

Impact of Hepatitis C Virus on HIV-Infected Individuals in Nigeria

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Introduction

Hepatitis C virus (HCV) infection occurs in 15–30% of persons with HIV coinfection in Europe and North America, and coinfection rates are even higher in injection drug users.¹ In these regions, where access to combination antiretroviral therapy (ARVs) is high, liver disease has emerged as a leading cause of death. HIV clearly accelerates HCV-related liver fibrosis progression, and rates of cirrhosis, decompensation, and hepatocellular carcinoma are higher in HIV/HCV compared to HCV monoinfected persons.^{1,2}

The effects of HCV on HIV-related disease progression has been more controversial. Some studies have found blunted CD4+ T cell recovery after ARV initiation in persons with HIV/HCV compared to those with HIV alone, but others have found no effect.³ Studies have been difficult to interpret, because the influence of injection drug use has been difficult to distinguish from the effects of HCV itself.

Nigeria, like other regions of West Africa, appears to have a higher endemic rate of HCV infection than East or Southern Africa, with estimated prevalence rates of 3–14%.^{4,5} The epidemiology of HCV acquisition is poorly understood, but factors that have been proposed include formal and informal health care with inadequately sterilized instruments, lack of screening of the blood supply for HCV until recently, and possibly sexual transmission. Injection drug use is very infrequent and does not drive the HIV or HCV epidemics. One study of 490 subjects with HIV infection in Nigeria found an overall prevalence of HCV Ab seropositivity of 5.7%, with 61% of HCV Ab+ cases having a history of blood transfusions and 39% having a history of needle injection at patent medicine stores.⁶ Only 3.6% of this HIV-infected cohort had ever injected drugs. Another study of 146 HIV infected patients in Nigeria found 8.2% were HCV RNA positive.⁷ We were interested in determining the effect of HCV on HIV-related outcomes in a primarily non-IDU population, and whether resources should be committed to testing for HCV in HIV-coinfected persons initiating ARVs.

Aims

•To determine the prevalence of HCV antibody seropositive (HCV Ab+) status in HIV infection

•To determine if subjects who are HCV Ab+ have a lower likelihood of achieving an undetectable HIV viral load and/or less of an increase in CD4+ T cell counts after initiation of ARVs, when compared to those with HIV alone.

•To compare the incidence of hepatotoxicity after ARV initiation in HIV/HCV coinfectd and HIV monoinfected subjects

Study Design

Antiretroviral naïve subjects were enrolled in the parent PEPFAR protocol, “A Study of the Safety, Efficacy and Adherence of Stavudine (Zeritid®), Lamivudine (Epivir®) and Nevirapine (Viramune®) to Treat HIV-1 Infection in Nigeria” at one of the study sites, Jos University Teaching Hospital (JUTH). Clinical data that were collected as part of the clinical protocol included demographics, medical history, clinical follow up, medication history, central pharmacy records, baseline hepatitis B surface antigen testing, and CD4+ T cell counts, HIV viral load, CBC and chemistries at baseline, 3–6 months after ARV initiation, and every six months thereafter. “Determine” test strips were used for HIV screening, and all positive tests were confirmed with Western blot. Baseline HCV antibody testing was performed with a third generation enzyme linked immunosorbent assay (DIA PRO Diagnostic Bioprobes, Milano, Italy). All laboratory values were measured on site at JUTH and data were also provided to a central database managed by the Harvard School of Public Health.

Hepatotoxicity was defined as ALT values that were increased at least 5 fold over the upper limit of normal range for the JUTH laboratory (ULN ALT = 41 IU/ml) or at least 3.5 fold if baseline ALT values were above the ULN. If multiple ALT values were obtained in a given time interval, the highest value was analyzed.

Statistical Analysis

Data were analyzed using Stata, version 9. Values are expressed as medians or percentages. Continuous variables were compared with the Wilcoxon rank-sum test or Kruskal-Wallis test. Categorical variables were compared with the Chi square test or Fisher’s exact test as appropriate. Significance was determined at p<0.05 and no adjustments were made for multiple comparisons.

Table 1: Hepatitis Serology

Total HIV+ subjects tested for HCV Ab and HBsAg	1963
Subjects with HCV Ab- and HBsAg- “HIV”	1,305
Subjects with HCV Ab+ and HBsAg- “HIV/HCV”	322
Subjects with HCV Ab+ and HBsAg+ (excluded from further analysis)	74
Prevalence of HCV Ab+	20.2%

Table 2: Baseline Demographics

Characteristics	HIV/HCV N=322	HIV N=1,305	p-value
Male sex	34%	35%	0.74
Mean Age (years)	37.9	35.6	<0.0001
Single	15%	19%	0.06
Ever Married	85%	81%	0.06

Table 3: Baseline Laboratory Values

Laboratory Values	HIV/HCV N=321	HIV N=1,302	p-value
CD4+ cell count (median, cells/mm ³)	123	130	0.82
HIV viral load	77,576	55,947	0.012
ALT (median, IU/ml)	23.8	19.5	0.0015
ALT above ULN	19.7%	17.0%	0.27

Table 4: Impact of HCV Status on Immune Reconstitution and HIV Virological Control after ARV Initiation

Lab Value	HIV/HCV	HIV	P value
CD4 count: month 3	246 (n=239)	237 (n=1071)	0.15
CD4 count: month 6	243 (n=234)	247 (n=959)	0.76
Percent with >50 CD4 cell increase between baseline and month 6	79% (n=234)	73% (n=956)	0.095
Percent with HIV VL <400 copies/ml at month 3	66% (n=218)	68% (n=924)	0.65
Percent with HIV VL <400 copies/ml at month 6	73% (n=218)	76% (n=874)	0.32

Table 5: Impact of HCV Status on Hepatotoxicity after ARV Initiation

Lab Value	HIV/HCV	HIV	P value
Median ALT: month 3	22.6 (n=235)	21.7 (n=1,043)	0.35
Hepatotoxicity at month 3	1.8% (n=235)	0.3% (n=1,043)	0.02
Median ALT: month 6	28.5 (n=231)	24.5 (n=929)	0.0006
Hepatotoxicity at either month 3 or month 6	2.7% ¹ (n=251)	1.0% (n=1088)	0.148
Subjects with baseline, month 3 and month 6 ALT: Hepatotoxicity at month 3 or 6	2.7% (n=187)	0.7% (n=766)	0.03

¹Subjects with hepatotoxicity at month 3 or 6 had a median age of 45 years (HIV/HCV versus 29.5 years (HIV; p<0.003) and were 60% female (HIV/HCV) versus 88% female (HIV; p=0.51)

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Conclusions

•A high prevalence of HCV Ab+ (20.2%) was found in this cohort of subjects with HIV

•At baseline, subjects with HIV/HCV coinfection had similar CD4+ cell counts and higher HIV viral load values than subjects with HIV alone

•There were no significant differences between HIV/HCV and HIV infected subjects in CD4+ cell count increases, percent subjects with at least 50 cell/mm³ increase, or percent subjects with undetectable HIV viral loads at months 3 and 6 after initiation of ARVs

•Subjects with HIV/HCV coinfection had significantly higher ALT values at baseline, although these effects were modest

•Subjects with HIV/HCV had modestly higher rates of hepatotoxicity over the first six months of ARV exposure

•Future goals include measuring HCV RNA levels in all HCV Ab+ subjects (including subjects with dual HCV and HBV infection) to determine the actual prevalence of chronic HCV infection, repeating all analyses in subjects with chronic HCV infection, and determining rates of hepatotoxicity at 1+ years of follow up

References

- Soriano V, Puoti M, Sulkowski M, Mauss s et al. Care of patients with hepatitis C and HIV coinfection. AIDS 2004; 18(1):1-12.
- Graham CS, Baden LR, Yu E, Mrus JM, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: A meta-analysis. CID 2001; 33:562-569.
- Miller MF, Haley C, Koziel MJ, Rowley CF. Impact of hepatitis C virus on immune reconstitution in HIV-infected patients who start highly active antiretroviral therapy: A meta-analysis. CID 2005; 41:713-720.
- Madhava V, Burgess C, Drucker E. Epidemiology of chronic hepatitis C virus infection in sub-Saharan Africa. Lancet Infectious Disease 2002; 2:293-302.
- Halim NK, Ajayi OI. Risk factors and seroprevalence of hepatitis C antibody in blood donors in Nigeria. East Africa Med J 2000; 77:410-412.
- Inyama PU, Uneke CJ, Anyanwu GI, Njoku OM, Idoko JH, Idoko JA. Prevalence of antibodies to hepatitis C virus among Nigerian patients with HIV infection. On J Health Allied Scs 2005; 2:2-6.
- Agwale SM, Tamimoto L, Womack C, Odama L, et al. Prevalence of HCV coinfection in HIV-infected individuals in Nigeria and characterization of HCV genotypes. J Clin Virol 2004; 31(Suppl 1):S3-6.