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Socio-demographic and ecological factors associated with anti-HCV prevalence in people who inject drugs: a systematic review

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Abstract

Background: The World Health Organization (WHO) aim to eliminate hepatitis C virus (HCV) as a public health threat by 2030. People who inject drugs (PWID) are a key risk group for HCV transmission globally. We explored socio-demographic and ecological variables associated with HCV antibody (anti-HCV) prevalence among samples of PWID.

Methods: We systematically searched for and screened journal articles and online reports published between January 2011 and June 2017. Serologically confirmed anti-HCV prevalence among PWID and other study-level socio-demographic variables were extracted. Country-level ecological indicators were sourced from online databases. We used generalized linear models to investigate associations between anti-HCV prevalence estimates and other study-level and country-level variables.

Results: There were 223 studies from 84 countries contributing 569 estimates of anti-HCV prevalence among PWID. Among study-level indicators, higher levels of anti-HCV prevalence were associated with higher HIV prevalence ($B=0.20$; 95% Confidence Interval [95%CI]=0.12, 0.29, $p<0.001$) and year of data collection ($B=-0.08$; 95%CI=-0.15, -0.02; $p=0.011$). At a national level, higher Human Development Index scores ($B=4.37$; 95%CI=0.12, 8.63, $p=0.044$) were associated with higher levels of anti-HCV in samples.

Implications: Serological surveillance data are increasingly available globally; however, there are still geographical gaps in quantification of HCV prevalence among PWID that must be addressed to inform efforts to achieve HCV elimination. Anti-HCV prevalence was lower in samples of PWID from countries with lower Human Development Index scores, which points to an opportunity to provide targeted intervention and potentially control transmission rates of infection in countries characterized by poor population health, education, and income.

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Keywords: Hepatitis C virus; people who inject drugs; HIV; ecological factors; global

1. Introduction

In response to the development of simple, well-tolerated and effective direct-acting antiviral therapies for hepatitis C virus (HCV) infection, the World Health Organization (WHO) has set a target to eliminate HCV as a public health threat globally by 2030 (World Health Organization (WHO), 2017). Currently, there are an estimated 6 million people who inject drugs (PWID) who are HCV positive (Degenhardt et al., 2017; Grebely et al., 2019), and there is currently no indication that this number is decreasing.

Previous work has emphasized the associations between individual-level factors and HCV prevalence and transmission (Diaz et al., 2001; Hagan et al., 2008; Lelutiu-Weinberger et al., 2009; Moss et al., 2002; Platt et al., 2017; Stone et al., 2018). Such factors include duration of injecting, ethnicity, recent incarceration, HIV comorbidity, engaging in injecting risk behaviors (e.g. sharing injecting equipment), as well as using services such as needle-syringe programs (NSP), and opioid agonist treatment (OAT). Due to the increase in available data particularly from low- and middle-income countries, there is an opportunity to update and expand on the work investigating individual risk factors for the prevalence of HCV antibodies (anti-HCV).

Less is understood about country-level ecological factors that might be associated with HCV prevalence. The economic or developmental context of a country may create structural barriers that inhibit implementation of, or access to, harm reduction services and therefore may be associated with HCV prevalence. Further, because HIV and HCV are both transmitted perinatally, associations between ecological characteristics and HIV prevalence among PWID might also be shared with HCV prevalence. These characteristics include harm reduction coverage, general population anti-HCV prevalence, and income inequality (Larney et al., 2019). Understanding the relationship between population and ecological variables and HCV can highlight targets for structural interventions to achieve this goal set by the WHO. Therefore, we aimed to explore socio-demographic and ecological variables associated with anti-HCV prevalence among populations of PWID.

2. Method

2.1. Data source

We used data from a comprehensive systematic review (PROSPERO registration numbers CRD42016052858 and CRD42016052853) of blood borne virus prevalence and sociodemographic characteristics of PWID (Degenhardt et al., 2017). Full methods have been published elsewhere (Degenhardt et al., 2017), and are in accordance with PRISMA and GATHER guidelines (Appendix 1-2). Briefly, we searched for journal articles indexed in Medline, Embase, and PsycINFO and online reports from government, intergovernmental, and non-governmental organisations published between January 2008 to June 2017, and sought-after data via expert requests.

PWID were defined as those injecting illicit or pharmaceutical drugs in the previous 12 months. All studies that reported serologically confirmed anti-HCV prevalence among PWID were considered for inclusion (see Appendix 3 for screening, detailed inclusion/exclusion criteria, and grading study quality). Studies were excluded from analyses if the sample was limited by age, sex, or drugs used as part of the study inclusion criteria.

For each identified study of anti-HCV prevalence among PWID, we extracted anti-HCV prevalence data and pre-defined socio-demographic, drug use, and risk behaviour characteristics of the sample. Extracted data included: median/mean age; median/mean duration of injecting; proportion female; (serologically confirmed) HIV positive; proportion who reported opioids or methamphetamine as their main drug injected; reported recent unstable housing; and within the previous 12 months or ever reported incarceration, engaging in sex work, engaging in injecting risk behaviours (this included but was not limited to sharing needles and syringes), and engaging in sexual risk behaviours (this included but was not limited to sex with a casual partner without a condom).

We further identified country-level ecological indicators of health, development, and inequality that may be associated with HCV infection (Gillespie et al., 2007; Meffre et al., 2010; Nikolopoulos et al., 2015). These included region, estimated national HCV population prevalence (Institute for Health Metrics and Evaluation, 2015), population injecting drug use (IDU) prevalence (Degenhardt et al., 2017), country income level (low/middle/high) (World Bank, 2017b), national incarceration rates (Walmsley, 2016), income inequality (measured by the Gini coefficient, with higher scores indicating greater inequality) (World Bank, 2017a), the Gender Inequality Index (high scores indicate greater inequality) (UNDP, 2016a), the Human Development Index (HDI; a score considering life expectancy at birth, expected and mean years of schooling, and gross national income, whereby a higher score indicates higher level of development) (UNDP, 2016b), NSP coverage, and OAT coverage (Larney et al., 2017).

2.2.Data analysis

To analyse the associations between anti-HCV prevalence and our study- and country-level predictor variables, we used generalised linear models. We decided not to build models for variables that were available for 25% or fewer of all anti-HCV prevalence estimates in the database; this meant we could not explore associations between anti-HCV prevalence in PWID and the proportion of the sample reporting homelessness, incarceration, sexual risk, sex work, or main drug injected.

Where a single study presented multiple estimates (e.g. for different locations), all estimates were included in the models, and clustered by country. As the outcome variable (anti-HCV prevalence in PWID) is a proportion, a logit transformation was performed by the formula $\ln(p/(1-p))$. The adjusted model included all variables from the unadjusted analyses that yielded p -values <0.05 . All analyses were conducted using STATA 14.2.

3. Results

3.1. Study characteristics

There were 569 estimates of anti-HCV prevalence among PWID from 223 studies in 84 countries (Appendix 4). Most of the studies were peer-reviewed journal articles (71.3%) and employed high quality methodological techniques for recruiting participants (72.5% were A- or B-grade). Of those estimates, 19.7% were nationally representative, 23.4% were representative of a sub-national region, and 56.9% were representative of a city.

3.2. Unadjusted analysis

Due to small numbers of studies, the following regions were combined in the generalised linear models: Central Asia and East and South East Asia; Caribbean, Latin America and Sub-Saharan Africa; and Middle East and North Africa and South Asia. Among study-level exposure variables, higher anti-HCV prevalence was associated with older median/mean sample age (coefficient estimate [B]=0.07; 95% confidence intervals [CI]=0.03, 0.11; $p=0.001$); higher HIV prevalence (B=0.17; 95%CI=0.09, 0.24; $p<0.001$); longer duration of injecting (B=0.09; 95%CI=0.03, 0.15; $p=0.002$); and studies with earlier data collection (B=-0.05; 95%CI=-0.11, 0.00; $p=0.040$) (Table 1). Gender distribution and injecting risk behaviours were not associated with anti-HCV prevalence among the samples.

Among country-level exposures, lower gender inequality (B=-1.24; 95%CI=-2.32, -0.17; $p=0.023$) and higher HDI scores (B=2.38; 95%CI=0.71, 4.05; $p=0.005$) were associated with higher anti-HCV prevalence among the samples. Compared to our referent category (Western Europe), anti-HCV prevalence was lower in studies from the Middle East, North Africa and South Asia. National anti-HCV prevalence, injecting drug use prevalence, Gini coefficient, incarceration rate, income level, NSP coverage, and OAT coverage were not associated with study-level anti-HCV prevalence. Scatterplots representing the associations where $p<0.05$ are presented in Figure 1 (scatterplots with associations where $p>0.05$ are presented in Appendix 5).

3.3. Adjusted analysis

We included mean sample age, HIV prevalence, year of data collection, gender inequality index score, HDI scores and region in the adjusted analysis model. We excluded duration of injecting as it was highly correlated with age and yielded less data points. In this model, age, gender inequality and region were no longer associated with anti-HCV prevalence. Study-level HIV prevalence (B=0.20; 95%CI=0.12, 0.29; $p<0.001$), year of data collection (B=-0.08; 95%CI=-0.15, -0.02; $p=0.011$), and HDI score (B=4.37; 95%CI=0.12, 8.63; $p=0.044$) all showed stronger associations in the adjusted analysis.

4. Discussion

Higher HDI (indicating a *higher* level of development) scores of a country were associated with higher anti-HCV prevalence but there was no association with national hepatitis C prevalence, income level or inequality, incarceration rate or treatment coverage. There was also no association with national gender inequality score after adjusting for HIV prevalence, age of the sample, year of data collection, region and HDI scores. It appears that at the current stage of the global HCV epidemic, developing countries may have less HCV among their PWID populations than developed countries. We also confirmed the association between higher anti-HCV prevalence and age, longer duration of injecting, higher prevalence of HIV, and calendar period.

Our results indicate a decline in HCV prevalence in populations of PWID over time. This relationship might reflect an influx of recent research from parts of the world, or areas within a country, where HCV is an emerging risk or generally low in prevalence among PWID based on other factors. For example, studies within a country might have previously targeted samples of PWID from regions where HCV prevalence was known or expected to be high and are now sampling PWID from regions where prevalence is relatively low. This may give the illusion of a decrease in prevalence, when there are simply more data available from areas with low prevalence. If so, this tells us that we may be effectively filling the gaps of HCV epidemiology in more recent years.

Due to small numbers of studies, we were unable to assess which regions made up of developing countries might be experiencing lower prevalence of anti-HCV. Although Africa has a high prevalence of HCV in the general population (Karoney and Siika, 2013), there is evidence to suggest that HCV prevalence remains low compared to regions with more established IDU populations (Degenhardt et al., 2017; Madhava et al., 2002). With that said, developing countries are also likely to have limited treatment resources and are characterised by quicker acquisition of HCV (Hagan et al., 2008). This offers an opportunity to intervene, and potentially control transmission rates, before the burden becomes as prevalent among PWID as it has in developed countries. Targeting PWID in regions such as Sub-Saharan Africa and Asia has been shown to result in a much higher rate of averted infections compared to their more economically developed counterparts (Trickey et al., 2019b).

Unlike HIV, anti-HCV prevalence among PWID does not seem to be associated with national-level factors such as income or population blood borne virus prevalence. Also, despite strong evidence that the implementation of needle-syringe programs and OAT results in a reduction in HCV transmission and reinfection (Des Jarlais et al., 2013; Hagan et al., 2011; Latham et al., 2019; Platt et al., 2017), we did not find an association between country-level coverage of these harm reduction strategies and study-level anti-HCV prevalence. Unfortunately, there was insufficient data to determine whether

study-level OAT engagement was associated with anti-HCV prevalence, which may have been a more effective method to answer this question.

Our findings are limited by the data that are available. Studies of PWID in the Caribbean, Latin America, Asia, and Africa were scarce, and no data were available from the Pacific Island states and territories. As a result, we were not able to examine regional variation to see how the prevalence of anti-HCV might vary geographically with respect to the variables of interest. Compared to high-income countries, PWID in low- and middle-income countries make up smaller proportions of the total HCV infected populations (Grebely et al., 2019) and HCV transmission (Trickey et al., 2019a), thus reducing country-level HCV transmission might require a broader range of strategies (e.g. eliminating unsterile medical syringe use).

We collected data on anti-HCV prevalence, which is indicative of exposure to, but not active, HCV infection. Therefore, this review does not address associations between the examined variables and chronic HCV infection. Since around one in four people spontaneously clear HCV infection (Micallef et al., 2006), future research into the associations between PWID with chronic HCV infection and ecological or sociodemographic variables is important, but will be difficult to undertake given very few studies report on the epidemiology of chronic HCV infection among PWID specifically (Grebely et al., 2019).

Although we did not find an association between population-level harm reduction coverage and anti-HCV prevalence, there is substantial evidence to suggest that implementing such strategies is an effective way to reduce the risk of transmission and reinfection of chronic HCV (Platt et al., 2017). Importantly, HCV research among PWID is now being undertaken in more parts of the world, which is vital to achieve the elimination goals set out by WHO (World Health Organization (WHO), 2017).

Table 1.

Models on HCV prevalence in current PWID	Unadjusted analysis					Adjusted analysis ^a				
	N	B	SE	95% CIs	p	N	B	SE	95% CIs	p
Study-level exposure variables										
Percentage of sample female	245	0.16	0.10	(-0.02,0.35)	0.090		--			
Median/mean age of sample	252	0.07	0.02	(0.03,0.11)	0.001	209	0.04	0.02	(0.00,0.08)	.059
Median/mean duration of injecting	164	0.09	0.03	(0.03,0.15)	0.002		--			
Percentage reporting injecting risk behaviours	236	0.06	0.11	(-0.15,0.27)	0.565		--			
Percentage of sample with HIV	456	0.17	0.04	(0.09,0.24)	<.0001	209	0.20	0.04	(0.12,0.29)	<.001
Year of data collection	568	-0.05	0.03	(-0.11,0.00)	0.042	209	-0.08	0.03	(-0.15,-0.02)	.011
Country-level exposure variables										
Population HCV prevalence	569	0.11	0.16	(-0.20,0.43)	0.483		--			
Population IDU prevalence	535	0.10	0.08	(-0.06,0.26)	0.231		--			
Gini Coefficient	539	0.02	0.02	(-0.02,0.06)	0.273		--			
Gender Inequality Index	559	-1.24	0.55	(-2.26,-2.32)	0.024	209	-0.01	1.94	(-3.81,3.78)	.994
Human Development Index	566	2.38	0.86	(0.69,4.06)	0.006	209	4.37	2.17	(0.12,8.63)	.044
National incarceration rate	404	0.07	0.06	(-0.04,0.18)	0.203		--			
NSP coverage	526	0.10	1.02	(-1.90,2.11)	0.921		--			
OST coverage	466	0.84	0.65	(-0.44,2.12)	0.199		--			
Country income level (Low/middle vs high)	567	0.26	0.21	(-0.15,0.67)	0.217		--			
Region	569					209				
Western Europe ^u		--					--			
Eastern Europe		-0.02	0.24	(0.94,0.45)	0.936		0.56	0.31	(-0.05,1.16)	0.07
Australasia		0.30	0.22	(0.16,0.73)	0.164		-0.22	0.24	(-0.69,0.26)	0.37
North America		0.24	0.19	(-0.12,0.60)	0.197		-0.55	0.35	(-1.23,0.13)	0.11
Central, East and South East Asia		0.14	0.34	(-0.52,0.80)	0.672		0.88	0.52	(-0.13,1.89)	0.09
Caribbean, Latin America and Sub-Saharan Africa		-0.03	0.94	(-1.86,1.81)	0.976		1.76	0.90	(-0.01,3.53)	0.05
Middle East and North Africa and South Asia		-0.78	0.22	(-1.22,-0.35)	<.001		-0.03	0.70	(-1.40,1.35)	0.97

Note. Bold indicates variables with a p-value <0.05.

^a Adjusted analysis was adjusted for variables where unadjusted analyses found p<0.05, except for duration of injecting (redundant due to inclusion of median/mean age of sample)

^u Referent category variable

Figure 1.

Figure Legend

Table 1. Unadjusted and adjusted associations of study-level socio-demographic and behavioural characteristics of people who inject drugs (PWID) and country-level indicators of health, development and inequality with anti-HCV prevalence among PWID

Figure 1. Associations of socio-demographic and behavioural characteristics of samples of people who inject drugs (PWID) with anti-HCV prevalence

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