Predictors of Liver-Related Death among People Who Inject Drugs in Vancouver, Canada: A 15-Year Prospective Cohort Study

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Background

- People who inject drugs (PWID) are known to have an elevated risk of both HIV and hepatitis C virus (HCV) infection.

- While HIV/AIDS remains one of the primary causes of death among PWID worldwide, a recent study from Australia has reported an increasing mortality burden of liver disease within this population.

- However, little is known about the contribution of HCV infection to mortality among PWID in other settings.

- Therefore, we sought to identify predictors of liver-related mortality among community-recruited cohorts of PWID in Vancouver, Canada.

Methods

- Data were derived from two prospective cohorts of PWID recruited through self-referrals and street outreach in Vancouver:
  - The Vancouver Injection Drug Users Study (VIDUS): a cohort of HIV-negative adult PWID.
  - The AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS): a cohort of HIV-positive adults who have used illicit drugs other than cannabinoids in the month prior to their baseline interview.

- At baseline and semi-annually thereafter, participants answered an interviewer-administered questionnaire, which elicited data on demographic characteristics, drug use patterns and related exposures, and underwent serologic testing for HIV and HCV.

- Participants were eligible for the present study if they: (1) completed the baseline and at least one follow-up visit for VIDUS or ACCESS between May 1, 1996 and December 31, 2011, and (2) reported having injected drugs during the previous 6 months at baseline.

- Cohort data were linked to the British Columbia Vital Statistics database to ascertain rates and causes of death.

- Liver-related death was defined as having any of the following 10th edition of the International Classification of Diseases (ICD-10) codes: viral hepatitis (B15–19), sequelae of viral hepatitis (B942), liver cancer (C22), alcoholic liver disease (K70) and non-alcoholic liver disease (K71–77) .

- We examined the relationship between HCV infection and liver-related mortality using multivariate Cox regression.

- A sub-analysis examined the effect of HCV/HIV co-infection.

Figure 1: Liver-related mortality rates among PWID in Vancouver, Canada, between 1996 and 2011.
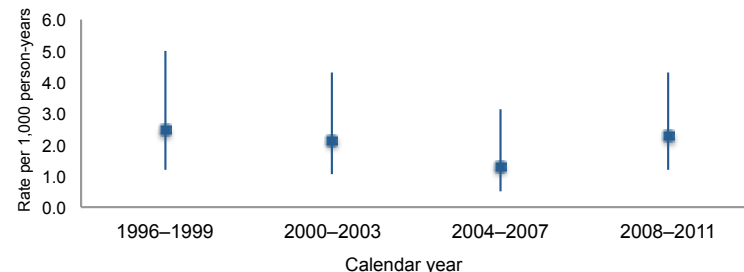
Results

- In total, 2,279 PWID participated in this study and were followed for a median of 60.9 months (interquartile range [IQR]: 34.4 – 113.2).

- Baseline characteristics of the sample are shown in Table 1. As shown, 1,519 (66.7%) were men, and the median age at baseline was 37 years (IQR: 29 – 44).

- In total, 1,921 (84.3%) participants had seroconverted to anti-HCV prior to baseline assessments, and 124 (5.4%) additionally seroconverted during follow-up.

- A total of 31 liver-related deaths were identified during the study period, yielding a liver-related mortality rate of 2.10 (95% confidence interval [CI]: 1.50 – 2.99) deaths per 1,000 person-years.

- As shown in Figure 1, liver-related mortality rates at four-year intervals were relatively stable over time.

- The primary underlying causes of liver-related death were viral hepatitis (38.7%), non-alcoholic liver disease (25.8%), and liver cancer (25.8%).

- Results of bivariate and multivariate Cox regression analyses are shown in Table 2. As shown, HCV seropositivity was not significantly associated with liver-related mortality (adjusted relative hazard [ARH]: 0.45; 95% CI: 0.15 – 1.37), but HIV seropositivity was (ARH: 2.67; 95% CI: 1.27 – 5.63).

- In sub-analysis, individuals with HIV/HCV co-infection had a 2.53 (95% CI: 1.18 – 5.46) times hazard of liver-related death compared with those with HCV mono-infection.

Table 1: Baseline characteristics of PWID participating in the VIDUS and ACCESS cohorts in Vancouver, Canada, between May 1996 and December 2011 (n = 2,279).

Characteristic	n (%)
Age (median, IQR)	37 (29 – 44)
Male gender	1,519 (66.7%)
Caucasian ethnicity	1,393 (61.1%)
Years since first injection (median, IQR)	14 (6 – 24)
Unstable housing[a]	1,602 (70.3%)
Daily heroin injection[a]	881 (38.7%)
Daily cocaine injection[a]	711 (31.2%)
Daily crack smoking[a]	545 (23.9%)
Alcohol consumption (> 4 drinks per day on average)[a]	366 (16.1%)
Engagement in sex work[a]	537 (23.6%)
Enrolment in methadone maintenance therapy[a]	514 (22.6%)
HIV seropositivity	620 (27.2%)
HCV seropositivity	1,921 (84.3%)

PWID: people who inject drugs; VIDUS: Vancouver Injection Drug Users Study; ACCESS: AIDS Care Cohort to Evaluate Access to Survival Services; IQR: interquartile range. [a] denotes activities during the six months prior to the interview.

Table 2: Bivariate and multivariate Cox proportional hazards regression analysis of factors associated with liver-related mortality among PWID in Vancouver, Canada (n = 2,279).

Characteristic	Relative Hazard (RH)	
	Unadjusted (95% CI)	Adjusted (95% CI)
Age[b]		
(Per 10 years older)	1.95 (1.36 – 2.80)	1.59 (0.90 – 2.82)
Gender		
(Male vs. Female)	3.01 (1.18 – 7.66)	2.38 (0.86 – 6.58)
Ethnicity		
(Caucasian vs. Others)	1.80 (0.82 – 3.96)	
Time since first injection		
(Per year longer)	1.05 (1.01 – 1.09)	1.02 (0.98 – 1.07)
Unstable housing[a, b]		
(Yes vs. No)	1.12 (0.55 – 2.29)	
Heroin injection[a, b]		
(Daily vs. < Daily)	0.62 (0.24 – 1.61)	
Cocaine injection[a, b]		
(Daily vs. < Daily)	1.10 (0.43 – 2.82)	
Crack smoking[a, b]		
(Daily vs. < Daily)	0.51 (0.20 – 1.34)	
Alcohol consumption[a, b]		
(> 4 drinks per day vs. ≤ 4 drinks per day)	1.11 (0.32 – 3.90)	
Engagement in sex work[a, b]		
(Yes vs. No)	0.25 (0.03 – 1.76)	
Enrolment in methadone maintenance therapy[a, b]		
(Yes vs. No)	0.84 (0.42 – 1.71)	
Incarceration events[b]		
(1-2 times vs. Never)	1.03 (0.45 – 2.32)	
(3-5 times vs. Never)	0.68 (0.22 – 2.05)	
(> 5 times vs. Never)	0.74 (0.19 – 2.83)	
HIV serostatus[b]		
(Positive vs. Negative)	2.17 (1.06 – 4.43)	2.67 (1.27 – 5.63)
HCV serostatus[b]		
(Positive vs. Negative)	0.85 (0.26 – 2.77)	0.45 (0.15 – 1.37)

PWID: people who inject drugs; CI: confidence interval; [a] refers to activities during the six months prior to interview. [b] denotes time-updated variables.

Discussion

- Our results demonstrate that liver-related mortality rates among PWID in Vancouver were stable between 1996 and 2011.

- In this study, HCV seropositivity did not predict liver-related mortality while HIV seropositivity did.

- Further, we found that HIV/HCV co-infection had a significantly higher risk of liver-related mortality than HCV mono-infection.

- The findings highlight the role of HIV infection rather than HCV infection in contributing to liver-related mortality among PWID in this setting.

- Collectively, these findings highlight the importance of promoting access to diagnostics and treatment for liver disease among HIV-positive PWID.