

Published in final edited form as:

*J Clin Virol.* 2008 April ; 41(4): 255–263. doi:10.1016/j.jcv.2007.08.021.

## Factors associated with hepatitis C viremia in a large cohort of HIV-infected and - uninfected women

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### Abstract

**Background**—Coinfection with hepatitis C virus (HCV) is common among HIV-infected women.

**Objective**—To further our understanding of the risk factors for HCV viremia and the predictors of HCV viral load among women.

**Study design**—We investigated sociodemographic, immunologic, and virologic factors associated with presence and level of HCV viremia among 882 HIV-infected and 167 HIV-uninfected HCV-seropositive women at entry into the Women's Interagency HIV Study.

**Results**—Plasma HCV RNA was detected in 852 (81%) of these 1,049 women (range: 1.2–7.8 log<sub>10</sub> copies/ml). HCV-viremic women were more likely to have an HIV RNA level >100,000 copies/ml ( $P=0.0004$ ), have reported smoking ( $P=0.01$ ), or to be Black ( $P=0.005$ ). They were less likely to have current or resolved hepatitis B infection. HCV RNA levels were higher in women who were >35 years old, or HIV-infected. Current smoking and history of drug use (crack/freebase cocaine, marijuana, amphetamines, or heroin) were each associated with both presence and level of viremia.

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**Conflict of interest** Authors do not have conflicts of interest in relation to the present manuscript.

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**Conclusions**—Substance abuse counseling aimed at eliminating ongoing use of illicit drugs and tobacco may reduce clinical progression, improve response to treatment, and decrease HCV transmission by lowering levels of HCV viremia in women.

## Keywords

Hepatitis C; Hepatitis C RNA levels; Hepatitis C viremia; HIV/hepatitis C virus coinfection

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## 1. Introduction

Approximately four million people in the U.S. are infected with hepatitis C virus (HCV) (Armstrong et al., 2006). Among high-risk populations (hemophiliacs, injection drug users, HIV-infected patients), HCV prevalence is 30–98% (Mohsen et al., 2002).

Following initial infection, HCV viremia clears in approximately 20% of individuals, ranging from 15% of transfusion recipients to 45% of infants and young women (Thomas and Seeff, 2005). Factors associated with persistence include older age, male gender, African-American race, immunosuppression, HLA subtypes and polymorphisms, and blunted innate immune response (Thomas and Seeff, 2005). HIV coinfection is associated with reduced HCV clearance, whereas hepatitis B virus (HBV) is associated with higher clearance (Zhang et al., 2006).

Compared with the general population, HIV co-infected individuals have higher plasma HCV RNA levels (Zhang et al., 2006), and more HCV-associated complications (Thomas and Seeff, 2005). Since the introduction of highly active anti-retroviral therapy (HAART), HCV has become a major source of morbidity and mortality in co-infected individuals (Winnock et al., 2004).

While most HCV studies evaluated predominantly male populations (Mohsen et al., 2002; Thomas and Seeff, 2005; Zhang et al., 2006), understanding factors influencing persistent HCV infection in women is important in considering candidates for anti-HCV therapy. Chronically-infected patients with lower HCV viral loads have better response to therapy (NIH Consensus Development Conference Statement, 2002; Torriani et al., 2004) and are less likely to transmit HCV (Chayama et al., 1995; Thomas et al., 1998; Hisada et al., 2000). To understand risk factors for HCV viremia and viral load, we evaluated HCV-seropositive women at entry into the Women's Interagency HIV Study (WIHS).

## 2. Materials and Methods

### 2.1. Participants

This investigation included 1,049 (882 HIV-infected, 167 HIV-uninfected) HCV-seropositive women at entry into WIHS. Briefly, 2,059 HIV-infected and 569 uninfected women were enrolled at six sites (Los Angeles and San Francisco, CA; Washington, DC; Brooklyn and Bronx, NY; Chicago, IL) in October 1994–November 1995 (Bacon et al., 2005). This cohort was augmented in October 2001–November 2002 (738 HIV-infected, 406 uninfected). The WIHS protocol was approved by local institutional review boards; informed consent was obtained.

### 2.2. Laboratory methods at entry visit

Plasma HIV RNA levels were measured using the NASBA/NucliSens HIV RNA assay (bioMerieux, Durham, NC), in laboratories certified by the NIH National Institute of Allergy and Infectious Diseases Virology Quality Assurance Certification Program.

HCV and HBV serology were performed using standard commercial assays by local clinical laboratories. HBV serology included hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) and hepatitis B core antibody (anti-HBc).

HCV RNA was measured in 352 HCV-seropositive women using the COBAS Amplicor Monitor 2.0 assay (Roche Diagnostics, Branchburg, NJ) with a linear range of 600–700,000 IU/ml. All samples were diluted 1:10. Samples negative for HCV RNA were retested undiluted using the qualitative Amplicor 2.0 HCV assay, with a lower detection limit of 50 IU/ml (Roche Diagnostics). Positive undiluted samples were retested with the quantitative assay. All specimens >500,000 IU/ml were retested 1:100. Remaining HCV-seropositive women were tested using the real-time polymerase chain reaction (PCR) assay, COBAS Taqman (Roche Diagnostics), with a linear range of 10– $2.0 \times 10^8$  IU/ml, after demonstrating concordance of results using the two assays. Specimens non-reactive by HCV quantitative and qualitative PCR were considered HCV RNA-negative. Women with undetectable HCV RNA were retested to confirm HCV-seropositivity by HCV 3.0 EIA (Ortho-Clinical Diagnostics, Raritan, NJ).

Lymphocyte subsets were measured using standard flow cytometry at local laboratories participating in the NIH Division of Acquired Immune Deficiency Syndrome Flow Cytometric Quality Assurance Program.

### 2.3. Statistical analysis

Logistic regression was used to relate HCV viremia to participant characteristics. Factors associated with HCV RNA level among HCV-viremic women were studied using ordinal logistic regression with a three-level outcome:  $>0$ – $<5.0$ ,  $5.0$ – $7.0$ , and  $>7.0$   $\log_{10}$  copies/ml. The following characteristics were investigated: age, race, education, history of injection drug use (IDU), amphetamine, cocaine, crack/freebase cocaine, heroin, marijuana/hash use, IDU in last six months, lifetime number of sex partners, sex with injection drug user or HIV-infected male, history of sex for drugs, money, or shelter, alcohol use, current smoking, blood transfusion, and HBV and HIV status. For HIV-infected women, additional characteristics included AIDS, HIV therapy, HIV plasma RNA, and CD4 and CD8 counts. Multivariate models included independent variables with  $P < 0.20$  in univariate analyses.

## 3. Results

The majority of HCV-seropositive women was over 35 years old, Black, had completed high school, and had serologic evidence of HBV infection (Table 1). Over 90% had used illicit drugs but most had not recently injected drugs. Among HCV-viremic women, the median  $\log_{10}$  HCV RNA level was 6.3 copies/ml for HIV-infected women and 5.8 copies/ml for uninfected women. Only 4% of HIV-infected women had received HAART, as 90% were enrolled before HAART was generally available. Almost 25% had an HIV RNA level  $>100,000$  copies/ml or CD4 count  $<200$  cells/ml.

Multivariate analysis of the presence of HCV viremia (Table 2) revealed positive associations for Black race, crack/freebase cocaine use, and smoking, and inverse associations with HBsAg and anti-HBc/anti-HBs positivity. There was no association with HIV status.

Multivariate analysis of factors associated with higher HCV RNA levels among the HCV-viremic women (Table 3) revealed that age  $>35$  years, marijuana/hash use, smoking, and HIV infection were positively, while heroin was inversely associated with viremia levels.

Among HIV-infected women (Table 4), presence of HCV viremia was positively associated with Black race, smoking, and HIV plasma RNA >100,000 copies, and inversely associated with HBsAg antigenemia. The associations with HCV levels observed for the entire cohort generally remained (Table 5). In addition, sex with an injection drug user was positively associated, while amphetamine use and CD8 counts <800 were inversely associated with viremia levels.

#### 4. Discussion

In this largest cross-sectional study of HCV-seropositive women, age >35 years, Black race, drug use, smoking, and HIV and HBV co-infections were associated with presence and level of HCV viremia.

Viremic women >35 years old had higher HCV RNA levels; age had no effect on presence of HCV. These observations support reports among blood donors, drug users and women (Thomas et al., 2001; Busch et al., 2006; Fishbein et al., 2006), although one study found no association of HCV RNA levels with age (Sherman et al., 1993). Age-related immunity may not affect persistence/clearance of infection, but may reduce control of established infection.

An interaction of HIV with HCV infection has been observed (Dieterich, 1999; Winnock et al., 2004). Higher HCV RNA is associated with HIV positivity and HIV RNA levels (Sherman et al., 1993; Cribier et al., 1995; Thomas et al., 2001; Fishbein et al., 2006). Consistent with earlier reports (Daar et al., 2001; Thomas et al., 2001), we found a positive association between presence of HCV viremia and HIV RNA only at HIV RNA >100,000 copies/ml, suggesting that advanced HIV disease and resulting immunosuppression influence HCV viremia. Alternatively, HCV infection may more likely occur in advanced HIV disease.

Black women were more likely to be HCV-viremic, consistent with reports in other populations (Alter et al., 1999; Villano et al., 1999; Thomas et al., 2000a; Busch et al., 2006), although one study found no such association after controlling for HIV infection (Piasecki et al., 2004). In HCV treatment studies, Blacks have lower viral response to therapy (Brau et al., 2006). HCV persistence is associated with class II HLAs and *HLA-DQB1\*0301* may be more strongly associated with HCV clearance in Blacks (Thio et al., 2001). The racial effect we observed might be due to class II allele differences.

Smoking increased the likelihood of HCV viremia, which may be related to immunosuppressive effects of smoking/nicotine (Nair et al., 1990; McAllister-Sistilli et al., 1998; Ouyang et al., 2000). Smoking is associated with higher prevalence and incidence of HPV infection among HIV-infected women, suggesting that smoking during HIV infection alters the natural history of other viruses (Minkoff et al., 2004).

*In vivo* and *in vitro* studies of HIV and cocaine found decreased antimicrobial activity, cytokine production (Baldwin et al., 1997), lymphocyte proliferation and CD4/CD8 ratio, and increased HIV replication (Thomas et al., 1996; Roth et al., 2002). These findings in HIV may relate the association of HCV viremia with crack cocaine we observed. Similarly, women who used marijuana had higher HCV RNA levels, which may reflect known effects of cannabinoids on the function of T, B, and NK cells and macrophages (Friedman et al., 2003), and suppression of host resistance to infections (Joy et al., 1999).

The negative association between heroin use and levels of HCV viremia is puzzling in view of the opiate-mediated suppression of immune cells (Friedman et al., 2003). However, opiates may have anti-inflammatory effects through increased TGF- $\beta$  and decreased TNF- $\alpha$  and IFN- $\gamma$  (Peterson et al., 1987; Chao et al., 1992; Chao et al., 1993). If inflammation

favors HCV replication, this may partially explain heroin's protective effect. Our finding that illicit drugs varied in their effects on HCV viremia supports reports that immunomodulatory effects of psychotropic drugs either enhance or suppress infections by modulating T-helper activity (Friedman et al., 2003).

That women with evidence of current or resolved HBV infection were less likely to be HCV-viremic supports a reciprocal viral interaction (Thomas et al., 2000a; Thomas et al., 2000b; Jardi et al., 2001; Piasecki et al., 2004; Sagnelli et al., 2006).

Associations of HCV viremia with modifiable risk factors (smoking and illicit drug use) have important clinical and public health implications. In addition to our findings, hepatotoxicity of cigarette smoke and progression of fibrosis with marijuana use occur among patients with chronic HCV infection (Pessione et al., 2001; Hezode et al., 2003, Hezode et al., 2005). Eliminating tobacco and recreational drugs may lead to less severe histological lesions and decreased HCV viremia, an important indicator of response to therapy (NIH Consensus Development Conference, 2002; Torriani et al., 2004). Similarly, because patients with lower HCV viral loads are less likely to transmit HCV (Chayama et al., 1995; Thomas et al., 1998; Hisada et al., 2000), it may be beneficial to aggressively encourage HCV-viremic patients and their sexual partners to stop smoking and drug use.

This study had some limitations. We used baseline data and assume that HCV viremia reflects chronic, not recent, infection. Although we do not know date of HCV infection or when drug-using women started injecting (a good proxy for time of HCV infection), it is likely to have been several years before study entry. This seems reasonable since 92% of the women reported past drug use, but most had not recently injected. Nevertheless, the factors for which we found associations were, or most likely were, present at the time of clearance (race, drug use, HBV infection, and smoking). Although HCV RNA levels are relatively stable in chronic HCV infection (Gordon et al., 1998; Thomas et al., 2000b; Yeo et al., 2001), a recent study reported HCV RNA levels increased over a 2-year period (Fishbein et al., 2006). The replication patterns in HBV/HCV co-infection are widely divergent and have dynamic profiles, making a longitudinal evaluation of both viruses essential (Raimondo et al., 2006). Although in injection drug users, HCV and HBV infections usually predate HIV infection (Villano et al., 1999), it would be important to establish the timing of these infections to elucidate the observed relationships. Finally, our identification of factors associated with high and low HCV RNA levels was constrained by small numbers. Nonetheless, this report identifies factors associated with HCV viremia in the largest cohort of women of which we are aware.

In conclusion, the relationships of demographic, lifestyle, viral, and immunologic factors with HCV viremia in women are complex. HIV RNA level, age, smoking and Black race were the strongest predictors of HCV viremia. Because modifiable factors affect HCV viremia, HCV-infected women should be aggressively counseled against cigarette smoking and drug use. Eliminating such factors may result in lower rates of HCV chronicity, lower HCV viremia levels, reduced risk of sexual and vertical transmission, and improved response to HCV therapy.

## Acknowledgments

This study was supported by grants RO1 AI052065 (AK) and RO1-AI0577006 (HS) from the National Institute of Allergy and Infectious Diseases). Data in this manuscript were collected by the Women's Interagency HIV Study (WIHS) Collaborative Study Group with centers (Principal Investigators) at New York City/Bronx Consortium (Kathryn Anastos); Brooklyn, NY (Howard Minkoff); Washington DC Metropolitan Consortium (Mary Young); The Connie Wofsy Study Consortium of Northern California (Ruth Greenblatt); Los Angeles County/Southern California Consortium (Alexandra Levine); Chicago Consortium (Mardge Cohen); Data Coordinating Center (Stephen Gange). The WIHS is funded by the National Institute of Allergy and Infectious Diseases with

supplemental funding from the National Cancer Institute and the National Institute on Drug Abuse (UO1-AI-35004, UO1-AI-31834, UO1-AI-34994, UO1-AI-34989, UO1-AI-34993, and UO1-AI-42590). Funding is also provided by the National Institute of Child Health and Human Development (UO1-CH-32632) and the National Center for Research Resources (MO1-RR-00071, MO1-RR-00079, MO1-RR-00083).

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## Abbreviations

<b>anti-HBc</b>	hepatitis B core antibody
<b>anti-HBs</b>	hepatitis B surface antibody
<b>EIA</b>	enzyme-linked immunoassay
<b>HAART</b>	highly active anti-retroviral therapy
<b>HBsAg</b>	hepatitis B surface antigen
<b>HBV</b>	hepatitis B virus
<b>HCV</b>	hepatitis C virus
<b>HIV</b>	human immunodeficiency virus
<b>HLA</b>	human leukocyte antigen
<b>IDU</b>	injection drug use
<b>IFN</b>	interferon
<b>NIH</b>	National Institutes of Health
<b>PCR</b>	polymerase chain reaction
<b>RNA</b>	ribonucleic acid
<b>TGF</b>	transforming growth factor
<b>TNF</b>	tumor necrosis factor
<b>WIHS</b>	Women's Interagency HIV Study



**Table 1**

Baseline characteristics of 1,049 anti-HCV-positive women evaluated for presence and level of HCV viremia

	<b>No. of participants (%)</b>	
	<b>HIV(+)</b> ( <i>n</i> =882)	<b>HIV(-)</b> ( <i>n</i> =167)
Age (years)		
<35	197 (22%)	51 (31%)
>35	685 (78%)	116 (69%)
Race		
White	157 (18%)	30 (18%)
Hispanic	172 (19%)	45 (27%)
Black	534 (61%)	87 (52%)
Other	19 (2%)	5 (3%)
Education		
<12 yrs	385 (44%)	80 (48%)
12 yrs	497 (56%)	87 (52%)
History of drug use		
No	70 (8%)	9 (5%)
Yes	812 (92%)	158 (95%)
Injection drug use in last 6 months		
No	683 (77%)	111 (66%)
Yes	196 (22%)	56 (34%)
Missing	3 (<1%)	0 (0%)
HBV status		
Seronegative	98 (11%)	37 (22%)
Seropositive <sup>a</sup>	637 (72%)	97 (58%)
Missing	147 (17%)	33 (20%)
HCV plasma RNA status		
HCV RNA(-)	159 (18%)	38 (23%)
HCV RNA(+)	723 (82%)	129 (77%)
HCV plasma RNA (log <sub>10</sub> copies/ml)		
(HCV RNA+ only)		
<5.0	61 (8%)	27 (21%)
5.0–7.0	601 (83%)	95 (74%)
>7.0	61 (8%)	7 (5%)
AIDS diagnosis (HIV+ only)		
No	556 (63%)	
Yes	326 (37%)	
HIV therapy (HIV+ only)		
None	336 (38%)	
Mono	287 (33%)	
Combo	225 (26%)	
HAART	32 (4%)	

	<b>No. of participants (%)</b>	
	<b>HIV(+) (n=882)</b>	<b>HIV(-) (n=167)</b>
Missing	2 (<1%)	

<sup>a</sup>Defined as presence of any marker: HBsAg, anti-HBc, anti-HBs

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**Table 2**

Factors associated with presence of HCV viremia among 1,049 HCV-seropositive women (882 HIV-infected and 167 HIV-uninfected) at baseline WIHS visit, multivariate analysis<sup>a</sup>

	Total no. of women	HCV-viremic (n, %)	OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>
Age (years)				
<35	248	190 (77%)	1.0	
>35	801	662 (83%)	1.1 (0.8–1.7)	0.54
Race				
White	187	145 (78%)	1.0	
Hispanic	217	152 (70%)	0.8 (0.5–1.3)	0.37
Black	621	538 (87%)	1.9 (1.2–2.9)	<b>0.005</b>
Other	24	17 (71%)	0.6 (0.2–1.7)	0.39
History of cocaine use				
No	785	622 (79%)		
Yes	262	228 (87%)	1.3 (0.8–2.0)	0.29
History of crack/freebase cocaine use				
No	714	556 (78%)	1.0	
Yes	333	294 (88%)	1.6 (1.0–2.6)	<b>0.04</b>
History of marijuana/ hash use				
No	760	608 (80%)		
Yes	285	240 (84%)	1.1 (0.7–1.6)	0.71
Alcohol use				
0/wk	474	372 (78%)		
<3/wk	219	180 (82%)	1.1 (0.7–1.7)	0.65
3–13/wk	179	148 (83%)	0.9 (0.5–1.5)	0.67
13+wk	147	127 (86%)	1.0 (0.6–1.8)	0.95
Current smoking				
No	236	172 (73%)	1.0	
Yes	811	678 (84%)	1.6 (1.1–2.4)	<b>0.01</b>
HBV status				
Seronegative	135	113 (84%)	1.0	
Anti-HBs only	23	20 (87%)	2.0 (0.4–9.5)	0.40
Anti-HBc(+)/anti-HBs(+)	341	260 (76%)	0.5 (0.3–0.9)	<b>0.02</b>
Anti-HBc(+) only	339	289 (85%)	0.8 (0.5–1.5)	0.58
HBsAg(+)	31	19 (61%)	0.2 (0.1–0.6)	<b>0.002</b>
HIV status				
HIV(–)	167	129 (77%)		
HIV(+)	882	723 (82%)	1.4 (0.9–2.2)	0.15

<sup>a</sup>Model includes all variables with  $P < 0.20$  on univariate analysis

<sup>b</sup>Odds ratio (95% confidence interval) from dichotomous logistic regression

<sup>c</sup> $P$ -values  $< 0.05$  are bolded

Table 3

Factors associated with level of HCV viremia among HIV-infected and HIV-uninfected women at baseline WHHS visit, multivariate ordinal logistic regression analyses using log HCV RNA level >0 to <5.0 as reference level<sup>a</sup>.

	No. of women by HCV RNA level (log <sub>10</sub> copies/ml)			HCV RNA level (log <sub>10</sub> copies/ml)			
	>0-4.99	5.0-7.0	>7.0	OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>	OR (95% CI)	p-Value
Age (years)							
<35	35	147	8	1.0		1.0	
35	53	549	60	2.2 (1.3-3.8)	<b>0.004</b>	4.0 (1.6-10.0)	<b>0.003</b>
Race							
White	24	108	13				
Hispanic	16	128	8	1.7 (0.8-3.7)	0.15	0.8 (0.2-2.6)	0.68
Black	45	448	45	1.7 (0.9-3.1)	0.11	1.1 (0.5-2.8)	0.78
Others	3	12	2	1.4 (0.3-6.8)	0.70	2.5 (0.3-22.4)	0.40
History of amphetamine use							
No	79	673	66	1.0		1.0	
Yes	9	22	1	0.5 (0.2-1.4)	0.19	0.2 (0.0-1.6)	0.13
History of heroin use							
No	55	506	51	1.0		1.0	
Yes	33	189	16	0.6 (0.3-1.0)	<b>0.03</b>	0.5 (0.2-1.1)	0.07
History of marijuana/hash use							
No	67	499	42	1.0		1.0	
Yes	21	195	24	1.5 (0.8-2.7)	0.22	2.3 (1.0-5.3)	<b>0.05</b>
Sex with HIV+ male							
No	60	401	39	1.0		1.0	
Yes	26	243	23	1.3 (0.8-2.2)	0.30	1.2 (0.6-2.6)	0.56
Alcohol use							
0/wk	44	299	29	1.0		1.0	
<3/wk	22	145	13	1.0 (0.5-1.8)	0.90	0.7 (0.3-1.8)	0.48
3-13/wk	13	119	16	1.2 (0.6-2.5)	0.58	1.8 (0.7-4.7)	0.22
13+/wk	8	111	8	1.8 (0.8-4.3)	0.17	0.9 (0.3-3.2)	0.90

	No. of women by HCV RNA level (log <sub>10</sub> copies/ml)			HCV RNA level (log <sub>10</sub> copies/ml)		
	>0-4.99	5.0-7.0	>7.0	5.0-7.0	>7.0	
Current smoking				<b>OR (95% CI)<sup>b</sup></b>	<b>p-Value<sup>c</sup></b>	<b>p-Value</b>
No	25	134	13	1.0	1.0	1.0
Yes	63	561	54	2.0 (1.1-3.5)	<b>0.02</b>	1.8 (0.8-4.3)
HIV status						
Negative	27	95	7	1.0	1.0	1.0
Positive	61	601	61	2.8 (1.6-4.8)	<b>0.0003</b>	3.9 (1.4-10.5)

<sup>a</sup>Model includes all variables with  $P < 0.20$  on univariate analysis

<sup>b</sup>Odds ratio (95% confidence interval) from dichotomous logistic regression

<sup>c</sup> $P$ -values < 0.05 are bolded

**Table 4**

Factors associated with presence of HCV viremia among 882 HIV-infected HCV-seropositive women at baseline WIHS visit, multivariate analysis<sup>a</sup>

	Total no. of women	HCV-viremic (n, %)	OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>
Race				
White	157	125 (80%)	1.0	
Hispanic	172	126 (73%)	1.1 (0.6–1.9)	0.84
Black	534	460 (86%)	1.7 (1.0–2.8)	<b>0.05</b>
Others	19	12 (63%)	1.0 (0.2–4.2)	0.97
History of cocaine use				
No	672	541 (81%)	1.0	
Yes	208	180 (87%)	0.9 (0.5–1.6)	0.81
History of crack/freebase cocaine use				
No	609	480 (79%)		
Yes	271	241 (89%)	1.7 (1.0–3.0)	0.07
History of marijuana/hash use				
No	641	517 (81%)	1.0	
Yes	237	202 (85%)	1.2 (0.7–2.0)	0.44
History of blood transfusion				
No	641	535 (83%)	1.0	
Yes	156	123 (79%)	0.6 (0.4–1.0)	0.07
Alcohol use				
0/wk	403	320 (79%)	1.0	
<3/wk	182	152 (84%)	1.2 (0.7–2.0)	0.61
3–13/wk	155	127 (82%)	0.9 (0.5–1.6)	0.68
13+/wk	120	104 (87%)	1.1 (0.6–2.4)	0.71
Current smoking				
No	213	155 (73%)	1.0	
Yes	667	566 (85%)	1.9 (1.2–2.9)	<b>0.005</b>
HBV status				
Seronegative	98	86 (88%)	1.0	
Anti-HBs only	18	16 (89%)	0.9 (0.2–5.2)	0.93
Anti-HBc(+)/anti-HBs(+)	281	219 (78%)	0.5 (0.2–1.1)	0.09
Anti-HBc(+) only	307	263 (86%)	0.7 (0.3–1.7)	0.49
HBsAg(+)	31	19 (61%)	0.2 (0.1–0.5)	<b>0.0017</b>
HIV therapy				
None	336	279 (83%)	1.0	
Mono	287	240 (84%)	0.9 (0.6–1.6)	0.80
Combo	225	177 (79%)	0.7 (0.4–1.3)	0.31
HAART	32	25 (78%)	0.6 (0.1–6.3)	0.66
HIV plasma RNA (copies/ml)				
4,000	275	209 (76%)	1.0	

	Total no. of women	HCV-viremic (n, %)	OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>
4,001–20,000	191	155 (81%)	1.3 (0.7–2.2)	0.37
20,001–55,000	113	92 (81%)	1.4 (0.7–2.6)	0.34
55,001–100,000	87	75 (86%)	1.8 (0.8–3.8)	0.16
>100,000	211	188 (89%)	3.5 (1.8–7.1)	<b>0.0004</b>
CD4 counts(cells/ml)				
>500	251	195 (78%)	1.0	
200–500	385	319 (83%)	1.1 (0.7–1.9)	0.66
<200	224	191 (85%)	1.1 (0.5–2.2)	0.81

<sup>a</sup>Model includes all variables with  $P < 0.20$  on univariate analysis

<sup>b</sup>Odds ratio (95% confidence interval) from dichotomous logistic regression

<sup>c</sup> $P$ -values  $< 0.05$  are bolded

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Table 5

Factors associated with level of HCV viremia among HIV-infected women at baseline WHHS visit, multivariate ordinal logistic regression analyses using log HCV RNA level >0 to <5.0 as reference level<sup>d</sup>

Variable	No. of participants by HCV RNA Level (log <sub>10</sub> copies/ml)			HCV RNA Level (log <sub>10</sub> copies/ml)			
	>0-4.99	5.0-7.0	>7.0	OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>	OR (95% CI)	P-Value
Age (years)							
<35	22	128	8	1.0		1.0	
35	39	473	53	2.2 (1.1-4.2)	<b>0.02</b>	3.5 (1.2-9.7)	<b>0.02</b>
Race							
White	15	98	12	1.0		1.0	
Hispanic	9	109	8	1.6 (0.6-4.3)	0.31	0.7 (0.2-2.9)	0.67
Black	35	386	39	1.4 (0.7-3.0)	0.39	0.7 (0.2-2.0)	0.50
Others	2	8	2	0.5 (0.1-3.1)	0.46	0.9 (0.1-8.6)	0.91
History of amphetamine use							
No	53	585	59	1.0		1.0	
Yes	8	15	1	0.2 (0.0-0.5)	<b>0.002</b>	0.7 (0.0-0.7)	<b>0.03</b>
History of marijuana/hash use							
No	46	433	38	1.0		1.0	
Yes	15	166	21	1.3 (0.6-2.9)	0.45	2.6 (1.0-6.9)	0.06
Ever had sex for drugs, money, shelter							
No	25	239	32	1.0		1.0	
Yes	36	361	28	0.9 (0.5-1.7)	0.73	0.5 (0.2-1.1)	0.10
Sex with injection drug user							
No	22	133	17	1.0		1.0	
Yes	38	458	43	2.1 (1.1-4.0)	<b>0.03</b>	1.4 (0.6-3.3)	0.51
Alcohol use							
0/wk	30	262	28	1.0		1.0	
<3/wk	16	126	10	0.9 (0.4-1.9)	0.81	0.5 (0.2-1.5)	0.23
3-13/wk	9	103	15	1.1 (0.4-2.6)	0.86	1.4 (0.5-4.5)	0.52
13+/wk	5	93	6	1.9 (0.6-5.6)	0.27	0.8 (0.2-3.7)	0.78



Variable	No. of participants by HCV RNA Level (log <sub>10</sub> copies/ml)			HCV RNA Level (log <sub>10</sub> copies/ml)		
	>0-4.99	5.0-7.0	>7.0	5.0-7.0		>7.0
				OR (95% CI) <sup>b</sup>	p-Value <sup>c</sup>	
Current smoking						
No	20	122	13	1.0	1.0	1.0
Yes	41	478	47	1.7 (0.9-3.4)	0.11	1.9 (0.7-4.9)
AIDS						
No	31	400	20	1.0	1.0	1.0
Yes	30	201	41	0.5 (0.2-0.9)	<b>0.02</b>	2.1 (0.9-5.3)
HIV therapy						
None	20	243	16	1.0	1.0	1.0
Mono	19	198	23	1.1 (0.5-2.5)	0.74	0.9 (0.3-2.8)
Combo	16	144	17	0.9 (0.4-2.2)	0.83	1.3 (0.4-4.1)
HAART	6	14	5	0.3 (0.1-1.0)	<b>0.05</b>	2.4 (0.5-12.3)
HIV plasma RNA (copies/ml)						
<4,000	19	175	15	1.0	1.0	1.0
4,000-20,000	9	136	10	1.4 (0.5-3.4)	0.50	0.7 (0.2-2.6)
20,000-100,000	15	141	11	0.9 (0.4-2.1)	0.79	0.7 (0.2-2.4)
>100,000	17	146	25	0.7 (0.3-1.9)	0.52	1.1 (0.3-4.0)
CD4 counts(cells/ml)						
>500	19	164	12	1.0	1.0	1.0
200-500	24	267	28	1.4 (0.6-3.2)	0.40	1.7 (0.6-5.2)
<200	16	158	17	1.8 (0.6-5.6)	0.29	1.7 (0.4-8.0)
CD8 counts(cells/ml)						
>1200	10	114	15	1.0	1.0	1.0
800-1200	16	168	18	1.0 (0.4-2.5)	0.97	0.9 (0.3-2.9)
<800	33	307	24	0.7 (0.3-1.7)	0.41	0.3 (0.1-0.8)

<sup>a</sup>Model includes all variables with  $P < 0.20$  on univariate analysis

<sup>b</sup>Odds ratio (95% confidence interval) from dichotomous logistic regression

<sup>c</sup>P-values < 0.05 are bolded