Prevalence and Associated Factors of Hepatitis C Infection (HCV) in a Multi-site Canadian Population of Illicit Opioid and Other Drug Users (OPICAN)

Michelle Firestone Cruz, MHS[1]
Benedikt Fischer, PhD[1,2]
Jayadeep Patra, MA, PhD[1,2]
Kate Kalousek, HonBA[1,3]
Brenda Newton-Taylor[1]
Jürgen Rehm, PhD[1,2]
Mark Tyndall, MD[4,5]

ABSTRACT

Background: Hepatitis C virus (HCV) infection is highly prevalent in illicit drug user populations, with three in four new HCV infections related to this risk behaviour and a growing HCV disease burden in Canada. Using data from a multi-site cohort study of illicit opioid users in five Canadian cities (OPICAN), this paper explores the prevalence and predictors of HCV status in this high-risk population.

Methods: HCV status of cohort participants was assessed by salivary antibody test. Univariate relationships of HCV status with select variables were examined on the basis of cohort baseline data, and subsequently multivariate models using logistic regression to determine independent predictors of HCV status were generated.

Results: 54.6% of the analysis sample (n=482) was HCV positive. Significant differences in terms of HCV prevalence existed across the sites. Significant variables in the final stepwise logistic regression model included age, site (Toronto), unprotected sex, injecting drug use, drug treatment and incarceration in past year, in addition to opioid use in combination with non-opioids.

Discussion: Besides drug injecting, various other socio-behavioural factors were associated with HCV status in our cohort. On this basis, interventions focusing solely on injection risks are overly limited in scope to prevent HCV transmission in the high-risk population of illicit drug users and need to be broadened. Prevention efforts should also target young injectors as a priority.

MeSH terms: Logistic regression; hepatitis C; illicit drug use; infectious disease; marginalization

La traduction du résumé se trouve à la fin de l'article.

1. Centre for Addiction and Mental Health, Toronto, ON
2. University of Toronto, Toronto
3. York University, Toronto
4. B.C. Centre for Disease Control, Vancouver, BC
5. University of British Columbia, Vancouver

Correspondence and reprint requests: Michelle Firestone Cruz, CAMH, 33 Russell St., Room 2035, Toronto, ON M5S 2S1, Tel: 416-535-8501, ext. 6921, Fax. 416-260-4156, E-mail: michelle_firestone@camh.net

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Hepatitis C virus (HCV) infection is highly prevalent in illicit drug user populations. Studies from North America and abroad consistently indicate HCV prevalence between 50-90%, with incidence rates varying considerably from 4 to 30 per 100 person-years.[1,2] HCV infection can lead to severe morbidity and/or mortality, and thus imposes an extensive disease burden on society.[3,4] In Canada, approximately 300,000 persons are HCV-infected. Injection drug use (IDU) is the primary risk factor for HCV transmission, with 3 out of 4 new HCV infections related to this risk behaviour.[5] Hence, successful reduction of the HCV disease burden can only occur through effective interventions with drug user populations.

This paper examines the predictors of HCV status in a multi-site cohort of illicit opioid users in Canadian cities. The role of several such predictors has been well documented. Drug injecting – via the sharing of injection equipment – is the main causal pathway for HCV transmission.[6,7] While this includes syringe sharing, the sharing of other equipment, e.g., cookers and filters, is an equally strong determinant of HCV transmission.[8,9] One study found that 54% of HCV infections in IDUs who did not share syringes were attributable to cooker/cotton sharing.[10]

Various other behavioural, social or virological factors have been identified as risk factors for HCV infection among illicit drug users. Length of injection career[11] and age[12] have been associated with HCV status since they are directly linked to virus exposure and most injectors become HCV-infected within the first year of injection use.[13] Furthermore, injection use of opioid/cocaine combinations can lead to high frequency injecting and unsafe injection practices, leading to increased HCV transmission risk.[14,15]

A few recent epidemiological studies have suggested an independent association between (oral) crack use and HCV infection status in high-risk populations including IDUs.[16-18] The current evidence is inconclusive, however, as to whether this reflects actual HCV transmission through crack use (i.e., via paraphernalia sharing) or is related to other risk characteristics for HCV common in crack users.

Increased HCV incidence has also been shown in drug users who are HIV-infected, likely attributable to HIV's strong

immuno-compromising effect, reducing the body's defense in case of HCV exposure.[14,19] Evidence points to the role of social marginalization in predicting HCV, e.g., the association between unstable housing (e.g., homelessness) and HCV infection in IDUs.[20,21] Previous exposure to incarceration[22,23] as well as sex work involvement have been associated with HCV status in IDUs.[14,24]

Addiction treatment studies have demonstrated low levels of HCV transmission risks or seroprevalence status in clients retained in opioid (e.g., methadone) maintenance treatment.[25,26] However, the overall effectiveness of such programs for reducing HCV transmission is limited,[2,27] likely due to the combined facts that many users, at least intermittently, relapse from treatment or co-use illicit drugs.

Evidently, HCV infection among illicit drug users is a severe public health problem, influenced by a multitude of factors. Existing interventions have been rather limited in containing the spread of HCV in this population. Our study explores the prevalence and predictors of HCV status in a Canadian multi-site cohort of illicit opioid and other drug users, providing a unique opportunity for pan-Canadian data on this issue.

METHODS

The multi-site OPICAN cohort study monitored health, drug use and social characteristics of illicit opioid and other drug users who a) used illicit opioids regularly for at least one year; and b) were not in treatment at time of recruitment in Vancouver, Edmonton, Toronto, Montreal and Quebec City. Baseline recruitment occurred by outreach-based snowball sampling in 2002. Study applicants were screened for eligibility and then assessed anonymously via a standardized protocol, consisting of an interviewer-administered questionnaire, mental health (i.e., depression) assessments and HCV and HIV salivary antibody testing (see Fischer et al., 2005).[28] Participants provided consent and received a $20 fee. Local research ethics boards approved the study.

The following analysis is based on the OPICAN baseline sample of n=677 cases. Cases excluded from this analysis included: 108 cases from Edmonton*; 22 cases where no salivary sample could be obtained; and 65 cases where samples could not be conclusively analyzed. The final analysis sample was n=482.

We explored univariate relationships of HCV status (positive vs. negative) as the dependent variable with hypothesized factors derived from the literature. Independent variables included: age (26 or older vs. all others); gender (male vs. female); sites (reference: Vancouver); current housing (stable vs. unstable; 'unstable' defined as temporary/transitional or homeless); income source (illegal vs. no illegal income; 'illegal income' defined as sex work, drug dealing and other criminal activity); injection drug use in lifetime (yes vs. no); crack use in the past 30 days (yes vs. no); opioid use in combination with non-opioids in the past 30 days (yes vs. no); engaging in unprotected sex in the past 6 months (yes vs. no); drug treatment in the past 12 months (yes vs. no); incarcerated in the past 12 months (yes vs. no); and current HIV status (negative vs. positive). The relationships were examined by cross-tabulation using Pearson's χ^2.

For multivariate analysis, a stepwise logistic regression model predicting HCV status was computed with the same variables as those analyzed at the univariate level. All data analyses were carried out using SPSS, Version 12 and SAS/ STAT software, Version 9.1.[29]

RESULTS

In the overall analysis sample (N=482), 54.6% were HCV positive. HCV prevalence rates varied significantly across the four sites, with the highest rate in Vancouver (see Table I).

In the univariate analysis, several sociodemographic, substance use and risk behaviour variables were associated with HCV status (see Table II). HCV-positive respondents were more likely to be older, have unstable housing and generate income from illegal activities. Virtually all of the HCV-positive respondents had injected drugs in their lifetime, and fewer HCV-positive respondents had engaged in unprotected sexual activity shortly prior to assessment. Crack use and opioid use in combination with other substances were associated with positive HCV status. HCV-positive respondents were less likely to have had any substance abuse treatment, but more likely to have spent time in detention in the past year. Overall, 15.6% of the sample tested HIV positive; of the HCV positives, 17.5% were also HIV positive.

TABLE I

Prevalence of HCV-positive Cases Across Sites and Total (n=482)

City ***	HCV Positive % (n)
Montreal	40.5% (49)
Quebec City	59.2% (45)
Toronto	49.2% (59)
Vancouver	66.7% (110)
TOTAL	54.6% (263)

*** p<0.001

The stepwise logistic regression analysis (LRA) included gender as a comparison variable, even though this was not significant at the univariate level. The following significant predictors of HCV status emerged from the LRA model (see Table III): opioid use in combination with non-opioid drugs, injection drug use (lifetime) and unprotected sexual activity, drug treatment (in past year), incarceration (in past year), age and site (Toronto). Overall, the model showed acceptable goodness of fit and discrimination between the two categories (positive vs. negative), as evidenced by the Hosmer and Lemeshow test (χ^2 =5.02, df=7, p>0.66) and an area under the receiver operating characteristic curve of 0.74. A discriminant analysis came to similar results (details not shown).

DISCUSSION

We investigated the prevalence of HCV infection and the relationship of possible predictor variables with HCV status among participants in the multi-site OPICAN cohort at baseline. The HCV prevalence rates observed in the local site samples (except for Montreal) fall within the range reported for other illicit drug user populations in North America and elsewhere.[1,30]

Injection history and age both emerged as significant predictors of HCV-positive status in the stepwise logistic regression analysis. Injecting – via the sharing of needles and other injecting equipment – is the primary risk factor for HCV transmission in illicit drug users.[7] Given that the vast majority of OPICAN subjects have injected drugs, this behaviour is likely responsible for most observed HCV transmissions and subsequent infections in our sample. Age is

* In Edmonton, the local REB did not allow for anonymous infectious disease testing

TABLE II

Socio-demographic Characteristics and Risk Behaviours by HCV status (%) (n=482)

	HCV Status	
	Negative (n=219)	Positive (n=263)
Age† (26 or older) ***	65.3 (143)	84.4 (222)
Gender: male[ns]	65.3 (143)	65.4 (172)
Unstable housing ****	49.3 (108)	62.0 (163)
Illegal income generation (past 30 days)*	47.0 (103)	57.0 (150)
Drug use by injection (lifetime)***	85.4 (187)	99.2 (261)
Crack use (past 30 days)****	44.3 (97)	57.0 (150)
Opioid use in combination - past 30 days*	65.8 (144)	74.9 (197)
Unprotected sex - past 6 months***	64.8 (142)	49.0 (129)
Drug Treatment - past 12 months****	29.2 (64)	18.6 (49)
Jail/Detention - past 12 months*	35.6 (78)	45.2 (119)
HIV-positive status[ns]	11.9 (26)	17.5 (46)

† Mean age (SD) for HCV positive 36.1 (8.9) and for HCV negative 32.6 (9.7)
* p<0.05; ** p<0.01; *** p<0.001; **** p≤0.005; ns = not significant

TABLE III

Factors Associated with HCV Status in Sample (n = 482)

	Stepwise Logistic Regression			
Effect†	Unadjusted OR	Adjusted OR	95% CIs	Exact p-values
Age group [26 or older]	2.878	3.548	2.173 - 5.791	0.0001
Sex [male]	1.005	0.791	0.512 - 1.222	0.2903[ns]
Toronto	0.749	0.542	0.335 - 0.877	0.0126
Ever injected - lifetime	22.319	25.821	5.962 - 111.836	0.0001
Opioid use in combination - past 30 days	1.555	1.595	1.030 - 2.470	0.0364
Unprotected sex - past 6 months	0.522	0.492	0.327 - 0.742	0.0070
Drug Treatment - past 12 months	0.555	0.495	0.309 - 0.793	0.0034
Jail/Detention - past 12 months	1.494	1.670	1.102 - 2.531	0.0156

† Age group and sex were controlled in every step of the model
Adjusted odd ratios and CIs are shown as in final model of stepwise logistic regression model
ns Not significant

a relevant factor, as it is typically associated with length of drug use (e.g., injection) history, and therefore determines exposure to HCV. Most IDUs are likely to be HCV-infected shortly after initiating injection use.[2,31] Age-related exposure dynamics are also the likely explanation for the lower HCV prevalence rate in Montreal, as this population was significantly younger (mean: 29 years; 48% under 26 years). The observed age dynamics must be considered when developing HCV interventions, since HCV is more preventable in younger users, while it is older users who are more likely to be HCV-infected and require consideration for treatment.

Further risk behaviours – i.e., opioid and non-opioid drug use and unprotected sex – predicted HCV status in our logistic model. Specifically, poly-drug use behaviours, like heroin/cocaine ('speedballing') or other opioid-stimulant combinations, can lead to "binge" injecting and related unsafe practices that heighten infectious disease transmission risks.[14,32] Interestingly, HCV-positive participants were less likely to report unprotected sex. In the context of illicit drug users often indicating risky sexual practices – often related to sex work – we can only speculate that knowledge of HCV-positive status may have initiated safer sexual practices.[33]

Two important intervention factors were significant predictors of HCV status in our sample. HCV-positive individuals were more likely to report recent incarceration, and less likely to have engaged in drug treatment in the past year. As demonstrated in the literature, illicit drug users exposed to incarceration tend to be more marginalized and isolated from health and other essential care; correctional facilities furthermore are high-risk environments for HCV transmission and provide barriers to infectious disease testing and care.[23,34] Conversely, recent engagement in drug treatment was significantly lower among HCV-positive participants, suggesting that this subgroup also experienced lesser access to therapeutic interventions. This is unfortunate, since addiction treatment programs (e.g., methadone treatment) can provide both preventive effects for infectious disease transmission as well as a useful conduit for the delivery of HCV treatment and primary care for this population.[27,35,36] Hence, the diametrically opposed effects of 'incarceration' and 'treatment' interventions are important to consider for comprehensive HCV intervention programming. Regarding the site variable of Toronto as a protective factor against HCV status, we undertook analyses exploring possible interactions between this and other significant variables in the model, yet none of these emerged significant, i.e., excluding the possibility that one of the underlying mechanisms impacted differentially in the Toronto site. We can only speculate that the overall lower prevalence of injection (vs. non-injection) drug use in our cohort in Toronto compared to the other sites may be mirrored by this effect.[28]

Our analysis has several limitations. First, HCV status was determined by a salivary antibody test. While the HCV EIA test is a standard screen for past or present HCV infection, HCV RNA testing is required for conclusive confirmation of active HCV infection.[37] This is important since spontaneous clearance of HCV may occur in between 10-30% of HCV-infected individuals, leading to possible overestimation of HCV infection prevalence.[38,39] Furthermore, our analysis is based on self-reported data, although their validity even on highly sensitive topics has been confirmed.[40] Finally, logistic regression models are typically used to assess potentially causal factors of an outcome, whereas our analyses assessed potential risk indicators post-hoc to HCV transmission at an unknown point in time, which mainly serve as proxies for past indicators.[41]

The demonstrated prevalence and predictors of HCV status in the OPICAN sample have underscored the multiplicity of factors associated with HCV infection among illicit drug users across Canada. Also, given the role of this population as the host of most new HCV transmissions, current intervention measures focusing mainly on injection risks are prohibitively narrow and rather need to address wider social and therapeutic determinants related to HCV transmission (e.g., incarceration, treatment access). Furthermore, targeted HCV prevention (e.g., via needle exchange programs, treatment) needs to be aimed primarily at younger users where the chance of successful prevention is highest.[42,43]

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RÉSUMÉ

Contexte : Le virus de l'hépatite C (VHC) est extrêmement répandu dans la population de consommateurs de drogues illicites, les trois quarts des nouvelles infections à VHC étant reliées à ce comportement à risque; ainsi donc, le fardeau de cette maladie s'accroît au Canada. Utilisant les données d'une étude de cohorte de consommateurs d'opiacés dans cinq villes canadiennes (OPICAN), notre article porte sur la prévalence et les indicateurs de l'état sérologique relativement au VHC dans cette population à risque.

Méthode : L'infection à VHC chez les participants de la cohorte a été évaluée au moyen d'un test salivaire de détection des anticorps. Les associations univariées entre l'état sérologique relativement au VHC et certaines variables ont été examinées d'après les données de base de la cohorte. Par la suite, des modèles multivariables ont été produits par régression logistique afin de déterminer les indicateurs indépendamment liés à l'état sérologique relativement au VHC.

Résultats : Une proportion de 54,6 % de l'échantillon d'analyse (n = 482) était atteinte du VHC. Il existait des différences significatives, d'une ville à l'autre, en ce qui a trait à la prévalence du VHC. Le modèle final, obtenu par analyse séquentielle de la régression logistique, montre que les facteurs de risque comprennent l'âge, le lieu (Toronto), les relations sexuelles non protégées, l'injection de drogues, les programmes de désintoxication et l'incarcération au cours de l'année antérieure, ainsi que la consommation d'opiacés en combinaison avec des drogues non opioïdes.

Discussion : Plusieurs facteurs socio-comportementaux autres que l'injection de drogues étaient associés à l'infection à VHC dans la cohorte. Par conséquent, les interventions qui visent seulement les risques d'injection sont trop limitées pour prévenir la transmission du VHC dans la population de consommateurs de drogues illicites, et doivent êtres élargies. Les efforts de prévention devraient aussi cibler, de façon prioritaire, les jeunes utilisateurs de drogues injectables.