Published in final edited form as:

J Viral Hepat. 2011 April ; 18(4): e153–e159. doi:10.1111/j.1365-2893.2010.01350.x.

GB virus C infection among young, HIV-negative injection drug users with and without hepatitis C virus infection

B. Boodram¹, R. C. Hershow¹, D. Klinzman², and J. T. Stapleton²

¹Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA

²Department of Internal Medicine, Division of Infectious Diseases, Iowa City Veterans Administration and the University of Iowa, Iowa City, IA, USA

SUMMARY

Our study examined the association between GB virus C (GBV-C) and (i) hepatitis C virus (HCV) infection status, (ii) biomedical indicators of liver disease (alanine and aspartate aminotransferases) and (iii) HCV RNA level among young injection drug users (IDUs) recruited using street outreach and respondent-driven methods. Cross-sectional and longitudinal analyses were completed. GBV-C (active or resolved) infection was significantly ($P < 0.05$) more prevalent among HCV antibody-positive (anti-HCV+) (65.1%) than antibody-negative (anti-HCV–) (32.3%) (OR = 3.9, 95% CI: 2.3–6.9) IDUs. The prevalence of resolved GBV-C infection was highest among those with chronic HCV infection (41.9%), followed by those with resolved HCV infection (34.4%) and significantly lower ($P < 0.05$) among anti-HCV participants (16.9%). Although not statistically significant ($P = 0.13$), a similar pattern was observed for active GBV-C infection. No association between GBV-C infection status and biomedical indicators of liver disease or HCV RNA level over time was observed. In conclusion, GBV-C infection prevalence was higher among anti-HCV+ compared to anti-HCV– young IDUs, similar to prior studies among older populations. In particular, chronically HCV-infected young IDUs had an increased rate of GBV-C clearance.

Keywords

co-infection; GB virus C; hepatitis C virus; injection drug users; prevalence

Hepatitis C (HCV) and GB virus C (GBV-C) are closely related RNA viruses with efficient parenteral transmission. An estimated 60% of all HCV infections is attributable to injection drug use [1], with 170 million persons infected worldwide [2]. As many as 56% of injection drug users (IDUs) have active [3–7] and up to 95% have prior [5] GBV-C infection. Chronic HCV infection ensues an estimated 75%–85% of the time [8] and is involved in about 40% of chronic liver disease [9], while nearly 75% of all GBV-C infections are cleared among immune competent individuals (reviewed in [10]). Most epidemiological studies have shown no direct association between GBV-C and liver or any other human diseases (reviewed in [10, 11]), although a recent study showed that GBV-C was associated with diminished hepatic fibrosis, liver-related death and cirrhosis among individuals also co-infected with HIV and HCV [12]. The suggested mechanism of this effect may be GBV-C-associated lower HIV RNA levels [13–15] and improved immune function [16,17], which may in turn reduce the severity and rate of HCV-related liver disease progression. Nonetheless, the role

of GBV-C co-infection with HCV on liver disease progression is unclear, especially among those without HIV co-infection [18–25]. However, humoral and/or cellular immune responses to one infection may alter the course of the other during co-infection.

Among a population of young, HIV-negative, HCV therapy-naïve IDUs, we examined the association between GBV-C and HCV infection status, biomedical indicators of liver disease and HCV RNA level.

MATERIALS METHODS

Study design and sample description

A cross-sectional and longitudinal study design using serological and interview data from a cohort of young (aged 15–35) IDUs who were recruited using street outreach and respondent-driven sampling methods for participation in two concurrent, longitudinal studies of young IDUs at the University of Illinois at Chicago. After HIV and HCV serostatus were determined at a baseline visit, HIV-negative and anti-HCV– IDUs were randomized into a behavioural intervention trial—the Collaborative Injection Drug User Study III (CIDUS III, 2002–2006), while HIV-negative and anti-HCV+ IDUs were simultaneously referred for participation in the Early Natural History of Hepatitis C Infection Among Young Injection Drug Users Study (NATHCV). The NATHCV study also enrolled a few (~10% of sample) anti-HCV+ participants from an earlier round of the CIDUS study (1997–1999).

The population for this study consisted of a random sample ($n = 124$ of 750) of IDUs from the CIDUS III and all NATHCV study participants ($n = 116$), with 74 of the latter group having chronic and 32 having resolved HCV infection. HCV-infected IDUs in this study were therapy-naïve and had been infected for a brief period (median = 2.5 years), which was estimated using either the midpoint of the interval between (i) the date of illicit drug injection initiation and the anti-HCV result or (ii) the last known anti-HCV– and first anti-HCV+ test result.

A secondary longitudinal analysis to evaluate whether the presence and/or level of GBV-C RNA or E2 antibodies was associated with changes in HCV RNA level over time was performed using IDUs with chronic HCV infection with at least two follow-up visits 6 months apart ($n = 64$ of 74).

Data collection

From the CIDUS III and NATHCV studies, a subset of identical demographic, sexual and injection-related questions pertaining to the previous 3 months that were collected using an audio-computed-assisted self-interview were combined for our analysis. Serological testing for HCV antibody was completed [enzyme immunoassay (EIA) 2.0 or 3.0, Ortho-Clinical Diagnostics, Raritan, NJ, USA], with all anti-HCV+ results with a signal to cut-off ratio of <3.8 verified using a recombinant immunoblot assay (RIBA, Chiron Corporation, Emeryville, CA, USA). Antibody testing was also performed for HIV (EIA 3.0, Ortho Diagnostic Systems, Inc., Raritan, NJ, USA), hepatitis A (anti-HAV; HAVAB, Abbott Laboratories, Abbott Park, IL, USA) and hepatitis B (anti-HBc; CORAB, Abbott Laboratories, Abbott Park, IL, USA). Anti-HCV+ participants were additionally tested for (i) HCV RNA level (HCV SuperQuant™, National Genetics Institute, Los Angeles, CA, USA) using a polymerase chain reaction (PCR) amplification assay with a linear range of 40 international units (IU)/mL to 2 million IU/mL, (ii) HCV genotype (TRUGENE 5'NC, Bayer HealthCare, Berkeley, CA, USA) for those with the laboratory minimum HCV RNA level of 4000 IU/mL ($n = 86$ of 116) and (iii) serum level of alanine aminotransferase (ALT), with a normal range of 10–40 IU/L and aspartate aminotransferase (AST), with a

normal range of 10–50 IU/L for the testing laboratory (Molecular Pathology Laboratory, University of Illinois, Chicago, IL, USA). As previously described [26], GBV-C RNA level was estimated using RT-PCR amplification of the conserved 5′ nontranslated region of the genome, while E2 glycoprotein antibodies (anti-E2) were detected using an enzyme-linked immunosorbent assay (μ Plate anti-HGenv test, Roche Diagnostics, Penzburg, Germany).

Measures

Active GBV-C infection was defined as having GBV-C RNA without the presence of E2 antibodies, while resolved infection was defined as having only E2 antibodies as suggested in prior studies (reviewed in [10]). Chronic HCV infection was defined as having detectable HCV RNA at baseline and at least one subsequent study visit at least 6 months later [8], while resolved HCV infection was defined as being anti-HCV+ with no RNA at baseline and a subsequent visit at least 6 months later [27].

Statistical analysis

Chi-square tests were used to compare categorical variables and the Kruskal–Wallis nonparametric test was used to assess continuous variables including $\log_{10}$ -transformed HCV RNA and GBV-C RNA levels. Multinomial logistic regression was used to evaluate the association between GBV-C and HCV infection status in the cross-sectional analysis, using anti-HCV+ participants as the referent group. The longitudinal analysis evaluated changes in $\log_{10}$ HCV RNA over time relative to the baseline level among those with chronic HCV infection using mixed-effects regression analysis. All statistical analyses were conducted using Statistical Analysis Software (SAS, version 9.1, SAS Institute, Cary, NC, USA). The Institutional Review Board at the University of Illinois at Chicago approved the study.

RESULTS

Table 1 reports characteristics of participants with chronic, resolved and without HCV infection by GBV-C infection status. Participants with chronic HCV infection did not significantly differ on any characteristic when examined by GBV-C status; a similar pattern was observed for those with resolved and those without HCV infection (Table 1). However, compared to participants without HCV infection, those with chronic or resolved HCV infection were significantly ($P < 0.05$) older and more likely to have been injecting drugs for 3 years. Evidence of resolved or active GBV-C infection was common (51.5%) among all IDUs, and significantly ($P < 0.05$) more prevalent among anti-HCV+ (65.1%) than anti-HCV− (32.3%) (OR = 3.9, 95% CI: 2.3–6.9) IDUs. Figure 1 shows that the prevalence of resolved GBV-C infection was highest among those with chronic HCV infection (41.9%), followed by those with resolved HCV infection (34.4%) and significantly lower ($P < 0.05$) among anti-HCV− participants (16.9%). Although not statistically significant ($P = 0.13$), a similar pattern was found for active GBV-C infection prevalence in the three groups (Fig. 1). Furthermore, among those with GBV-C infection ($n = 109$), the ratio of resolved to active GBV-C infection was higher among those with chronic and resolved HCV infection (1.6:1 for both) compared to anti-HCV− (1.1:1) participants ($P < 0.01$).

In multinomial logistic regression analysis, compared to HCV-negative IDUs, those with chronic HCV infection were significantly older, more likely to have been injecting for 3 years, injected drugs more frequently, and were more likely to have resolved GBV-C infection (Table 2). A similar pattern was found for those with resolved HCV infection, with fewer reaching statistical significance partly because of a small sample size. Table 3 shows that $\log_{10}$ HCV RNA, ALT and AST levels were similar among anti-HCV+ IDUs regardless of GBV-C status. In the longitudinal analysis among those with chronic HCV infection, a

significant ($P = 0.01$) average decrease of $0.06 \log_{10}$ HCV RNA level relative to the baseline value was observed after adjusting for demographic and injection-related behaviours; GBV-C infection status was not associated with this decline.

DISCUSSION

This study showed that GBV-C prevalence among young IDUs was similar to that reported among older IDUs [3–5,7,19], especially among those with HCV infection. The proportion of GBV-C-negative IDUs with chronic or resolved HCV infection (31%) was similar to the proportion of anti-HCV– with active or resolved GBV-C infection (32%) (data not shown), suggesting a similar background prevalence and transmission efficiency for both viruses among young IDUs. Moreover, the high prevalence of GBV-C among anti-HCV– IDUs is suggestive of more sexually related transmission because these IDUs were significantly younger and less likely to engage in risky injection-related behaviours than anti-HCV+ participants.

The higher ratio of resolved to active GBV-C infection among all anti-HCV+ compared to anti-HCV– IDUs may have implications for those at high risk for HIV infection. Given the observation that active GBV-C infection was beneficial on HCV-related disease progression among patients co-infected with HIV [12], a propensity to resolve GBV-C infection may increase unfavourable outcomes for anti-HCV+ participants in our study who are at high risk for HIV acquisition. Prior studies [5] have suggested that age might explain this phenomenon because older participants are more likely to experience the protective effect of prior infection; however, there was no significant interaction between age and GBV-C infection status in our multivariable analysis. An alternative explanation may relate to cellular immune responses to HCV. Specifically, given the reported high level of amino acid conservation in HCV and GBV-C nonstructural proteins (NS3 and NS5) (reviewed in [10]), HCV-specific virus T-cell immune responses may cross-react with GBV-C and influence GBV-C clearance. It is conceivable that a robust T-cell response to regions homologous to HCV and GBV-C may result in a higher propensity for resolution for GBV-C, but not HCV. Alternatively, GBV-C has significantly less genetic diversity than HCV, which may decrease the ability of GBV-C to evade host immune responses (reviewed in [28,29]).

This study agrees with prior research suggesting that GBV-C and HCV co-infection does not appear to alter HCV replication [18,19,30,31]. Interestingly, among those with active GBV-C infection, HCV infection was also not associated with GBV-C RNA level, which was similar among participants with chronic, resolved or no HCV infection (Kruskal–Wallis test of comparison of $\log_{10}$ GBV-C RNA, $P = 0.29$; data not shown). GBV-C did not appear to increase liver injury in those with HCV infection, as measured by ALT and AST levels, similar to other studies (reviewed in [11], [19,21,23,25,32]).

An important consideration when interpreting this study's findings is that, in this population, loss of GBV-C RNA is not always accompanied by the appearance of E2 antibodies. Moreover, duration of GBV-C infection may play a role in E2 antibody detection, which has been shown to decline in serum over time after an immune response, with one study showing that 5% of HIV-negative and 29% of HIV-positive patients lost the antibody over a 10.7-year period [33]. These two observations suggest that E2 antibody may not accurately identify resolved infection. Nonetheless, given the young age and short interval of injection, it is unlikely that there were many subjects who lost E2 antibodies.

There are several limitations to this study. First, the cross-sectional design limits the ability to determine the order of GBV-C or HCV infection acquisition. Second, only a few sexual risk factor-related questions were available for analysis. Third, study groups with resolved

HCV infection and groups stratified by HCV and GBV-C infection status had relatively small numbers (Table 1). Fourth, this study did not evaluate the role of GBV-C genotypes on HCV infection status. Fifth, our study is limited by the use of aminotransferases as indicators of liver disease or injury, which are not as precise as histological measures.

In summary, GBV-C and HCV co-infection was common in this cohort of young, HIV-negative IDUs. GBV-C did not appear to influence HCV infection status or HCV-related liver disease, and interference between HCV and GBV-C replication is not supported. Chronically HCV-infected people appear to have an increased rate of GBV-C clearance. If these individuals become HIV-infected, this would obviate the reported potential beneficial effect on liver disease severity and progression among those co-infected with GBV-C and HIV [12].

Acknowledgments

The authors thank Sylvia Furner, Donald Hedeker and Lawrence Ouellet for their thoughtful review of this manuscript. This study was funded in part by a cooperative agreement from the Centers for Disease Control and Prevention for the CIDUS III study (U64/CCU317662, U64/CCU517656, U64/CCU917655, U64/CCU217659, U64/CCU017615), the National Institute of Drug Abuse for the NATHCV study (5R01DA013765-05), the National Institutes of Health (RO1 AI58940-06) and a Veteran's Administration Merit Review (Jack Stapleton).

Abbreviations

ALT	alanine aminotransferase
AST	aspartate aminotransferase
EIA	enzyme immunoassay
HAV	hepatitis A virus
HCV	hepatitis C virus

REFERENCES

1. Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med.* 1999; 341:556–562. [PubMed: 10451460]
2. WHO. Global surveillance and control of hepatitis C. Report of a WHO Consultation organized in collaboration with the Viral Hepatitis Prevention Board, Antwerp, Belgium. *J Viral Hepat.* 1999; 6:35–47. [PubMed: 10847128]
3. Kennedy N, Tong CY, Beeching NJ, et al. Hepatitis G virus infection in drug users in Liverpool. *J Infect.* 1998; 37:140–147. [PubMed: 9821088]
4. Schreier E, Hohne M, Kunkel U, Berg T, Hopf U. Hepatitis GBV-C sequences in patients infected with HCV contaminated anti-D immunoglobulin and among i.v. drug users in Germany. *J Hepatol.* 1996; 25:385–389. [PubMed: 8895019]
5. Thomas DL, Nakatsuji Y, Shih JW, et al. Persistence and clinical significance of hepatitis G virus infections in injecting drug users. *J Infect Dis.* 1997; 176:586–592. [PubMed: 9291303]
6. Yan J, Dennin RH. A high frequency of GBV-C/HGV coinfection in hepatitis C patients in Germany. *World J Gastroenterol.* 2000; 6:833–841. [PubMed: 11819705]
7. Stark K, Bienzle U, Hess G, Engel AM, Hegenscheid B, Schluter V. Detection of the hepatitis G virus genome among injecting drug users, homosexual and bisexual men, and blood donors. *J Infect Dis.* 1996; 174:1320–1323. [PubMed: 8940225]
8. Thomas DL, Seeff LB. Natural history of hepatitis C. *Clin Liver Dis.* 2005; 9:383–398. vi. [PubMed: 16023972]
9. NIH. NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consens State Sci Statements.* 2002; 19:1–46.

10. Stapleton JT. GB virus type C/Hepatitis G virus. *Semin Liver Dis.* 2003; 23:137–148. [PubMed: 12800067]
11. Alter HJ. G-pers creepers, where'd you get those papers? A reassessment of the literature on the hepatitis G virus. *Transfusion.* 1997; 37:569–572. [PubMed: 9191815]
12. Berzsenyi MD, Bowden DS, Kelly HA, et al. Reduction in hepatitis C-related liver disease associated with GB virus C in human immunodeficiency virus coinfection. *Gastroenterology.* 2007; 133:1821–1830. [PubMed: 18054555]
13. Jung S, Knauer O, Donhauser N, et al. Inhibition of HIV strains by GB virus C in cell culture can be mediated by CD4 and CD8 T-lymphocyte derived soluble factors. *AIDS.* 2005; 19:1267–1272. [PubMed: 16052081]
14. Mohr EL, Stapleton JT. GB virus type C interactions with HIV: the role of envelope glycoproteins. *J Viral Hepat.* 2009; 16:757–768. [PubMed: 19758271]
15. Xiang J, George SL, Wunschmann S, Chang Q, Klinzman D, Stapleton JT. Inhibition of HIV-1 replication by GB virus C infection through increases in RANTES, MIP-1alpha, MIP-1beta, and SDF-1. *Lancet.* 2004; 363:2040–2046. [PubMed: 15207954]
16. Lefrere JJ, Roudot-Thoraval F, Morand-Joubert L, et al. Carriage of GB virus C/hepatitis G virus RNA is associated with a slower immunologic, virologic, and clinical progression of human immunodeficiency virus disease in coinfecting persons. *J Infect Dis.* 1999; 179:783–789. [PubMed: 10068572]
17. Williams CF, Klinzman D, Yamashita TE, et al. Persistent GB virus C infection and survival in HIV-infected men. *N Engl J Med.* 2004; 350:981–990. [PubMed: 14999110]
18. Chu C, Hwang S, Luo J, et al. Clinical, virological, immunological, and pathological significance of GB virus C/hepatitis G infection in patients with chronic hepatitis C. *Hepatol Res.* 2001; 19:225–236. [PubMed: 11251305]
19. Goeser T, Seipp S, Wahl R, Muller HM, Stremmel W, Theilmann L. Clinical presentation of GB-C virus infection in drug abusers with chronic hepatitis C. *J Hepatol.* 1997; 26:498–502. [PubMed: 9075655]
20. Manolakopoulos S, Morris A, Davies S, Brown D, Hajat S, Dusheiko G. Influence of GB virus C viraemia on the clinical, virological and histological features of early hepatitis C-related hepatic disease. *J Hepatol.* 1998; 28:173–178. [PubMed: 9514527]
21. Pereira LM, Spinelli V, Ximenes RA, et al. Chronic hepatitis C infection: influence of the viral load, genotypes, and GBV-C/HGV coinfection on the severity of the disease in a Brazilian population. *J Med Virol.* 2002; 67:27–32. [PubMed: 11920814]
22. Saitoh H, Moriyama M, Matsumura H, Goto I, Tanaka N, Aarakawa Y. The clinical significance of GBV-C/HGV exposure in C-viral chronic liver disease and blood donors. *Hepatol Res.* 2002; 22:288–296. [PubMed: 11929714]
23. Shev S, Bjorkman P, Norkrans G, et al. GBV-C/HGV infection in hepatitis C virus-infected deferred Swedish blood donors. *J Med Virol.* 1998; 54:75–79. [PubMed: 9496362]
24. Slimane SB, Albrecht JK, Fang JW, et al. Clinical, virological and histological implications of GB virus-C/hepatitis G virus infection in patients with chronic hepatitis C virus infection: a multicentre study based on 671 patients. *J Viral Hepat.* 2000; 7:51–55. [PubMed: 10718943]
25. Tan D, Matsumoto A, Conry-Cantilena C, et al. Analysis of hepatitis G virus (HGV) RNA, antibody to HGV envelope protein, and risk factors for blood donors coinfecting with HGV and hepatitis C virus. *J Infect Dis.* 1999; 179:1055–1061. [PubMed: 10191204]
26. Souza IE, Allen JB, Xiang J, et al. Effect of primer selection on estimates of GB virus C (GBV-C) prevalence and response to antiretroviral therapy for optimal testing for GBV-C viremia. *J Clin Microbiol.* 2006; 44:3105–3113. [PubMed: 16954234]
27. Hoofnagle JH. Course and outcome of hepatitis C. *Hepatology.* 2002; 36:S21–S29. [PubMed: 12407573]
28. Farci P, Purcell RH. Clinical significance of hepatitis C virus genotypes and quasispecies. *Semin Liver Dis.* 2000; 20:103–126. [PubMed: 10895435]
29. Orii K, Tanaka E, Rokuhara A, et al. Persistent infection mechanism of GB virus C/hepatitis G virus differs from that of hepatitis C virus. *Intervirology.* 2000; 43:139–145. [PubMed: 11044807]

30. Tanaka E, Alter HJ, Nakatsuji Y, et al. Effect of hepatitis G virus infection on chronic hepatitis C. *Ann Intern Med.* 1996; 125:740–743. [PubMed: 8929008]
31. Oshita M, Hayashi N, Mita E, et al. GBV-C/HGV infection in chronic hepatitis C patients: its effect on clinical features and interferon therapy. *J Med Virol.* 1998; 55:98–102. [PubMed: 9598928]
32. Ramezani A, Gachkar L, Eslamifar A, et al. Detection of hepatitis G virus envelope protein E2 antibody in blood donors. *Int J Infect Dis.* 2008; 12:57–61. [PubMed: 17629534]
33. Devereux H, Sabin CA, Kinson Z, et al. Influence of HIV-1 infection on GBV-C infection in multiply infected haemophilic patients. *J Med Virol.* 1998; 56:316–320. [PubMed: 9829635]

Fig. 1. GBV-C infection among IDUs with chronic, resolved and without HCV infection. GBV-C, GB virus C; HCV, hepatitis C; IDUs, injection drug users. Among participants with chronic or resolved HCV infection, the prevalence of resolved and active GBV-C infection are similar ($P = 0.58$), but significantly higher when compared to those without HCV infection ($P < 0.05$).

Participant characteristics by HCV and GBV-C infection status

Characteristic/behaviour	Participants with chronic HCV (n = 74)			Participants with resolved HCV (n = 32)			Participants without HCV (n = 124)					
	RNA (n = 20) *	E2 (n = 31) *	Neg (n = 23) *	RNA (n = 7) *	E2 (n = 11) *	Neg (n = 14) *	RNA (n = 19) *	E2 (n = 21) *	Neg (n = 84) *	P [†]	P [‡]	P [§]
Age												
15–23	30	26	39	57	36	36	42	43	65	0.57	0.07	0.05
24–35	70	74	61	43	64	64	58	57	34			
Median (Range: 16–32)	25	26	24	23	26	27	24	25	22			
Gender												
Male	70	55	65	71	36	57	58	48	67	0.52	0.39	0.25
Female	30	45	35	29	64	43	42	52	33			
Race/ethnicity												
Non-Hispanic white	75	52	65	43	45	43	61	65	73	0.33	0.79	0.73
Hispanic	20	23	22	43	18	36	28	30	22			
All other race/ethnicities	5	26	13	14	36	21	11	5	5			
Years of injecting drugs												
<3 years	35	17	35	29	30	38	53	57	64	0.26	0.11	0.59
3 years	65	83	65	71	70	62	47	43	36			
Median	5	5	5	4	5	4	3	3	3			
How frequently injected drugs in the last year												
Median [¶]	35	45	27	57	40	50	47	57	61	0.4	0.81	0.57
>median	65	55	72	43	60	50	53	43	39			
How often inject with new, sterile syringe												
1/2 the time	58	62	36	43	67	55	68	65	65	0.19	0.71	0.97
<1/2 the time	42	38	64	57	33	45	32	35	35			
Divide drugs with others using a single syringe												
No	45	43	68	57	60	77	78	70	65	0.16	0.69	0.54
Yes	55	57	32	43	40	23	22	30	35			
Number of sex partners												
0	35	20	18	29	20	21	0	11	12	0.68	0.83	0.58

\$watermark-text

\$watermark-text

\$watermark-text

Characteristic/behaviour	Participants with chronic HCV (<i>n</i> = 74)			Participants with resolved HCV (<i>n</i> = 32)			Participants without HCV (<i>n</i> = 124)		
	RNA (<i>n</i> = 20) *	E2 (<i>n</i> = 31) *	Neg (<i>n</i> = 23) *	RNA (<i>n</i> = 7) *	E2 (<i>n</i> = 11) *	Neg (<i>n</i> = 14) *	RNA (<i>n</i> = 19) *	E2 (<i>n</i> = 21) *	Neg (<i>n</i> = 84) *
1	40	43	50	43	30	50	56	44	41
2	25	37	32	29	50	29	44	44	46
Traded sex for drugs or money									
No	100	84	91	100	90	100	79	81	86
Yes	0	16	9	0	10	0	21	19	14
Hepatitis A infection ^{**}									
No	83	85	85	100	88	73	84	90	95
Yes	17	15	15	0	12	27	16	10	5
Hepatitis B infection ^{**}									
No	95	77	87	71	82	71	89	76	92
Yes	5	23	13	29	18	29	11	24	8
Ever had an STD ^{††}									
No	75	84	91	86	70	79	NA	NA	NA
Yes	5	16	9	14	30	21			
Hepatitis C genotype ^{††, ‡‡}									
Genotype 1	80	73	71	NA	NA	NA	NA	NA	NA
All other genotypes	20	27	29						

HCV, hepatitis C; GBV-C, GB virus C; RNA, active GBV-C infection; E2, resolved GBV-C infection; neg, negative for GBV-C RNA and E2 antibodies; STD, sexually transmitted disease.

* Column proportions are based on persons without missing data and may not add up to 100% due to rounding.

[†] Among those with chronic HCV infection, $P < 0.05$ indicates significantly different proportions of participants with chronic, resolved and no GBV-C infection using Chi-square statistic.

[‡] Among those with resolved HCV infection, $P < 0.05$ indicates significantly different proportions of participants with chronic, resolved and no GBV-C infection using Fisher Exact statistic due to small group sizes.

[§] Among those without HCV infection, $P < 0.05$ indicates a significant different proportions of participants with chronic, resolved and no GBV-C infection using Chi-square statistic.

[¶] Overall median number of times injected drugs during the past year (930 times) for all study participants ($n = 230$).

^{**} Antibody test does not distinguish between active or resolved infection.

^{††} Data only available for participants with chronic and resolved HCV infection.

\$watermark-text

\$watermark-text

\$watermark-text

†† Only participants with HCV RNA level >4000 IU/mL were tested due to laboratory requirement.

Table 2

Multinomial logistic model: Risk factors for chronic and resolved HCV infection

Characteristic/risk behaviour	AOR (95% CI)	
	Chronic HCV infection [*] (<i>n</i> = 74)	Resolved HCV infection [*] (<i>n</i> = 32)
Age		
24–35 vs. 15–23	1.6 (1.1, 2.2)	1.1 (0.7, 1.7)
Race/ethnicity		
All others vs. Non-Hispanic white	1.0 (0.7, 1.5)	1.5 (1.0, 2.4)
Years injecting drugs		
3 vs. <3 years	1.7 (1.2, 2.4)	1.6 (1.1, 2.6)
Drug injection frequency in the past year [†]		
>Median vs. median	1.6 (1.1, 2.3)	1.3 (0.9, 2.0)
GB virus C infection		
Active vs. negative	14 (0.8, 2.3)	1.2 (0.6, 2.4)
Resolved vs. negative	1.7 (1.0, 2.8)	1.3 (0.7, 2.5)

HCV, hepatitis C; GBV-C, GB virus C; AOR, adjusted odds ratio; CI, confidence interval.

^{*} Referent category is participants without HCV infection (*n* = 124).[†] Overall median number of times injected drugs for the past year (930 times) for all study participants (*n* = 230).

Table 3

Association between GBV-C infection and HCV infection status, aminotransferases and HCV RNA

	Log₁₀ HCV RNA (mean, median, std IU/mL)	ALT* (mean, median, std IU/L)	AST* (mean, median, std IU/L)	χ^2 P-value
Participants with chronic HCV infection (<i>n</i> = 74, 69.8%)				
No GBV-C	4.9, 5.5, 1.4	63.6, 53.0, 54.5	48.5, 42.0, 31.9	0.59 [†]
Active GBV-C	5.3, 5.5, 1.1	72.3, 50.0, 57.2	57.1, 38.0, 47.5	0.36, 0.65 [‡]
Resolved GBV-C	4.9, 5.3, 1.6	95.8, 56.0, 82.4	58.2, 41.0, 40.7	
Participants with resolved HCV infection (<i>n</i> = 32, 32.2%)				
No GBV-C	NA	18.6, 17.5, 7.0	22.6, 22.5, 5.3	–
Active GBV-C	NA	32.1, 26.0, 32.1	28.9, 25.0, 15.1	0.24, 0.39 [‡]
Resolved GBV-C	NA	22.6, 22.5, 5.3	21.3, 21.0, 5.0	

HCV, hepatitis C; RNA, viremia level; GBV-C, GB virus C; IU/mL or L, international units per millilitre or litre; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

* Laboratory normal range for serum ALT was 10–40 IU/L and 10–50 IU/L for AST.

[†] Kruskal–Wallis nonparametric test was used to examine differences in log₁₀ HCV RNA across the three groups.

[‡] Kruskal–Wallis nonparametric test was used to examine differences in ALT and AST, respectively, across the three HCV study groups.