



Nearly One-Third of Veterans with Hepatitis Delta Virus Infection in the United States have Already Developed Cirrhosis or Hepatocellular Carcinoma at Time of Diagnosis

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Background and Aims

- Hepatitis delta virus (HDV) infection is associated with more rapid disease progression to cirrhosis, hepatocellular carcinoma (HCC) and liver-related mortality.
- Delays in timely diagnosis and treatment of HDV contribute to more severe liver disease at presentation.
- This is due to low awareness and low rates of testing for HDV among patients with chronic HBV.
- Earlier diagnosis of concurrent HDV can facilitate timely linkage to care and appropriate treatment to prevent further liver disease progression and liver-related complications.
- We aim to evaluate the prevalence and predictors of advanced liver disease (AdvLD) at presentation among a national cohort of United States Veterans co-infected with chronic hepatitis B and HDV.

Results

Table 1. Characteristics of the Cohort

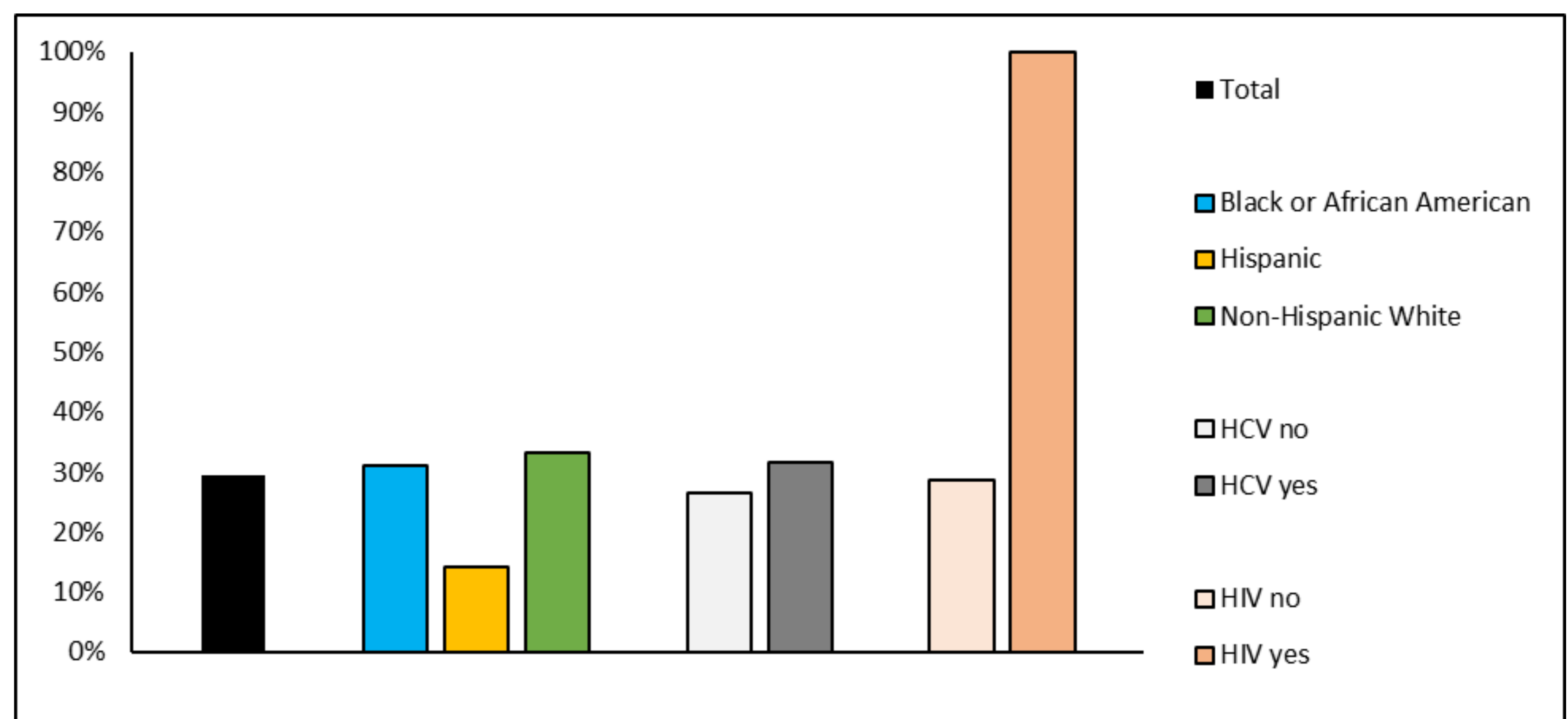
Variables	HDV positive (%)	Frequency (N)	HDV negative (%)	Frequency (N)	p-value
Total	3.1	109	96.9	3,462	
HBeAg Status					
HBeAg negative	89.2	66	75.6	1,835	0.01
HBeAg positive	10.8	8	24.4	593	
Antiviral Treatment					
No	66.1	72	65.8	2,279	0.96
Yes	33.9	37	34.2	1,183	
Sex					
Female	2.8	3	6.8	237	0.09
Male	97.2	106	93.2	3,225	
Race/Ethnicity					
Asian or Pacific Islander	8.7	9	15.3	503	
Black or African American	55.8	58	43	1,411	
Hispanic	6.7	7	4.3	141	
Non-Hispanic White	28.8	30	36.9	1,210	
Age (mean ± SD)	(58.9 ± 12.0)		(57.0 ± 12.7)		
BMI (mean ± SD)	(27.4 ± 5.7)		(28.6 ± 5.8)		
Comorbidities					
Diabetes	16.5	18	27.9	967	0.01
Hypertension	63.3	69	54.5	1,888	0.07
HCV	55.0	60	19.1	662	<.0001
HIV	0.9	1	1.2	41	0.80
Alcohol Use Categories					
Never	60.6	63	54.5	1,769	0.03
Low Risk Alcohol Use	22.1	23	33.4	1,086	
High Risk Alcohol Use	17.3	18	12.1	392	
Drug Use Categories					
No	74.3	81	87.2	3,020	<.0001
Yes	25.7	28	12.8	442	
Fibrosis-4 Categories					
FIB-4 Score < 1.45	37.9	36	46.2	1,321	0.0009
FIB-4 Score 1.45-3.25	29.5	28	36.2	1,034	
FIB-4 Score > 3.25	32.6	31	17.6	502	

- Among 29,061 CHB patients, 3,571 (12.3%) completed HDV testing, among whom 109 (3.1%) were positive and 3,462 (96.9%) were negative.
- Compared to HDV negative, HDV positive patients were more likely to be Black/African American (55.8% vs. 43.0%) or Hispanic (6.7% vs. 4.3%), less likely to be Asian/Pacific Islander (8.7% vs. 15.3%), p<0.05.
- HDV positive patients were more likely to have concurrent HCV infection (55.0% vs. 19.1%, p<0.01).
- When evaluating risk behaviors, compared to HDV negative, HDV positive patients were more likely to have high risk alcohol use (17.3% vs. 12.1%, p<0.05), current or past history of drug use (25.7% vs. 12.8%, p<0.01), and active tobacco use (53.8% vs. 39.9%, p<0.01).

Study Design and Methods

- We performed a retrospective cohort study using longitudinal data on all Veterans receiving care within Veteran health systems in the U.S. from 1/1/2010 to 12/31/2023.
- HDV diagnosis among Veterans with chronic HBV was confirmed based on laboratory testing (anti-HDV and HDV RNA).
- Prevalence of cirrhosis and cirrhosis-related complications (such as ascites and hepatic encephalopathy) were identified with ICD-9/10 diagnostic coding.
- Presence of HCC was also determined using established ICD-9/10 based diagnostic coding.
- The prevalence of AdvLD (cirrhosis, cirrhosis-related complications, or HCC) at time of HDV diagnosis was compared between groups using chi-square testing.
- We performed a sensitivity analysis focusing specifically on patients with documented viremic HDV (detectable HDV RNA) although few patients had follow up testing for HDV RNA after positive anti-HDV.

Figure. Prevalence of Advanced Liver Disease at Presentation Among HDV Positive Veterans



- At the time of diagnosis, HDV positive patients had greater prevalence of cirrhosis (25.7% vs. 11.5%) or HCC (7.3% vs. 2.0%), p<0.01, compared to CHB patients without HDV.
- Overall, 29.4% of HDV positive patients had AdvLD at presentation, the prevalence of which was higher in black/African American vs. Hispanics (31.0% vs. 14.3%) and trended higher among those with concurrent HCV infection (31.7% vs. 26.5% in HCV negative) or concurrent HIV infection (100% vs. 28.7%), p=0.12).
- HDV patients who reported concurrent high-risk alcohol use also trended towards greater prevalence of AdvLD compared to low risk alcohol use (22.2% vs. 17.4%, p=0.13).
- On sensitivity analyses of patients with viremic HDV only, 36.4% had AdvLD at presentation with similar trends seen across subgroup comparisons.

Conclusion

- **Among a national cohort of US Veterans with CHB and HDV, nearly 1 in 3 had already developed cirrhosis or HCC at time of HDV diagnosis, reflecting dangerous delays in diagnosis and treatment. Implementing effective programs for early HDV detection are urgently needed to facilitate timely linkage to care and treatment to prevent liver-related morbidity and mortality.**

Reference

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