Prevalence and incidence of hepatitis C virus infection among Aboriginal young people who use drugs: results from the Cedar Project

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ABSTRACT

Background: We sought to estimate the prevalence and incidence of hepatitis C virus (HCV) infection among Aboriginal young people who use drugs and to identify risk factors associated with HCV infection in this population.

Methods: The Cedar Project is a longitudinal study involving Aboriginal young people living in Vancouver and Prince George, British Columbia. Eligibility criteria include age from 14 to 30 years and self-reported use (smoking or injection) of illicit drugs (e.g., crystal methamphetamine, crack cocaine, heroin or other opiates, and cocaine) at least once in the month before enrolment. At each visit, participants completed a detailed questionnaire administered by an Aboriginal interviewer. For this analysis, we included information for 512 participants who were recruited between September 2003 and April 2005.

Results: Among the 512 participants, the prevalence of HCV infection was 34.8% (95% confidence interval [CI] 30.6%–38.9%); the rates were similar in Prince George and Vancouver (34.5% and 35.0% respectively, $p = 0.37$). Among those who reported the use of injection drugs at baseline (n = 286), the prevalence of HCV infection was 59.4% (95% CI 53.8%–65.1%); the rate in this group was slightly higher in Prince George than in Vancouver (62.4% v. 57.1% respectively, $p = 0.37$). The prevalence was 3.5% among participants who reported smoking drugs (n = 226). In the multivariate logistic regression analysis, factors significantly associated with HCV infection among participants who used injection drugs included daily injection of opiates (adjusted odds ratio [OR] 2.7, 95% CI 1.0–7.4), reuse of syringes (adjusted OR 2.4, 95% CI 1.3–4.4), having at least 1 parent who attended residential school (adjusted OR 1.9, 95% CI 1.1–3.4), female sex (adjusted OR 1.9, 95% CI 1.1–3.4) and duration of injection drug use (per year) (adjusted OR 1.4, 95% CI 1.3–1.5). The crude incidence rate of HCV infection was 10.6% and the incidence density estimate was 9.9 per 100 person-years in this cohort.

Interpretation: The prevalence of HCV infection was elevated among Aboriginal young people living in Prince George and Vancouver who use drugs. Culturally based prevention, treatment and harm-reduction programs are urgently needed in this population.

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Little is known about the extent of the hepatitis C (HCV) epidemic among Aboriginal people in North America.[1,2] In Canada, the reasons for this include limited surveillance data, underreporting of HCV infection and inconsistent documentation of ethnicity between the provinces.[3] As a result, national surveillance data can offer only a minimum estimate of the number of infected people. Regrettably, alarming trends have already emerged. The Public Health Agency of Canada estimates that the prevalence of HCV infection is 0.8% in the general population of Canada and that it is 7-fold higher among Aboriginal people than among non-Aboriginal people.[3] Estimates also suggest that the number of new cases is 2.5 times higher among Aboriginal people than in the general population.[4] These data, however, represent Aboriginal people who live in urban areas and may not be generalizable to the entire Aboriginal population. A recent analysis conducted by Health Canada's First Nations, Inuit and Aboriginal Health Branch found that Status Indians represented 4% of the population of the province of British Columbia but accounted for 10% of cases of HCV infection reported in 2001.[4] Other data indicate that the prevalence of HCV infection in Aboriginal populations in different regions of Canada ranges between 0.4% and 29.3%.[1]

Indigenous people's vulnerability to HCV infection and other infectious diseases is becoming increasingly apparent worldwide. A better understanding of the factors and processes that cause drug-related harm among Aboriginal young people is urgently required. Aboriginal scholars have long suggested that any discussions related to addictions and concomitant vulnerability to infectious disease must be framed within the context of the legacy of colonization, including the residential school system, which removed more than 100 000 Aboriginal children from their families between 1874 and 1986[5–7] in an attempt to assimilate and Christianize the youngest generations of Aboriginal people in the absence of their parents and leaders.[8] Although some factors unique to the transmission of infectious disease among young people who use injection drugs are known, studies addressing sex- and drug-related harm and the impact of the residential school system among Aboriginal young people are lacking, particularly in smaller cities and in reserve communities.[9]

Aboriginal leaders and HIV/AIDS service providers are concerned about the impact of the HIV and HCV epidemics, not only in small and large cities but in rural settings as well.[10] We conducted this study to estimate the prevalence and incidence of HCV infection among Aboriginal young people who use drugs and reside in Prince George, a forestry and mining town in the northern interior of British Columbia, and in Vancouver. In addition, we sought to identify demographic and behavioural factors associated with HCV infection in this population.

Methods

Study design and population. We followed the guidelines provided in the Canadian *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*[11] in the development and conduct of this study. We paid particular attention to section 6.0, which pertains to research involving Aboriginal subjects. Our First Nations collaborators, including Aboriginal HIV/AIDS service organizations, were involved in the conception, design and implementation of the Cedar Project. They also reviewed the results of this analysis and approved this manuscript for publication. The study design was approved by the University of British Columbia/Providence Health Care Research Ethics Board.

The Cedar Project is an ongoing prospective cohort study involving Aboriginal young people who use drugs and live in Prince George and Vancouver, with target recruitments of 300 participants in each city. Eligibility criteria include age from 14 to 30 years and use (smoking or injection) of illicit drugs (e.g., crystal methamphetamine, crack cocaine, heroin or other opiates, and cocaine) in the month before enrolment. Participants were eligible to participate if they had been residing in the greater Vancouver or Prince George regions and provided written informed consent. Nonrandom samples of participants were recruited from both cities through a variety of methods, including referral by health care providers, community outreach, participant referral and word of mouth. Based on 2001 Census data, there are an estimated 14 080 Aboriginal people between 15 and 34 years of age residing in the Northern Health Authority (Prince George) and 7675 in the Vancouver Coastal Health Authority (Vancouver).

Data collection and laboratory testing. All participants met with a single study coordinator, who explained procedures, sought informed consent and confirmed study eligibility. Venous blood samples were drawn and tested for HIV and HCV antibodies. At enrolment, participants completed an interviewer-administered questionnaire to elicit sociodemographic data and data on their use (smoking or injection) of illicit drugs, injection practices, sexual risk behaviours and use of health care services. Various sections of the Vancouver Injection Drug User Study (VIDUS) questionnaire were tested and included in our baseline questionnaire.[12] Aboriginal

study personnel conducted all of the interviews; interviewers were blinded to the HIV and HCV status of the participants.

We used algorithms for HCV serologic testing similar to those used in other studies conducted in this region.[13] In brief, AxSYM HCV version 3.0 (Abbott Laboratories, Chicago, Ill.) was used to screen all plasma samples. Negative samples did not undergo further testing. All positive samples underwent further testing with the recombinant Ortho HCV 3.0 ELISA test system (Ortho Clinical Diagnostic Inc., Rochester, NY). Samples that tested positive with both assays were classified as positive. Samples that tested positive by the AxSYM HCV test and negative by the Ortho HCV test were classified as negative.

All eligible participants had private interviews, including pre- and post-test counselling with trained nurses. Participants were requested to return for their HCV test result, at which time referral for HIV/AIDS and hepatitis C care was provided if requested. In addition, subjects were referred to clinics for immunization against hepatitis A and B.

Participants were given a small stipend at each study visit as compensation for their time and to facilitate transportation.

Estimation of HCV prevalence and incidence. To estimate the prevalence of HCV infection, we used a cohort of 512 participants who were recruited between September 2003 and April 2005, had completed their baseline interview during this period and had an HCV antibody test result from this visit.

To estimate the incidence of HCV infection, we used a cohort of 198 participants who completed their enrolment visit between September 2003 and October 2004, were HCV-negative at enrolment and completed at least 1 follow-up HCV antibody test during the observation period (September 2003 to April 2005). The event of interest in this analysis was time to HCV infection. For participants with new infection, we calculated time to HCV infection as the duration (in months) from the date of enrolment to the date of the first positive antibody test result. Follow-up time for event-free participants was calculated as the duration from enrolment to the date of their most recent negative antibody test result. We determined estimates of HCV incidence using crude rates and incidence density methods. To assess the strength of association between factors of interest and HCV infection, we calculated both unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). The low number of HCV seroconversions (n = 21) during the study period did not permit a thorough analysis of risk factors for incident infection.

Because of the known association between HCV infection and parenteral drug use, we stratified prevalence rates of HCV infection by injection and noninjection drug use. We restricted analyses of risk factors to participants who reported injection of drugs. Variables of interest included age, incarceration and housing (stable v. unstable). Participants considered to have stable housing were those living in their own house or apartment. Unstable housing was defined as living arrangements that included single-room occupancy hotels, transitional living arrangements ("couch surfing") and homelessness. Risky injection practices included borrowing and lending of previously used syringes. Drug use behaviours included frequent injection, type of drug, bingeing behaviour and overdose experience. As in previous reports, we defined frequent injection as injection of cocaine, heroin or "speedballs" (cocaine and heroin combined) once or more per day. We defined bingeing as periods when drugs were injected more frequently than usual. Risky sexual behaviours in the 6 months before enrolment and in the 6 months before each follow-up visit included having an HCV-positive sexual partner and exchanging money or drugs for sex.

Statistical analysis. We analyzed bivariate categorical data using the Pearson χ^2 test. We used the Fisher exact test to analyze bivariate categorical data when 25% or more of the expected cell frequencies in a contingency table were less than 5. We compared numeric variables (e.g., age at enrolment, age at first injection) between HCV-positive and HCV-negative participants using the Wilcoxon rank-sum test. We used multivariate logistic regression analysis to model the independent association of demographic variables and behavioural risk factors with HCV infection. Variables that were at least marginally significant in unadjusted analyses ($p < 0.10$) were included in the multivariate logistic regression model. We calculated unadjusted ORs and 95% CIs using logistic regression analysis. All reported p values are 2-sided.

Results

The demographic characteristics of the 512 participants are summarized in Table 1. A total of 178 participants were HCV positive at enrolment, for a prevalence of 34.8% (95% CI 30.6%–38.9%). The prevalence was similar in both locations (34.5% in Prince George and 35.0% in Vancouver, $p = 0.37$). Of the 286 participants at baseline who reported using injection drugs, 170

Table 1: Demographic characteristics of 512 Aboriginal young people who participated in the Cedar Project between September 2003 and April 2005

Characteristic	No. (%) of participants* *n = 512*
Female sex	265 (51.8)
Age at enrolment, yr, median (range)	23 (14–30)
Heterosexual social/sexual identity	456 (89.1)
Single marital status	390 (76.2)
High school not completed	423 (82.6)
Unstable housing	230 (44.9)
≥ 1 parent attended residential school	286 (55.9)
Taken from biological parents (ever)	327 (63.9)
Age when first taken from biological parents, yr, median (range)	5 (1–19)
Nonconsensual sex (ever)	244 (47.7)
Age at first nonconsensual sex, yr, median (range)	7 (1–25)
Attempted suicide (ever)	187 (36.5)
Incarcerated (ever)	342 (66.8)
Age at first incarceration, yr, median (range)	16 (10–28)
Pregnancy (ever) among female participants	201 (39.3)
Involvement in survival sex work† (ever)	195 (38.1)
Age at first involvement in survival sex work, yr, median (range)	16 (10–28)
Injection drug use	286 (55.9)

*Unless stated otherwise.
†Exchanging sex for such things as food and shelter.

were HCV positive, for a prevalence of 59.4% (95% CI 53.8%–65.1%); 38% of these HCV-positive participants reported that they had been injecting drugs for 2 years or less. The prevalence among those who used injection drugs was higher in Prince George than in Vancouver (62.4% v. 57.1%); this difference was not statistically significant (p = 0.37). The prevalence among the 226 participants at baseline who reported noninjection use of drugs was 3.5%.

A total of 199 participants who were HCV negative at enrolment were followed for a median of 11 months. These participants contributed 212.7 person-years of observation (data not shown). During the observation period, 21 new infections were recorded in this cohort, for a crude incidence rate of 10.6% and an incidence density estimate of 9.9 per 100 person-years. The incidence of HCV infection was higher in Prince George than in Vancouver (12.9 v. 7.5 per 100 person-years); this difference was not statistically significant ($p > 0.10$). The incidence density was 22.6 per 100 person-years among the participants who reported injection drug use (n = 71) and 6.7 per 100 person-years among those who reported noninjection drug use (n = 128). Of the 21 participants with new HCV infection, 14 (67%) reported use of injection drugs at enrolment. Of the 7 (33%) who reported noninjection drug use at enrolment, all 7 reported use of injection drugs at 1 or more follow-up visits.

In the univariate analysis, we found that HCV infection at enrolment among the participants who reported use of injection drugs was significantly associated with daily injection of drugs (Table 2): speedballs (unadjusted OR 5.6, 95% CI 1.6–19.3), morphine (unadjusted OR 3.7, 95% CI 1.0–12.9), cocaine (unadjusted OR 3.3, 95% CI 1.8–6.1), hydromorphone (unadjusted OR 3.1, 95% CI 0.9–11.2) and heroin (unadjusted OR 2.0, 95% CI 1.1–3.5). HCV infection at enrolment was also significantly associated with female sex, having at least 1 parent who attended residential school, involvement in sex work, incarceration, current or past methadone treatment and reuse of syringes. Other significant risk factors were duration of drug use and age (Table 2): participants who were HCV positive at enrolment reported significantly longer periods of drug use (injection drugs, unadjusted OR 1.42 [95% CI 1.26–1.56]; noninjection drugs, unadjusted OR 1.12 [95% CI 1.05–1.20) and were older (unadjusted OR 1.11, 95% CI 1.03–1.18) than the HCV-negative participants.

In the multivariate analysis, we combined responses for daily use of some opiates (morphine, hydromorphone or speedballs) into 1 variable (i.e., daily injection of opiates) because the numbers were small for both HCV-positive and HCV-negative participants. We found that the following risk factors were independently associated with HCV infection in the multivariate analysis: daily injection of opiates (adjusted OR 2.7, 95% CI 1.0–7.4), reuse of syringes (adjusted OR 2.4, 95% CI 1.3–4.4), having at least 1 parent who attended residential school (adjusted OR 1.9, 95% CI 1.1–3.4), female sex (adjusted OR 1.9, 95% CI 1.1–3.4) and duration of injection drug use (adjusted OR 1.4, 95% CI 1.3–1.5) (Table 3). Estimates of risk for the variables in this multivariate model were similar after adjustment for geographic location.

Interpretation

In this group of Aboriginal young people who use injection drugs in Prince George and Vancouver, HCV infection spread to levels above 55%, and the incidence rate of HCV infection was 10.6%. These findings were unexpected and reflect how rapidly this virus can spread even in the early period just after injection drug use begins.[13–16] Aboriginal and non-Aboriginal scholars agree that the relation between the cumulative effects of historical and current trauma are directly related to the HIV epidemic

Table 2: Demographic and behavioural characteristics of HCV-positive and HCV-negative participants who reported use of injection drugs at enrolment

Variable	HCV status; % of participants*			Unadjusted odds ratio (95% CI)
	HCV positive, %	HCV negative, %	*p* value	
Age, yr, median (IQR)	25 (14–30)	24 (15–30)	0.004	1.11 (1.03–1.18)
Female sex	62.4	47.4	0.012	1.9 (1.1–3.0)
Living in Prince George	45.9	40.5	0.369	1.2 (0.8–2.0)
Completed high school or attended technical school, college or university	19.1	16.5	0.587	1.2 (0.6–2.2)
Unstable housing	51.9	57.7	0.344	0.8 (0.5–1.2)
≥ 1 parent attended residential school	62.4	50.0	0.038	1.7 (1.0–2.7)
Taken from biological parents (ever)	62.4	63.8	0.804	0.9 (0.6–1.5)
Sexual behaviour				
Nonconsensual sex (ever)	54.1	54.3	0.974	1.0 (0.6–1.6)
Sex with client in previous 6 mo	44.7	26.7	0.002	2.2 (1.3–3.7)
Paid for sex (ever)	57.1	39.7	0.004	2.0 (1.3–3.3)
Attempted suicide	37.7	43.1	0.355	0.8 (0.5–1.3)
Detained by police	83.5	78.5	0.278	1.4 (0.8–2.5)
Incarcerated (ever)	81.2	69.8	0.026	1.9 (1.1–3.2)
Enrolment in alcohol or drug treatment program (ever)	80.6	71.6	0.075	1.7 (0.9–2.8)
Methadone treatment program (ever)	35.9	12.1	< 0.001	4.1 (2.1–7.7)
Methadone treatment program (current)	14.1	4.3	0.007	3.6 (1.4–9.9)
Daily drug use (≥ 1 injections per day)				
Speedballs†	13.0	2.6	0.002	5.6 (1.6–19.3)
Morphine	8.8	2.6	0.033	3.7 (1.0–12.9)
Cocaine	36.5	14.7	< 0.001	3.3 (1.8–6.1)
Hydromorphone	7.6	2.6	0.068	3.1 (0.9–11.2)
Heroin	32.9	19.8	0.015	2.0 (1.1–3.5)
Crystal methamphetamine	6.1	7.6	0.655	0.8 (0.3–2.1)
Reuse of syringes	41.2	21.5	< 0.001	2.5 (1.5–4.4)
Borrowing of injection equipment	20.0	12.9	0.119	1.7 (0.9–3.3)
Difficulty accessing clean needles	15.5	11.1	0.355	1.5 (0.6–3.4)
Binge drug use	20.0	16.4	0.439	1.3 (0.7–2.4)
Help required to inject drugs	27.1	36.2	0.100	0.7 (0.4–1.1)
Duration of drug use, yr, median (IQR)				
Injection drugs	5 (< 1–15)	1 (< 1–10)	< 0.001	1.42 (1.26–1.56)
Noninjection drugs	7 (< 1–17)	4 (< 1–15)	< 0.001	1.12 (1.05–1.20)

Note: CI = confidence interval, HCV = hepatitis C virus, IQR = interquartile range.
*Unless stated otherwise.
†Cocaine and heroin combined.

among indigenous peoples in North America. The prevalence of HCV infection among the Aboriginal young people who reported use of injection drugs in our study (59%) was higher than the prevalence in a previous study involving young people who were using injection drugs in Vancouver (46%).[17] Furthermore, the prevalence of HCV infection among the Aboriginal young people in our study who live in the northern community of Prince George mirrored the prevalence among young people using injection drugs in Vancouver's Downtown Eastside. Given that Vancouver has consistently been described as an epicentre of the HIV and HCV epidemics in British Columbia and in Canada since the 1990s, these findings indicate that the faces of these epidemics are changing.

We found that daily injection of opiates, reuse of syringes, having at least 1 parent who attended residential school, female sex and duration of injection drug use were independent risk factors for HCV infection at baseline. The strong association between frequent use of opiates and HCV prevalence is a relatively new finding in this setting. A persistent risk factor for blood-borne infection in Vancouver's Downtown Eastside is frequent injection of cocaine.[16,17] The fact that young people in our study

Table 3: Factors independently associated with HCV infection among participants who reported use of injection drugs

Risk factor	Adjusted odds ratio (95% CI)*
Daily injection of opiates (speedballs, morphine or dilaudid)	2.7 (1.0–7.4)
Reuse of syringes	2.4 (1.3–4.4)
≥ 1 parent attended residential school	1.9 (1.1–3.4)
Female sex	1.9 (1.1–3.4)
Duration of injection drug use (per year)	1.4 (1.3–1.5)

Note: HCV = hepatitis C virus, CI = confidence interval.
*Adjusted for enrolment in methadone treatment program (ever and current), daily injection of cocaine, sex with client in previous 6 months, paid for sex (ever), daily injection of heroin and incarceration (ever).

reported injecting a wide array of opiates (morphine, hydromorphone and speedballs) along with cocaine on a daily basis and that daily opiate use, and not cocaine use, was associated with HCV seropositivity warrants further investigation. Methadone maintenance therapy is the primary treatment of opiate addiction in Canada and has proven effective in preventing HIV infection.[18] Unfortunately, the evidence supporting its effectiveness in reducing HCV incidence is less substantial.[19,20] In this study, methadone maintenance therapy was not associated with a reduction of risk for HCV infection. Despite this lack of evidence, methadone maintenance therapy continues to be recommended, in part because it helps to reduce the number of daily opiate injections and because injection episodes are presumed to be safer when they occur. Increased efforts must be made to determine the barriers to receiving such treatment for Aboriginal young people, particularly in smaller city centres.

We found that reusing injection equipment was another significant risk factor for HCV infection in our study. Because of previously demonstrated associations between other high-risk behaviours related to accessibility of clean syringes,[18] we compared participants in our study who reported reusing syringes during the 6 months before enrolment with those who did not reuse injection equipment. Indeed, participants who reported reusing their syringes were significantly more likely to report borrowing and sharing injection equipment, bingeing with injection drugs and requiring assistance injecting during that period.

In recent years the federal government and Aboriginal communities across Canada have been debating the relative toll of the cumulative and intergenerational effects of historical trauma related to the Indian residential school system.[19] The forced removal of children from their homes and placement in boarding schools is considered by many researchers, based on testimony given by family and community, to be directly responsible for poor health outcomes among survivors, including the abuse of drugs and alcohol.[20] Currently, there are an estimated 80 000 survivors of the residential school system alive in Canada, of whom 35 000 are in British Columbia.[21] As affected communities raise their children and grandchildren, the intergenerational effects of abuse and familial fragmentation become evident.[22,23] Several Aboriginal HIV/AIDS service providers have suggested that drug use is just one way that people deal with the complex effects of poverty, despair, discrimination, loss of language and traditional territories and the erosion of culture.[24] Previous research has identified a bivariate relation between having a parent who attended residential school and involvement in the child welfare system with sexual abuse among Aboriginal young people who use drugs in British Columbia.[25] The mechanism of effect between having a parent who attended residential school and increased risk of HCV infection should be the subject of further study.

We found that female sex was significantly associated with HCV infection, even after we adjusted for demographic and behavioural risk factors. Although the majority of these infections can be attributed to injection-related risk behaviours, many young Aboriginal women are intimately involved with men who are usually older and who use injection drugs themselves.[26,27] Indeed, research has demonstrated that, for women who rely on their partners for drug acquisition, preparation and injection, the distribution of power and control in sexual and injection relationships often lies with drug-injecting men who control the money and the drugs.[28,29] Combined, these factors lead to an increased likelihood of unsafe sex and of the female partner being "second on the needle."[12]

Our study has several limitations. We used self-reported behavioural data obtained from a non-probability sample of individuals. Consequently, there is potential for recall bias, socially desirable reporting and misclassification of exposure variables. Responses to questions concerning drug use and sexual behaviours may have been influenced by the participants' knowledge of their HCV antibody status. In addition, recall problems may exist with reporting of past traumatic life events (e.g., being taken from biological parents, whether parents attended residential school, and sexual abuse or nonconsensual sex). The effect of memory on our estimates of risk for these factors is difficult to assess. Nondifferential misclassification of an exposure variable and the resultant bias can lead to a

relative risk estimate that may be either toward or away from the null hypothesis.[30] Furthermore, our estimate of the incidence of HCV infection may have been affected by differential drop-out. We found that participants who were lost to follow-up were younger and more frequent drug users than those who completed follow-up visits. Therefore, our estimates of incidence may be lower than their true values.

Despite these limitations, we believe these data provide important epidemiologic information about the prevalence and incidence of HCV infection in a high-risk Aboriginal population. In the absence of postexposure prophylaxis for HCV infection and an effective vaccine against HCV, primary prevention programs must focus on safer injection practices and reducing the number of people who initiate injection drug use. The high baseline prevalence rates in our study underscore the importance of carefully examining the effectiveness of current harm reduction initiatives in both rural and urban settings. Culturally based prevention, treatment and harm-reduction programs are urgently needed for young people who use injection drugs. Acknowledging the intergenerational trauma related to the residential school system may be one way that Aboriginal leadership and addiction specialists can begin to mitigate the potential impact of the HCV epidemic in their communities.

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