*	218
Absolute FIB4	1.25	1.19*	1.12*	0.92*	1.82*	1.16
Absolute APRI	0.34	0.33	0.31*	0.30*	0.71*	0.33
FIB 4 >3.25	9%	6%*	6%*	4%*	17%*	5%
APRI >2	5%	3%*	3%*	2%*	15%*	3%
Platelets <140,000	13%	10%	10%*	7%*	21%*	7%

All data presented as median value unless otherwise specified
* P < 0.01, indicated group compared with isolated HBcAb patients

Table 3
Risk of Advanced Fibrosis
(Non-Immune HBV as Referent Group)

	Referent: Non-Immune HBV	Isolated HBcAb	Resolved HBV	HBsAb+ only	HBsAg+
HIV/HCV					
FIB 4 >3.25	---	1.32 (1.09-1.60)	0.98 (0.80-1.21)	0.80 (0.56-1.13)	1.76 (1.32-2.35)
APRI >2.0	---	1.15 (0.92-1.44)	0.82 (0.64-1.04)	0.61 (0.40-0.94)	1.69 (1.23-2.32)
Platelets <140,000	---	1.27 (1.05-1.54)	1.07 (0.88-1.30)	1.17 (0.86-1.60)	1.66 (1.26-2.20)
HIV Alone					
FIB 4 >3.25	---	1.04 (0.78-1.39)	0.91 (0.73-1.14)	0.83 (0.58-1.18)	3.29 (2.51-4.32)
APRI >2.0	---	1.41 (0.96-2.10)	1.23 (0.91-1.66)	0.85 (0.54-1.36)	6.60 (4.82-9.04)
Platelets <140,000	---	1.16 (0.93-1.46)	1.20 (1.03-1.41)	1.02 (0.79-1.30)	2.36 (1.87-2.99)

All data presented as Odds Ratio (95% confidence interval)
Analyses were adjusted for age, race/ethnicity, CD4 count, log HIV VL, diabetes, body mass index, alcohol, drug use, smoking

Compared with patients with non-immune HBV infection, HIV+/HCV+ patients with isolated HBcAb had a higher OR for advanced hepatic fibrosis by FIB-4 and platelets , 140,000, but not APRI (OR 1.15, 0.92-1.44). No association between isolated HBcAb status and advanced hepatic fibrosis was seen among HCV- patients.

Results

Table 4
Risk of Advanced Fibrosis
Isolated HBcAb versus Other Serological Patterns

	Referent Group			
	Resolved HBV	Non-Immune HBV	HBsAb+ only	HBsAg+
HIV/HCV				
FIB 4 >3.25	1.34 (1.15-1.58)	1.32 (1.09-1.60)	1.65 (1.20-1.44)	0.75 (0.58-0.98)
APRI >2.0	1.40 (1.15-1.71)	1.15 (0.92-1.44)	1.88 (1.25-2.84)	0.68 (0.51-0.91)
Platelets <140,000	1.19 (1.02-1.40)	1.27 (1.05-1.54)	1.09 (0.82-1.44)	0.76 (0.60-0.99)
HIV Alone				
FIB 4 >3.25	1.14 (0.85-1.53)	1.04 (0.78-1.39)	1.26 (0.84-1.89)	0.32 (0.23-0.44)
APRI >2.0	1.16 (0.79-1.70)	1.42 (0.78-1.40)	1.67 (0.99-2.82)	0.22 (0.15-0.32)
Platelets <140,000	0.97 (0.78-1.22)	1.16 (0.93-1.46)	1.15 (0.86-1.54)	0.49 (0.37-0.65)

All data presented as Odds Ratio (95% confidence interval)
Analyses were adjusted for age, race/ethnicity, CD4 count, log HIV VL, diabetes, body mass index, alcohol, drug use, smoking

Compared with patients with HIV/HCV+ patients with isolated HBcAb also had a higher OR for advanced hepatic fibrosis by FIB-4 versus patients who were non-immune HBV or who were HBsAb+ only. Similar results were seen with APRI >2.0 (HBsAb+ only) and platelets <140,000/µL (non-immune HBV). Again, no association between isolated HBcAb status and advanced hepatic fibrosis was seen among HCV- patients.

In all comparisons, the risk of advanced fibrosis was less in patients with isolated HBcAb than in those who were HBsAg+.

Conclusions

- Isolated HBcAb is very common among HIV/HCV (37%) and HIV monoinfected patients (12%).
- HIV+/HCV+ persons with isolated HBcAb have evidence of a higher prevalence of advanced hepatic fibrosis, as assessed by thrombocytopenia, FIB-4 or APRI scores compared to persons who are non-immune to HBV, who have resolved HBV, or who are HbsAb+ only.
- In adjusted analyses, HIV+/HCV+ persons with isolated HBcAb have evidence of a higher risk of advanced hepatic fibrosis. While most clearly seen using a FIB 4 threshold of >3.25, similar results were seen with an APRI threshold of >2.0 or a platelet count of < 140,000.
- No increased risk of advanced hepatic fibrosis was seen among isolated HBcAb patients who were HCV-uninfected.
- These findings suggest that HIV+/HCV+ persons with isolated HBcAb may be at increased risk of clinical liver complications, and are consistent with prior studies showing an increased prevalence of occult HBV infection in such individuals.