HDV RNA Prevalence: Comparison of HBV/HIV and HBV Monoinfected Patients

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707

Abstract

Background: Hepatitis D virus (HDV), a defective RNA virus leads to the most aggressive form of viral hepatitis. HDV is thought to be relatively uncommon in the U.S. and its prevalence and significance in those with HIV is virtually unknown. We sought to assess the prevalence of HDV in a Midwestern cohort of patients with Hepatitis B (HBV)-HIV coinfection and a comparison group with HBV alone.

Methods: We developed and validated a qRT-PCR methodology for detection of HDV RNA. Briefly, viral RNA was extracted using a QIAamp viral RNA mini kit, followed by qRT-PCR in a BioRad CFX96 platform. A 93 BP region was amplified. The assay was validated by sequence analysis of the amplicon products with comparison to published sequences. The initial cohort was then tested and associated clinical data was obtained.

Results: 138 subjects (48 HBV-positive/HIV-negative and 90 HBV-positive/HIV-positive) were evaluated. The mean age was 38. 83% were male. 17% were on HBV active therapy. The mean ALT level in the HDV positives was 228 vs. 96 in HDV negative. Two subjects were found to be HDV RNA positive, both from the HBV/HIV group. Both were African-American, but one was born in the U.S. and the other in Africa. Cirrhosis was not present. Neither reported IDU as a risk factor. No samples were positive in the cohort with HBV alone.

Conclusions: Our analysis suggests HDV prevalence in those with HBV/HIV coinfection of 2% (p = 0.2, CI 0-5.3%) as compared to 0% in the HIV-negative cohort. Cirrhosis was not present in either subject found to have HDV coinfection though mean ALT level was higher. Further analysis of larger cohorts appears warranted because presence of HDV RNA was unsuspected in these patients

Background

- Hypothesized that 5% of the HBV-infected population co-infected with HDV, which portends worse clinical outcomes
- HDV rarely reported in the U.S. and few studies have examined its prevalence
- Few studies have investigated viral interplay in those also co-infected with HIV
- Methodology for HDV RNA testing not readily available

Goals

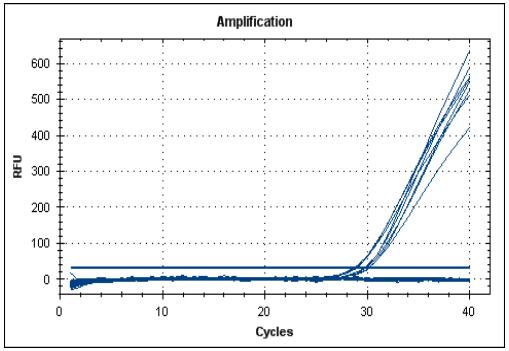
- Develop an HDV RNA RT-PCR assay
- Investigate prevalence of HDV in a Midwest population among a cohort of HBV-positive/HIV-positive or HBV-positive/HIV-negative
- Evaluate clinical outcomes when HDV co-infected

Supported in part by NIH NIDDK K24 070528 to KES

Methods

- Plasma samples selected from HBV-infected population, both HIV-positive and HIV-negative, enrolled in repository protocols between 1994 and 2014.
- HDV RNA RT-PCR assay developed, amplifying area of genome most conserved amongst eight established HDV genotypes
  - RNA isolated from serum samples using QIAamp viral RNA mini kit
  - Converted to cDNA and amplified with qRT-PCR in a BioRad CFX96 platform
  - Assay validated by sequence analysis of the amplicon products with comparison to published sequences
- Clinical data (risk factors for HDV contraction, AST/ALT level, presence of cirrhosis) evaluated specifically in patients found to have HDV RNA present
- Statistical analysis was performed using Statistix 10.0

Results



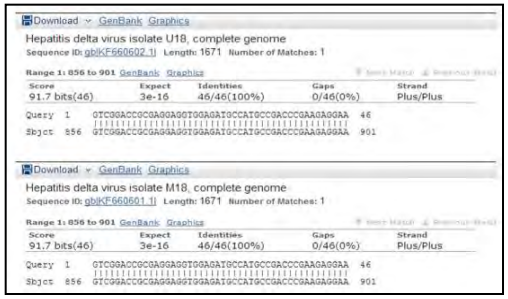
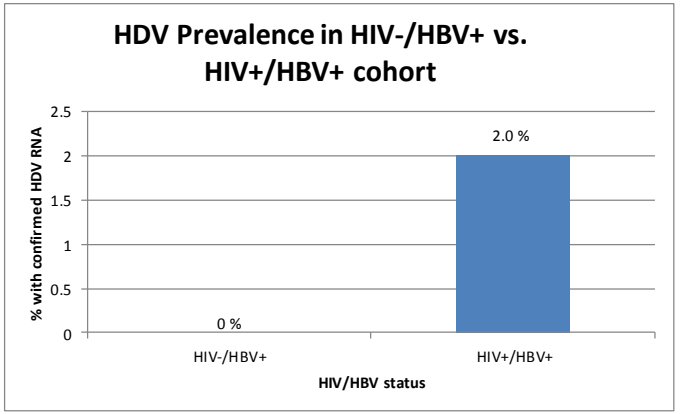


Figure 1A: RT-PCR curve. **Figure 1B**: HDV sequencing results.

Demographics and Clinical Data in all patients

	HIV-/HBV+ (n = 48)	HIV+/HBV+ (n = 90)
Age, mean/range yr	37.5 (18-66)	37.4 (18-57)
Gender, n (%)	Male – 28 (61%) Female – 18 (39%)	Male – 86 (96%) Female – 4 (4%)
Mean ALT, n (units/L)	107	201
Cirrhosis presence, n (%)	0/48 (0%)	0/90 (0%)
HDV presence, n (%)	0/48 (0%)	2/90 (2%)



Demographics and Clinical Data in HDV+ (n = 2)

Patient 1079	47 y/o black man, born in U.S. ALT 73. Cirrhosis not present. Unknown risk factors for HDV.
Patient 1790	45 y/o black man, born in Africa. ALT 383. Cirrhosis not present. Unknown risk factors for HDV.

Conclusions

- Preliminary data suggests a prevalence of 2% (p = 0.2, 95% C.I. 0-5.3%) in the HBV/HIV co-infected population as compared to 0% in the HBV+/HIV-negative cohort
- Cirrhosis not present in either of subject with HDV co-infection
- Larger sample size needed to assess prevalence, determine demographics, and draw definitive conclusions