

Prevalence and Characteristics of Hepatitis C Virus Coinfection in a Human Immunodeficiency Virus Clinical Trials Group: The Terry Beirn Community Programs for Clinical Research on AIDS

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The baseline prevalence of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) coinfection among 2705 patients enrolled in HIV clinical trials in the Community Programs for Clinical Research on AIDS (CPCRA) was 16.6%. For men, multivariate logistic regression showed that the baseline prevalence of HIV-HCV coinfection was positively associated with history of injection drug use, older age, antiretroviral therapy naive status, African American or Latino ethnicity, and no history of having sex with men. No association was found with baseline CD4⁺ cell count or HIV RNA level. The prevalence of HCV coinfection in a diverse HIV clinical trials cohort provides additional information about risk behaviors and demographic factors that can be used in the analysis of clinical and virologic outcomes.

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The treatment of patients coinfecting with HIV-1 and hepatitis C virus (HCV) is a concern for clinicians because of the morbidity and mortality attributed to chronic liver disease [1–5] and the possible acceleration of both HIV and HCV disease in coinfecting patients [6–11]. A recent report of the Adult AIDS Clinical Trials Group (AACTG) described the estimated prevalence of coinfection in a large, diverse cohort of patients participating in randomized HIV clinical trials of antiretroviral therapy (ART) [12]. Our objective is to determine the prevalence of HIV and HCV coinfection inpatient enrolled in the Terry Beirn Community Program for Clinical Research on AIDS (CPCRA), a multicenter HIV clinical trials group funded by the National Institutes of Health, and to describe associations between patients' demographic characteristics and HIV-HCV acquisition risk behaviors. The purpose of the CPCRA is to promote clinical HIV research in community-based settings where patients receive their primary care, and to include traditionally underrepresented groups, such as women, minorities, and injection drug users.

Knowledge of the interplay between risk behaviors and demographic characteristics for HIV-HCV coinfection in the context of longitudinal, randomized clinical trials may provide information about ART and clinical outcomes that is distinct from data in observational cohorts.

PATIENTS AND METHODS

The study population included 2705 individuals who enrolled in 1 of 5 CPCRA studies at 16 CPCRA units located across the United States during September 1998 through September 2001. The 5 studies were 4 randomized clinical trials for strategies of ART and 1 natural history study of ART-naive patients. HCV serostatus was determined for all 2705 participants at the time of entry into a study. Positive HCV antibody results were accepted from any time in the past. HCV serological tests were performed locally at baseline for patients with no HCV antibody results on record or with negative results from >1 year before randomization. No specific HCV antibody assay was required.

Baseline characteristics described include age, sex, ethnic group, CD4⁺ cell count, plasma HIV load, ART status (naive or experienced), history of same-sex sexual contact, and a history of injection drug use (IDU) since 1977. Univariate and multivariate logistic regression analyses were performed to identify baseline covariates associated with the prevalence of HCV infection at baseline.

Appropriate informed consent was obtained for all participants, and guidelines for human experimentation of the US Department of Health and Human Services were followed in the conduct of clinical research.

RESULTS

Table 1 reports the baseline characteristics of the study participants overall and by HIV-HCV coinfection status. Of the 2705 patients enrolled, 449 (16.6%) were HCV antibody positive. Older age, African American or Latino-Hispanic ethnicity, and history of IDU were associated with increased prevalence of HIV-HCV coinfection, whereas having a history of engaging in male homosexual sex was associated with decreased prevalence of HIV-HCV coinfection.

Table 1. Baseline characteristics of study participants, by hepatitis C virus (HCV) infection status.

Characteristic	All participants (n = 2705)	HCV-HIV– coinfected patients (n = 449)	HIV–monoinfected patients (n = 2256)	P	
				Unadjusted	Adjusted ^a
Age, mean years ± SD	39.1 ± 9.1	43.2 ± 7.1	38.2 ± 9.2	<.0001	<.0001
Male sex	80.7	77.3	81.3	.05	.03
Ethnic group				<.0001	<.0001
Latino/Hispanic	14.5	16.9	14.0		
African American	45.3	56.3	43.1		
White	37.6	24.7	40.1		
Other	2.6	2.0	2.7		
CD4 ⁺ cell count, cells/mm ³					

Mean ± SD	350.5 ± 309.2	341.0 ± 298.6	349.2 ± 279.3	.77	.08
Median	322.0	305.0	325.5		
CD4 ⁺ cell count of <200 cells/mm ³	37.0	38.1	36.8	.59	.21
Log ₁₀ HIV RNA copies/mL					
Mean ± SD	4.3 ± 1.4	4.3 ± 1.3	4.3 ± 1.4	.73	.12
Median	4.6	4.6	4.6		
HIV RNA level of >400 copies/mL	82.0	85.5	81.3	.03	.06
Antiretroviral therapy naive	88.1	89.3	87.9	.39	.52
Injection drug use ^b	14.7	61.9	5.3	<.0001	—
History of same-sex sexual contact ^c					
Male (<i>n</i> = 2182)	69.3	32.3	76.3	<.0001	<.0001
Female (<i>n</i> = 523)	7.3	9.8	6.7	.27	.96
Overall	57.3	27.2	63.3	<.0001	<.0001
HCV positive	16.6	100.0	0.0		

NOTE. Data are percentage of patients, unless otherwise indicated.

^a Adjusted for history of injection drug use.

^b Self-reported use of injection drugs anytime since 1977.

^c Self-reported history of same-sex sexual contact anytime since 1977.

The following baseline covariates were used in a multivariate logistic regression model to find variables associated with HIV-HCV coinfection: age, CD4⁺ cell count, HIV RNA level, sex, ART status at baseline, history of IDU (yes/no), history of same-sex sexual contact (yes/no), ethnic group (African American/Latino or white/other), and the interactions between IDU, same-sex sexual contact, and ethnic group. A history of IDU, age, being naive to antiretroviral drugs, having a history of same-sex sexual contact, and the 2-factor interactions with a history of same-sex sexual contact were significantly associated (data not shown). Table 1 reports that, although 69.3% of men had a history of same-sex sexual contact, only 7.3% of women had such a history. To explore the relationship between history of same-sex sexual contact and HIV-HCV coinfection, we repeated the analyses separately for both sexes. For the female cohort, the only significant baseline covariates were age and history of IDU.

For the analyses of the male cohort, we first looked at the distribution of HIV-HCV coinfection by history of IDU and history of male-male sexual contact. As expected, the prevalence of HIV-HCV coinfection is highest in those with a history of IDU (data not shown). However, for both those with and those without a history of IDU, the prevalence of HIV-HCV coinfection is lower among those with a history of male-male sexual contact. We next considered another multivariate logistic regression model that included indicators for the 4 possible combinations of history of IDU and history of male-male

sexual contact. Table 2 reports the ORs, 95% CIs, and *P* values for HIV-HIV coinfection from that model.

Table 2. ORs for the risk of HIV–hepatitis C virus coinfection from the multivariate logistic regression model adjusting for certain explanatory variables (male-only cohort).

Baseline characteristic	OR (95% CI)	<i>P</i>
Age, years (1-year increments)	1.42 (1.23–1.65)	<.001
Age squared	0.997 (0.995–0.998)	<.001
CD4 ⁺ cell count, cells/mm ³ (50-cell increment)	1.02 (0.98–1.05)	.39
HIV RNA level, log ₁₀ copies/mL	1.01 (0.88–1.19)	.85
Antiretroviral therapy naive	1.86 (1.09–3.04)	.02
African American or Latino	1.92 (1.35–2.74)	<.001
History		
IDU but not male-male sex	69.77 (43.93–110.81)	<.001
IDU and male-male sex	11.86 (7.28–19.32)	<.001
Neither IDU nor male-male sex	1.75 (1.16–2.64)	.007
Male-male sex but not IDU	1.0	—

NOTE. IDU, injection drug use.

CD4⁺ cell count and HIV RNA level were not associated with HIV-HCV coinfection. The ORs for age and age squared are both statistically different from 1, so there is not a simple effect for age. Parameter estimates indicate that the maximum prevalence of HCV antibody positivity occurs at ~52 years of age. Being ART naive at baseline is associated with HCV antibody positivity at baseline (OR, 1.86; 95% CI, 1.09–3.04; *P* = .02). The OR for African American or Latino to white/other ethnicity is 1.92 (95% CI, 1.35–2.74; *P* < .001). For the interactions between history of IDU and male-male sexual contact, we let those with no history of IDU but with a history of male-male sexual contact be the reference group. The ORs for those with a history of IDU (regardless of history of male-male sexual contact) and those with no history of IDU and no history of male-male sexual contact are significantly greater than the ORs for the reference group. Also, the 95% CIs of the ORs for the groups formed by history of IDU and history of male-male sexual contact do not overlap, indicating that each of those ORs is different.

DISCUSSION

The prevalence of HCV infection in a demographically diverse population of HIV-infected patients enrolled in 5 CPCRA studies in the United States varied not only with age and a history of IDU but also by a history of male-male sexual contact and ethnic group. As in most HIV cohorts, the seroprevalence

of HCV coinfection in the CPCRA cohort (16.6%) is proportional to the number of patients reporting a history of IDU (14.7%). In the AACTG cohort, an overall estimate of the prevalence of HCV infection was determined to be 16.1% from a subset of patients [12]. The Johns Hopkins AIDS service (2237 patients) reported a prevalence of HCV infection of 44% in a population in which 39% of persons have a history of IDU [11].

Among the men, the older age and HCV infection reported here and in several studies reflect the cohort effect of persons infected during 1970–1990, the time of the highest incidence of HCV infection [13]. CD4⁺ cell counts and HIV RNA levels were not significantly associated with HIV-HCV coinfection at baseline. The OR for coinfection was greater for those who were ART naive than for those who were ART experienced, a finding that has been reported in other observational cohorts [11, 13, 14]. The prevalence of ART-naive status for coinfecting patients may reflect several issues: delayed entry into care for those with a history of IDU, delayed prescription of ART, or a reluctance to enter clinical trials on the part of provider and/or patients.

In our male cohort, African American and Latino patients had a higher prevalence of HIV-HCV coinfection than did white patients or other groups. Previous data from the United States indicate that HCV infection is not associated with racial or ethnic group independently of other sociodemographic factors [13]. Possible unreported factors that could explain the difference among ethnic groups include different numbers of sexual contacts, more sexual contact with IDUs, or other unreported high-risk behaviors [15, 16].

An interesting distribution of HCV infection prevalence is noted in this analysis. As expected, the ORs for men with a history of IDU are higher than those for men with no history of IDU, regardless of history of male-male sexual contact. However, the ORs for HCV infection are lower for men who have sex with men than for men with no history of male-male sexual contact, regardless of history of IDU. The results of earlier studies differ from our results and show similar coinfection rates for men with and men without a history of homosexual contact [17, 18]. Recently, the Aquitaine cohort showed a similar low rate for HCV coinfection among patients reporting IDU and male-male sexual contact [19]; the Hopkins AIDS clinic patients also had a lower rate of HCV coinfection among those individuals reporting homosexual or bisexual contact [11]. The lower prevalence of HCV coinfection among those with a history of male-male sexual contact is surprising, because it does not support the studies of behaviors among urban IDUs and sexual practices (e.g., sex for drugs or money or needle sharing) [20, 21].

Among IDUs, those with a history of male-male sexual contact may differ from those with no history of male-male sexual contact in drug use behaviors or frequency of drug use (e.g., using different types of illicit drugs or injecting drugs with varying frequency). Those with a history of male-male sexual contact may also practice risk-reduction behaviors that could reduce the risk of HCV acquisition (e.g., cleaning needles and other drug paraphernalia, not using shooting galleries, and substituting other drugs) [17, 18]. Among those with no history of IDU, the reason for the lower prevalence of HCV antibody positivity at baseline for those who had a history of male-male sexual contact compared with those who did not have a history of male-male sexual contact is less clear [22–26].

Study of HIV-HCV-coinfecting populations enrolled in randomized trials for antiretroviral drugs such as the CPCRA, which represent geographically and racially diverse populations, can provide additional insight to the complex interactions of race, sexual practice, and drug use in the context of long-term clinical strategy trials for HIV. Further study is needed to elucidate the interplay between sexual behavior, IDU, and the risk of acquisition of HIV-HCV coinfection.

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