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Chronic hepatitis C virus infection and increases in viral load in a prospective cohort of young, HIV-uninfected injection drug users

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Abstract

Background—Chronic hepatitis C (HCV) infection, defined as persistent RNA (viral load) for at least 6 months, accounts for up to 50% of all cirrhosis, end-stage liver disease and liver cancer cases. Moreover, elevated HCV viral load is consistently associated with high infectivity and poor therapy response. This study aims to identify modifiable behavioral correlates both chronic HCV infection and increases in viral load over time among injection drug users (IDUs).

Methods—Cross-sectional and longitudinal analyses were performed using self-interview and serological data from a prospective cohort study (2002–2006) among young (age 18–35), HIV-negative, HCV therapy-naïve IDUs (n=113) from metropolitan Chicago, Illinois, USA.

Results—After adjustment for age, gender and race/ethnicity, using drugs measured or mixed in someone else's syringe (odds ratio=2.7, 95% confidence interval: 1.1, 6.7) was associated with chronic (n=75, 66%) versus resolved (n=38, 34%) HCV infection status. Among chronically-infected IDUs, injecting with a new, sterile syringe infrequently (< 1/2 half the time when injecting) compared to frequently (1/2 the time or more when injecting) was associated with increases in viral load over time after adjusting for age, gender, race/ethnicity and time effects.

Conclusions—Reductions in risky injection-related practices among young IDUs may ameliorate both the burden of chronic HCV infection-related liver disease and elevated viral load-related poor treatment response.

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Contributors

As principal and co-investigators, Ronald Hershow, Lawrence Ouellet and Scott Cotler contributed at every step of the study including design, protocol development and implementation. Basmattee Boodram was the Project Director for the entire study period (2002–2006), as well as managed the literature searches and summaries of previous related work, undertook the statistical analysis and wrote the first draft. All authors contributed to and approved the final manuscript.

Conflict of interest

The authors have no conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the work submitted that could inappropriately influence, or perceived to influence, their work.

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Keywords

Hepatitis C; chronic; injection drug use; longitudinal; viral load

1. Introduction

Hepatitis C virus (HCV) infection has an estimated worldwide prevalence of 2.2% (Global Burden of Hepatitis C Work Group, 2004). The primary mode of HCV transmission in developed countries is illicit drug injection (Alter, 2007). Despite humoral and cellular immune responses, an estimated 75%–85% of all HCV infections will become chronic or life-long without treatment (Hoofnagle, 2002). Chronic HCV infection accounts for 60%–70% of all cases of chronic hepatitis, and up to 50% of cases of cirrhosis, end-stage liver disease and liver cancer (Alter, 1995; Alter et al., 1992; Shakil et al., 1995). Although the relationship between viral load and liver disease progression remains controversial (Hisada et al., 2005; McCormick et al., 1996; Poynard et al., 1997; Puoti et al., 1999), elevated viral load is consistently associated with high infectivity and poor HCV treatment response (Idrees and Riazuddin, 2009; Poynard et al., 1998; Torriani et al., 2004).

Some similar reported risk factors for both chronic HCV infection status and elevated viral load include older age at the time of infection (Operskalski et al., 2008; Thomas et al., 2000b), male gender (Alter et al., 1999; Armstrong et al., 2006; Minuk, 1999; Sylvestre and Clements, 2004; Thomas et al., 2000a), African American race (Alter et al., 1999; Pyrsopoulos and Jeffers, 2007; Sylvestre and Clements, 2004), genotype 1 (Berger et al., 1996; Soriano et al., 2008; Strasfeld et al., 2003), specific human leukocyte antigen (HLA) subtypes and polymorphisms (Thomas and Seeff, 2005; Thomas et al., 2009), co-infection with the human immunodeficiency virus (HIV) (Cribier et al., 1995; Soriano et al., 2008; Thomas and Seeff, 2005), an absence of hepatitis B (HBV) infection (Operskalski et al., 2008; Soriano et al., 2008; Thomas et al., 2000a; Thomas et al., 2000b), drug abuse (Operskalski et al., 2008), and parenteral risk behaviors (Operskalski et al., 2008; Quinn et al., 1999; Soriano et al., 2008; Strasfeld et al., 2003; Thomas et al., 2000a; Thomas et al., 2000b; Thomas et al., 2001).

It has been suggested that HCV infection acquired through parenteral exposure results in a higher initial viral burden or reflects the impact of repetitive exposures to either the same or multiple viral genotypes (Quinn et al., 1999). In addition, HCV exists within infected individuals as a heterogeneous population of closely related quasispecies (Martell et al., 1992). Evidence increasingly suggests that the quasispecies nature of HCV may allow the virus to circumvent the immune response, leading to chronic infection (Farci et al., 2000; Martell et al., 1992). Therefore, factors that augment HCV viral heterogeneity within the individual, such as repeated exposure to the viral population of other injection drug users (IDUs), may be associated with chronic HCV infection status.

The progression from HCV infection to liver disease is often clinically silent, and some patients are not known to have HCV until they present with the complications of end-stage liver disease decades later. As such, little is known about the early course of HCV infection. Moreover, liver disease progression is complicated by the presence of infections such HIV and other co-morbidities. This study addresses some of the issues by studying young (age 18–35, median=25 years) IDUs who are estimated to have been infected with HCV for a median of 2.5 years at enrollment. This study aims to identify modifiable factors for both chronic HCV infection and increases in HCV viral load over time. Injection-related practices such as sharing contaminated injection equipment are proposed surrogates for repeated

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exposure to the HCV virus, which are hypothesized to be associated with both HCV chronicity and elevated viral load over time.

2. Methods

2.1. Study design and participants

This study examines data from the Early Natural History of Hepatitis C Among Young Injection Drug Users Study (2002–2006), a longitudinal study that followed HCV antibody-positive IDUs from metropolitan Chicago, Illinois, U.S.A. every 6 months for up to 4 years to identify viral, host, and environmental factors that may affect the early course of HCV infection.

Study participants were recruited from an established pool of participants in three concurrent or recently completed longitudinal studies of young drug users conducted at the same study sites as this study. These were the Chicago, Illinois site of two U.S. multi-city studies: the Second Collaborative Injection Drug User Study (CIDUS II, 1997–99, n=776 [Chicago, Illinois], other cities [Baltimore, Maryland; Los Angeles, California; New Orleans, Louisiana, New York, New York], HCV prevalence at baseline=39% [Chicago, Illinois] and CIDUS III (2002–04, n=796, other cities [Baltimore, Maryland; Los Angeles, California; New York, New York; Seattle, Washington], HCV prevalence=14% [Chicago, Illinois] as well as the Non-Injecting Heroin User Study (NIHU, 2002–2005, Chicago, Illinois, n=689, HCV prevalence=2.3%). Of note, NIHU evaluated transitions into drug injection and included former IDUs who had previously injected >6 months ago; the latter group was screened for participation in our study and were eligible if they resumed injection within 6 months of our study's baseline visit. Descriptions of the methods for each study are detailed elsewhere (Broz and Ouellet, 2010; Garfein et al., 2007; Latka et al., 2001). Briefly, all three studies recruited similar types of participants using similar methods at the same locations within high drug traffic neighborhoods throughout Chicago. Potential participants for CIDUS III and NIHU were recruited using a coupon-based recruitment strategy based on respondent-driven sampling methods described by Heckatorn (Heckathorn, 1997) as well as targeted advertising and street outreach by program staff (Broz and Ouellet, 2010; Garfein et al., 2007). CIDUS II participants were recruited using street outreach and word of mouth (Latka et al., 2001).

HCV antibody-positive participants from the three parent studies were recruited at their HCV test result counseling visit or at a subsequent follow-up visit and were eligible for enrollment in this study if they were between the ages of 18 and 35 and had injected illicit drugs in the past 6 months. Most HCV-positive participants of our study were recruited from the CIDUS III (77%) or an earlier round of this study (CIDUS II, 14%), with fewer from NIHU (9%). This study had a high participation rate, with >85% of those approached from the parent studies enrolling into the study.

Of the 125 IDUs enrolled in this study, 6 were excluded due to HIV co-infection since this small number impeded evaluation of HIV as a risk factor for chronic infection status or changes in HCV viral load. An additional 6 participants were excluded because they did not have the minimum 2 study visits needed for outcome classification. All participants in the final study sample were HCV antiviral therapy-naïve at enrollment (n=113), with 3 commencing treatment at follow-up. Since treatment would affect the viral load measurements, the study visits after commencing treatment were excluded from the longitudinal analysis.

The study evaluation design is comprised of two parts. First, a cross-sectional analysis examined socio-demographic and injection-related risk factors for chronic (n=75) compared

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to resolved (n=38) HCV infection. Second, a longitudinal analysis evaluated the association between the same factors and increases in viral load over time among those with chronic HCV infection without key missing demographic or serological data (n=3). For the latter, the final sample was 72 individuals with a total of 404 study visits.

2.2. Data collection

Audio computer-assisted self-interview (ACASI) software was used at baseline and at every follow-up visit to administer a questionnaire to collect socio-demographic and risk behavior data pertaining to the previous 6 months. Serological tests that were completed at each study visit include HIV enzyme immunoassay (EIA-3.0, Ortho Diagnostic Systems, Inc., Raritan, NJ, USA) and HCV viral load (HCV RNA SuperQuant™, National Genetics Institute, Los Angeles, CA, USA) using polymerase chain reaction (PCR) amplification with a linear range of 40 international equivalent units per milliliter (IU/mL) to 2 million IU/mL. Antibody tests for hepatitis A (HAV) (anti-HAV; HAVAB, Abbott Laboratories, Abbott Park, IL) and hepatitis B (HBV) (anti-HBc; CORAB, Abbott Laboratories, Abbott Park, IL, USA) were performed only at the baseline visit, and all antibody-negative participants were offered hepatitis A and B vaccinations. HCV genotyping (TRUGENE 5'NC, Bayer HealthCare, Berkeley, CA, USA) was performed in most chronically-infected participants who had the laboratory minimum viral load of ≥ 4,000 IU/mL (60 out of 75).

2.3. Measures and definitions

The outcome in the cross-sectional study—chronic HCV infection—is defined as persistent RNA for at least 6 months as suggested in prior studies (Fishbein et al., 2006; Kuramoto et al., 2002; Thomas and Seeff, 2005). Conversely, resolved HCV infection is defined as having undetectable viral load for the same period. Measures representing independent variables included demographic characteristics (age, gender, race/ethnicity), alcohol use, injection-related behavioral practices (frequency of injection drug use, frequency of injecting with a new syringe, using drugs measured or mixed in someone else's syringe, injecting with a syringe used before by someone else), and a history of sexually transmitted disease). Two variables were estimated at every study visit. Length of injection history represents the interval between the date of illicit drug injection initiation and the study visit date. Years of HCV infection was estimated as the midpoint of the interval between the date of illicit drug injection initiation and the first positive HCV antibody test result (80% of participants) or the interval between the last known negative and the first positive HCV antibody test result (20% of participants).

To reduce sparse categories in key injection-related variables, those with similar odds ratios (OR) for chronic HCV infection status were combined. For instance, the question 'how often did you inject with a new, sterile syringe in the past 6 months?' had four response categories: less than 1/2 the time, about 1/2 the time, more than 1/2 the time but not always, and always. In this case, the first two categories were collapsed due to similar ORs, as were the latter two.

2.4. Statistical analyses

For the cross-sectional analysis of factors associated with chronic compared to resolved HCV infection, the OR and 95% confidence interval (CI) were used to compare these groups for categorical variables and the Student's t-test for continuous variables; a multivariable logistic model was developed based on a previously reported risk factors and guided by the study's hypothesis. Select variables (age, race/ethnicity, gender) were included in all models regardless of statistical significance. Stepwise and forward selection procedures were used to evaluate injection-related and other variables for model inclusion if $p<0.05$.

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For the longitudinal analysis, risk factors for change in $\log_{10}$ HCV viral load over time relative to the baseline level were examined using mixed-effects regression by maximum likelihood for continuous outcomes. This method essentially adjusted for the baseline viral load for each participant, which is expected to be affected by the length of the infection period. Due to inconsistent adherence to scheduled study visit dates, time was examined as a continuous variable to account for this variability. Both fixed and time-varying covariates were examined in mixed effects regression for changes in $\log_{10}$ viral load over time.

All data analyses were conducted using Statistical Analysis Software (SAS version 9.1, SAS Institute, Cary, NC). The study was approved by the Institutional Review Board of the University of Illinois at Chicago, and all participants provided informed consent at the baseline visit. Throughout the study, all participants were offered harm reduction and drug cessation counseling, HIV testing, HAV and HBV vaccinations, and HCV treatment referrals.

3. Results

3.1. Cross-sectional: Correlates of chronic HCV infection

Among the 113 study participants in the cross-sectional analysis, 75 (66%) were chronically infected with HCV, while 38 (34%) had resolved infection. Table 1 illustrates that these two groups were similar on most characteristics at baseline with a few exceptions. Injecting with a syringe that had been used by someone else and injecting drugs measured or mixed in someone else's syringe was more common among IDUs with chronic compared to those with resolved HCV infection. Of note, it was unfeasible to evaluate the role of HCV genotype on chronic infection status since individuals with resolved infection did not have the required laboratory minimum RNA level for genotype determination. In a multivariable logistic model that adjusted for age, gender, race/ethnicity (all $p>0.05$), using drugs measured or mixed in someone else's syringe (OR=2.7, 95% CI: 1.1, 6.7) remained a significant correlate of chronic HCV infection status. For many of the other injection-related variables listed on Table 1, a positive, albeit statistically insignificant ($p>0.05$), association with chronic HCV infection status was found in multivariable analysis; therefore, no additional variables were included in the final model.

3.2. Longitudinal: Factors associated with increases in viral load over time

Among those with chronic HCV infection who met the criteria for inclusion in the longitudinal analysis (n=72), the mean and median baseline $\log_{10}$ HCV viral load, respectively was 5.3 and 5.7 with a standard deviation (s.d.) of 1.2. Table 1 includes the baseline mean and median $\log_{10}$ HCV viral load by covariates of interest. Compared to their counterparts, men, those who consumed alcohol > 1 day per week, and those with genotype other than 1 had significantly ($p<0.05$) higher mean baseline HCV viral load (Table 1). Although not statistically significant ($p>0.05$), IDUs aged 18–23 in this sample had higher mean baseline HCV viral load compared to those aged 24–35, while little variation was found by race/ethnicity; however, our sample was predominantly non-Hispanic white (61.3%) or Hispanic (21.3%), with fewer non-Hispanic black (8.0%) and other race/ethnicity (9.3%) (Table 1). Compared to their counterparts, a higher but statistically insignificant ($p>0.05$) mean baseline HCV viral load was noted for those who had been injecting drugs longer (> 3 years), those who used drugs measured or mixed in someone else's syringe, those with prior or current HAV or HBV infection, and those with HCV genotype other than 1 (Table 1).

Over time, there was an overall decline in HCV viral load for all participants (-0.06 $\log_{10}$ for every 6 months in the study, $p=0.02$) relative to the baseline level. However, two notable

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covariate effects were also found. First, compared to those who injected with a new, sterile syringe frequently (1/2 half the time or more), those who injected with a new syringe infrequently (less than 1/2 the time) exhibited a slight (p=0.05) average increase of 0.18 $\log_{10}$ per 6 months of study enrollment. Second, men compared to women had a significant average decrease in $\log_{10}$ HCV RNA (−0.37, p=0.04) over time. Nonetheless, men and women had similar risk factors for changes in HCV viral load over time in stratified models, supporting a combined multivariable model for both genders. In the final longitudinal model, injecting with a new syringe ≤ 1/2 the time was associated with a significant (p=0.02) average increase in HCV viral of 0.19 $\log_{10}$ per 6 months of study enrollment, after adjusting for age, gender, race/ethnicity and time effects (Table 2). Similar to the cross-sectional analysis, many of the injection-related variables on Table 1 showed a positive, albeit statistically insignificant, (p>0.05) association with an increase in HCV viral load over time in multivariable analysis. As such, no additional variables were included in the final model.

4. Discussion

To the authors' knowledge, this is the first study to examine factors associated with chronic HCV infection and increases in viral load over time in a population of young (median age=25, range 18–35), HIV-negative, HCV therapy-naïve IDUs. This study showed a slightly lower chronic HCV infection prevalence (66%) among young IDUs compared to that reported in the literature (75%–85%). Given the young age of the study population, this finding is consistent with prior studies that suggest older age at the time of infection may be associated with chronic HCV infection (Operskalski et al., 2008; Thomas et al., 2000b). The main finding was a positive association between risky injection practices and both chronic HCV infection status and increases in viral load over time.

Consistent with earlier studies (DuBois et al., 1994; Thomas et al., 2000b), higher viral load at baseline and over time was observed among men compared to women. In multivariable longitudinal analysis, the parameter estimate (−0.38) suggests that men had an overall decline in viral load over time. However, this is due to the referent group (women) exhibiting more fluctuation, with an average increase of 0.38 over time. As such, men had higher, more stable HCV viral load over time compared to women. Since no significant differences in age, race/ethnicity and injection practices were found by gender (data not shown), this finding may be partly due to a slightly longer estimated period of infection for in men compared to women (median=2.8 vs. 2.2 years, p=0.06), which would provide more time for infections to stabilize. Moreover, the smaller sample for women (n=28) compared to men (n=44) may have impeded detection of additional differences that may facilitate interpretation of this finding.

This study does not provide strong support for an association between older age and chronic HCV infection. However, in multivariable analysis, older age (24–35 vs. 18–23) was a borderline predictor (OR=2.5, 95% CI: 1.0, 6.5), which lends some support to prior findings (Operskalski et al., 2008; Thomas et al., 2000b) (data not shown) The largest portion of the study population was non-Hispanic white (56%), which is consistent with recent studies showing that this is the dominant racial/ethnic group currently initiating injection drug use (Broz and Ouellet, 2008; Neaigus et al., 2006). Nonetheless, evaluation of black race/ethnicity was impeded by a small sample for this group (8% of sample).

Previous studies have shown HCV viral loads to be relatively stable over time in various populations (Gordon et al., 1998; Hollingsworth et al., 1996; Yeo et al., 2001; Yoshimura et al., 1997), while others have shown considerable fluctuation (Eyster et al., 1994; Fishbein et al., 2006; Halfon et al., 1998). These conflicting results may in part be due to study design

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issues, including small sample sizes, short periods of follow-up, and variable quantification methods. In a prior study, needle sharing as a marker for HCV re-infection was positively associated with viral load among IDUs (Thomas et al., 2000b), which is supported by this study's findings using similar risky injection markers (Tables 1 and 2). However, after adjusting for these injection-related practices, age, gender, race/ethnicity, a significant ($p=0.02$) average decrease in viral load was observed. Since visits after commencing of any antiviral therapy were excluded for applicable participants, one suggested explanation may be related to participant experiences throughout the study period. All participants received ongoing harm reduction education and services (e.g., syringe exchange, counseling, viral load data), which may have led them to reduce risky behavior. It is possible that the cumulative effect of positive injection-related behavioral modification may have reduced re-exposure to the HCV virus over time. It is also important to note that several variables reported on Table 1 (injecting with a new, sterile syringe, using drugs measured or mixed in someone else's syringe, injecting with a syringe used before by someone else) were moderately correlated (Pearson's correlation (r): 0.6–0.7). While all of these variables might indicate similar measures for repeated exposure to the HCV virus, some IDUs might have modified one behavior over time, but not others. This is a suggested explanation for why using drugs measured or mixed in someone else's syringe was a significant correlate of chronic HCV infection, while injecting with a new, sterile syringe was a correlate for increases in HCV viremia over time.

There are several notable limitations of this study. First, the temporal relationship between risk behaviors and HCV chronicity cannot be firmly established for our cross-sectional analysis. Second, although socially desirable responding regarding injection behaviors is probable, the use of computerized self-interviews instead of a face-to-face interview has been shown to minimize this occurrence (Des Jarlais et al., 1999; Turner et al., 1998). Third, misclassification of chronic infection is possible, though not likely given the stringent criteria used for classification including the requirement of detectable viral load for at least two study visits ≥ 6 months apart and allowance for sufficient time for viral loads stabilization among those with recent HCV seroconversion. Nonetheless, resolution followed by re-infection may have occurred between study visits, which could affect the analysis of viral load changes over time. While this study lacked histological or genetic-distance examinations to ascertain re-infection, these methods still would not exclude re-infection since it is impossible to examine all variants in the HCV quasispecies (Thomas et al., 2000b). Moreover, this study did not measure IL-28B polymorphism, which is strongly associated with HCV chronic infection status (Thomas et al., 2009). Finally, the study sample size is somewhat small (n=113), especially the longitudinal analysis sample (n=72); however, the longitudinal study is adequately powered to detect viral load fluctuations since it is based on a large number of participant visits (total=404). Nonetheless, although most participants had more than 2 years of follow-up, some had less than a year. It is feasible that a longer period of follow-up may have shown greater increases in viremia (i.e. >0.5 log10) associated with injection-related practices.

This study also includes notable strengths. Our study focused on young HIV-negative IDUs in the early stages of HCV infection, which reduces over-representation of IDUs who survived HCV disease progression. Since our participants were recruited using street outreach and participant-driven methods, they may be different from those recruited in clinical settings.

An adequate explanation for why HCV infection evolves into chronicity in most people and resolves spontaneously in others remains elusive. This study reports modifiable injection-related correlates chronic HCV infection and increases in viral load over time. Reductions in risky injection-related practices among young IDUs may ameliorate both the burden of

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chronic HCV infection-related liver disease and elevated viral load-related reduced therapy response. The differences between men and women in viral load fluctuation over time warrant further investigation. Future studies are also needed to examine whether surrogates of repeated exposure to the HCV virus, such as sharing contaminated injection equipment, are associated with an increase in viral heterogeneity, which may in turn lead to increased risk of chronic HCVs infection among IDUs.

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Table 1

Participant baseline characteristics and risk factors for chronic versus resolved hepatitis C infection (n=113)

	Chronic HCV infection (n=75)	**Resolved HCV infection (n=38)**	**Odds ratio (95% CI[a]**	**Baseline Log_{10} HCV viral load[b] Mean[c], Median[c]**
Characteristics and behaviors[d]	%	%		
Age				
18–23	30.7	42.1	1.0	5.4, 6.1
24–35	69.3	57.9	1.6 (0.7, 3.7)	5.2, 5.5
Gender				
Female	41.3	44.7	1.0	4.9, 5.5
Male	58.7	55.3	1.1 (0.5, 2.5)	5.5 [c], 5.9
Race/ethnicity				
White	61.3	44.7	1.0	5.2, 5.8
Black	8.0	10.5	0.6 (0.4, 2.2)	5.3, 5.4
Hispanic (All)	21.3	34.2	0.5 (0.2, 1.1)	5.4, 6.0
Other	9.3	10.5	0.5 (0.2, 1.1)	5.4, 5.7
Alcohol consumption in past 6 mo				
≤1 day/week	73.3	81.6	1.0	5.2, 5.7
> 1 day/week	26.7	18.4	1.6 (0.6, 4.2)	5.6[c], 5.7
Years injecting illicit drugs				
≤3 years	18.1	26.3	1.0	5.2, 5.5
>3 years	81.9	73.7	1.6 (0.6, 4.1)	5.4, 5.8
Estimated years of hepatitis C infection[e]				
<2 years	34.3	42.1	1.0	5.4, 5.5
≥ 2 years	65.7	57.9	1.4 (0.6, 3.1)	5.3, 5.8
Injected with a syringe used before by someone else in past 6 mo				
No	64.9	84.2	1.0	5.3, 5.7
Yes	35.1	15.8	2.9 (1.1, 7.8)	5.3, 5.8
Frequency of injection with a new, sterile syringe in past 6 mo				
> 1/2 the time	55.4	65.8	1.0	5.4, 5.6
≤ 1/2 the time or less	44.6	34.2	1.5 (0.7, 3.5)	5.2, 5.7
Using drugs measured or mixed in someone else's syringe in past 6 months				
No	54.0	73.7	1.0	5.3, 5.6
Yes	46.0	26.3	2.4 (1.0, 5.6)	5.4, 6.1
Injected drugs daily in past 6 months				
No	32.4	44.7	1.0	5.4, 5.8
Yes	67.6	55.3	1.7 (0.8, 3.8)	5.2, 5.6
Prior or current HAV infection				
No	82.0	86.0	1.0	5.3, 5.7

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	Chronic HCV infection (n=75)	Resolved HCV infection (n=38)	Odds ratio (95% CI)[a]	Baseline Log_{10} HCV viral load[b] Mean[c], Median[c]
Yes	18.0	14.0	1.4 (0.4, 3.8)	5.4, 5.8
Prior or current HBV infection				
No	87.0	86.0	1.0	5.3, 5.7
Yes	13.0	14.0	0.9 (0.3, 3.0)	5.5, 5.7
Ever had an sexually transmitted disease				
No	80.0	79.0	1.0	5.6, 5.9
Yes	20.0	21.0	0.9 (0.4, 2.5)	5.4, 5.7
HCV genotype				
1	59.0	0.0	NA	5.5, 5.8
All others	21.0	0.0	NA	5.8[c], 6.1
Indeterminate[g]	20.0	100.0	NA	NA

CI, confidence interval; HAV, hepatitis A; HBV, hepatitis B; HCV, hepatitis C; IDU, injection drug user; std, standard deviation, NA, not available

[a] Odds ratio was used to compare the listed characteristics between those with chronic versus resolved HCV infection.

[b] To facilitate direct comparison of these data to the multivariable results for the longitudinal analysis, only the sample meeting the criteria for the latter (n=72 out of 75) are reported here. The overall mean and median was 5.3 and 5.7, respectively.

[c] The t-test was used to compare mean viral load across categories of each characteristic. Those categories indicated was significantly ($p>0.05$) when compared to the referent group; A non-parametric test (median test) was used to similarly evaluate the medians, with no differences ($p>0.05$) found.

[d] Referent group for odds ratio, t-test and non-parametric median test is listed first for each covariate.

[e] Estimated using the midpoint of the time interval between a known HCV antibody-negative and positive test or the midpoint between the date of illicit drug injection initiation and the study's HCV antibody-positive test result.

[f] Did not meet laboratory minimum HCV viremia level of ≥4,000 IU/ml for genotyping.

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Table 2

Mixed effects longitudinal regression model: Change in log10 hepatitis C viremia level relative to the baseline level among chronically-infected participants (n=72)

Characteristics and behaviors	Parameter estimate	Standard error	P-value
Age at baseline			
24–35 vs. 18–23	0.12	0.15	0.33
Gender			
Male vs. female	−0.38	0.18	0.04
Race/ethnicity			
Hispanic (All) vs. white	0.24	0.21	0.24
All others vs. white	0.21	0.24	0.48
Frequency of injection with a new syringe in past 6 mo			
≤ 1/2 the time vs. > 1/2 the time	0.19	0.08	0.02
Time (every 6 months)			
Linear trend	−0.06	0.02	0.01
Quadratic trend	0.00	0.01	0.92

IDU, injection drug user.