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RELATIONSHIP BETWEEN HUNGER, ADHERENCE TO ANTIRETROVIRAL THERAPY AND PLASMA HIV RNA SUPPRESSION AMONG HIV-POSITIVE ILLICIT DRUG USERS IN A CANADIAN SETTING

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Abstract

Food insecurity may be a barrier to achieving optimal HIV treatment-related outcomes among illicit drug users. This study therefore, aimed to assess the impact of severe food insecurity, or hunger, on plasma HIV RNA suppression among illicit drug users receiving antiretroviral therapy (ART). A cross-sectional Multivariate logistic regression model was used to assess the potential relationship between hunger and plasma HIV RNA suppression. A sample of n = 406 adults was derived from a community-recruited open prospective cohort of HIV-positive illicit drug users, in Vancouver, British Columbia (BC), Canada. A total of 235 (63.7%) reported "being hungry and unable to afford enough food," and 241 (59.4%) had plasma HIV RNA < 50 copies/ml. In unadjusted analyses, self-reported hunger was associated with lower odds of plasma HIV RNA suppression (Odds Ratio = 0.59, 95% confidence interval [CI]: 0.39–0.90, p = 0.015). In multivariate analyses, this association was no longer significant after controlling for socio-demographic, behavioral, and clinical characteristics, including 95% adherence (Adjusted Odds Ratio [AOR] = 0.65, 95% CI: 0.37–1.10, p = 0.105). Multivariate models stratified by 95% adherence found that the direction and magnitude of this association was not significantly altered by the adherence level. Hunger was common among illicit drug users in this setting. Although, there was an association between hunger and lower likelihood of plasma HIV RNA suppression, this did not persist in adjusted analyses. Further research is warranted to understand the social-structural, policy, and physical factors shaping the HIV outcomes of illicit drug users.

Keywords

HIV; antiretroviral therapy; plasma viral load suppression; food security; hunger; adherence

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INTRODUCTION

The universal uptake and effective use of antiretroviral therapy (ART) among injection drug users constitutes a key strategy to reduce AIDS-related deaths and HIV incidence (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2010). ART use has shown to predictably suppress plasma HIV RNA to undetectable levels, reducing HIV-related morbidity, mortality, sero-discordant transmission (Abdool Karim et al., 2010; Cohen et al., 2011; Grant et al., 2010), and HIV incidence (Das et al., 2010; Fang et al., 2004; Montaner et al., 2006). However, illicit drug users face multiple, individual, and socio-structural barriers to achieving optimal HIV outcomes (Krüsi, Wood, Montaner, & Kerr, 2010; Wood, Kerr, Tyndall, & Montaner, 2008).

Illicit drug users are known to be vulnerable to food insecurity, defined as a state where people lack “physical, social, and economic access to sufficient, safe, and nutritious food that meet their dietary needs and food preferences for an active and healthy life” (Food and Agriculture Organization [FAO] of the United Nations, 2012), and often experience multiple forms of malnutrition (Hendricks & Gorbach, 2009; Smit et al., 1996). Among HIV-positive drug users, food insecurity and malnutrition have been associated with increased behavioral risk of HIV transmission (Shannon et al., 2011), suboptimal ART adherence (Kalichman et al., 2011), HIV-related wasting (Campa et al., 2005) and mortality (Anema et al., in press; Baum, 2000). Little is known, however, about the potential relationship between food insecurity, adherence to ART, and virologic response to ART in this population. Therefore, the present study was conducted to assess the possible impact of severe food insecurity on plasma HIV RNA suppression among HIV-positive illicit drug users in a Canadian context.

METHODS

Study population

Data were derived from the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), a prospective cohort of HIV-positive illicit drug users in Vancouver, British Columbia (BC) described elsewhere (Wood et al., 2004; Wood, Hogg et al., 2008). Briefly, the participants were recruited by snowball sampling and street-based outreach, and eligible for the participation if they were aged ≥ 18 years, HIV-seropositive, and used illicit drugs other than cannabis within a month of enrollment. Participant surveys were linked to clinical and laboratory profiles within a centralized, province-wide HIV/AIDS Drug Treatment Program database. Research ethics approval was obtained from the Providence Health Care/ University of British Columbia Research Ethics Board.

The primary outcome variable was plasma HIV RNA suppression, defined as < 50 copies/mL (Thompson et al., 2010), measured using the Roche Amplicor Monitor assay (Roche Diagnostics, Laval, Quebec, Canada). A value for each participant was calculated by dichotomizing the mean plasma HIV RNA within the past six months. The primary explanatory variable was severe food insecurity, or hunger, understood as responding “yes” to: “I am hungry, but don’t eat because I can’t afford enough food”. Definitions and measures of food insecurity vary between international organizations, and require unique consideration in the context of HIV (Anema et al., 2013). In the USA, hunger is seen to arise

from occasional or chronic inadequate food intake due to the lack of resources and includes physical sensations of hunger (Briefel & Woteki, 1992). The hunger variable used in this study was extracted from the US-based Radimer/Cornell food insecurity scale (Radimer, Olson, & Campbell, 1990), has been validated for use in low-income populations in North America (Frongillo, 1999; Kendall, Olson, & Frongillo, 1995; Radimer et al., 1990) and also included in the Canadian Community Health Survey (Health Canada, 2004). Secondary explanatory variables hypothesized to confound the relationship between hunger and HIV RNA suppression included: age (per 10 year increase); gender (male vs. female); Aboriginal ancestry (yes vs. no); homelessness (no fixed address, street vs. other); educational attainment (≥ high school vs. other); monthly income (≥ CAD$1,050 vs. < CAD$1,050, based on median split); money spent on drugs per day (≥ CAD$60 vs. < CAD$60, based on median split); daily heroin injection (yes vs. no); noninjection crack use (yes vs. no); injection crack use (yes vs. no); any injection or noninjection drug binging (yes vs. no); daily alcohol use (≥4 drinks vs. <4 drinks, based on median split); symptoms of depression in the past week (≥16 CES-D score vs. <16 CES-D score) (Andresen,1994); year of ART initiation; plasma HIV RNA (per log 10); CD4 cell count (per 100 cells/μl), recorded using flow cytometry and fluorescent monoclonal antibody analysis (Beckman Coulter, Inc., Mississauga, Ontario, Canada); and ART adherence (≥95% vs. < 95%), measured by prescription refill compliance in the past 12 months (Wood, Hogg et al., 2003). All behavioral variable definitions were identical to previous reports (Wood, Hogg et al., 2008) and based on a recall period of six months, unless specified otherwise.

Statistical analyses

Univariate statistics were used to determine the factors associated with hunger. To estimate the independent effect of hunger on plasma HIV RNA suppression, a multivariate model was also constructed using a manual backward stepwise approach described previously (Maldonado & Greenland, 1993; Rothman & Greenland, 1998). To test whether the relationship between hunger and plasma HIV RNA suppression was modified by ART adherence level, additional multivariate models were constructed, stratified by ≥95% vs. <95% adherence. All statistical analyses were completed using R v2.10.1 (R Foundation, Vienna, Austria).

RESULTS

A total of 406 participants were interviewed between 5 December 2005 and 16 March 2008 and deemed eligible for the present analysis. Overall, the median age within the sample was 44.4 years [interquartile range (IQR): 38.9–48.8 years]; 134 (33.0%) were female; and 158 (38.9%) reported Aboriginal ancestry. A total of 235 (63.7%) participants were reported being hungry and unable to afford enough food, and 165 (40.6%) had plasma HIV RNA < 50 copies/ml at the time of interview.

As shown in Table 1, the unadjusted factors associated with self-reported hunger among illicit drug users included: younger age (Odds Ratio [OR] = 0.75, 95% Confidence Interval [CI]: 0.56–0.99, p = 0.045); homelessness (OR = 2.89, 95% CI: 1.24–6.75, p = 0.014); spending ≥ $60/day on drugs (OR = 2.23, 95% CI: 1.43–3.48, p < 0.001); incarceration (OR

= 1.71, 95% CI: 1.04 – 2.82, p < 0.035); and symptoms of depression (OR = 3.54, 95% CI: 2.26–5.55, p < 0.001).

Adjusted analyses of factors associated with plasma HIV RNA suppression among illicit drug users receiving ART are presented in Table 2. Hunger was no longer significantly associated with virologic suppression after controlling for age, homelessness, daily expenditure on drugs, monthly income, and 95% adherence (adjusted odds ratio [AOR] = 0.64, 95% CI: 0.37–1.10, p = 0.105). To assess the possibility of a Type II error, we conducted post hoc power calculations which showed that power = 0.74 (β = 26%) (Hsieh, Bloch, & Larsen, 1998). A significant association between hunger and HIV RNA suppression was uncovered only after deleting homeless and age from the final model.

In adjusted analyses stratified by levels of adherence, among the participants with ≥ 95% adherence, hunger was not significantly associated with reduced odds of plasma HIV RNA suppression (AOR: 0.61, 95% CI: 0.23–1.58, p = 0.307). Similarly, among individuals with <95% adherence, hunger was not significantly associated with a lower odds of plasma HIV RNA suppression (AOR: 0.56, 95% CI: 0.26–1.22, p = 0.144).

DISCUSSION

Over two-thirds of HIV-positive illicit drug users reported severe food insecurity in this sample, double that reported among HIV-positive people in diverse high resource settings (Anema et al., 2011; Kalichman et al., 2010; Vogenthaler et al., 2010), and over 20 times greater than prevalence reported in the general Canadian population (Health Canada, 2007). Approximately half of the participants in this setting had suppressed viral loads. While hunger was inversely associated with this outcome in univariate analysis, the strength of association weakened after controlling for socio-demographic, behavioral, and clinical characteristics. Varying levels of adherence did not significantly alter the magnitude or direction of this association (data available from corresponding author).

To the best of our knowledge, this study is the first to evaluate the potential impact of hunger on virologic outcomes in a setting with access to universal health care and free ART, independent of the potential confounding effect of financial barriers. The direction of association observed in the final model was consistent with studies in the USA that have found inverse associations between food insecurity and virologic suppression (Kalichman et al., 2011; Wang et al., 2011; Weiser et al., 2009). The lack of a statistically significant association between hunger and virologic suppression in the adjusted analysis may be due to several factors. First, the local environment has subsidized HIV treatment and support, which may have a protective effect in this setting. Second, the residual confounding may be present due to the categorization of continuous variables, confounder misclassification or failure to include unobserved and unknown confounders (Altman & Royston, 2006; Szklo & Nieto, 2007). Finally, the sample may have been underpowered to detect a true association due to limited variability in the predictor variable, the cross-sectional study design or the fact that drug use is itself a strong predictor of poor virologic outcomes (Krüsi, Milloy et al., 2010). However, the latter is not supported by post hoc power calculations (data not shown).

In multivariate models stratified by varying ART adherence levels, the direction and magnitude of the association between hunger and plasma HIV RNA viral load suppression remained unaltered, suggesting that adherence was not significant effect modifier in this relationship or that residual confounding influenced the effect estimate. These findings are counterintuitive and as such suggest a need for further studies that explore the association between hunger, adherence, and virologic suppression in larger or pooled samples of illicit drug users and for studies to explore potential nonbehavioral (i.e., mental health and nutritional) pathways (Weiser et al., 2011) in the relationship between hunger and virologic suppression. Of note, the measure of adherence used in this study is based on refill compliance. While, we have previously shown this measure of adherence to reliably predict both the virological suppression (Low-Beer, Yip, O'Shaughnessy, Hogg, & Montaner, 2000; Palepu et al., 2001; Wood, Montaner et al., 2003) and mortality (Wood, Hogg et al., 2008, Wood, Hogg et al., 2003), it is possible that refill compliance may be an incomplete surrogate of true drug exposure in this setting.

The high prevalence of hunger suggests that illicit drug users in this setting have inadequate individual-level and environmental supports (Rhodes, 2002; Rhodes, Singer, Bourgois, Friedman, & Strathdee, 2005). Given the role of food insecurity and malnutrition in HIV disease progression (Anema, Vogenthaler, Frongillo, Kadiyala, & Weiser, 2009; de Pee & Semba, 2010), interventions to mitigate hunger should be piloted and evaluated, including food support, within existing harm reduction and HIV-services. Operational research should ensure robust study designs, adequate sample size, validated food security and nutrition instruments, and harmonized composite HIV endpoints, to foster generalizability and comparability of findings (Chandrasekhar & Gupta, 2011; Wittkop et al., 2010). Low ART adherence among illicit drug users remains a concern in this setting (Nolan et al., 2011; Wood, Montaner et al., 2003) and was the most important predictor of virologic suppression in this study. Addressing known socio-structural barriers to ART adherence among illicit drug users, including incarceration (Milloy et al., 2011), homelessness (Milloy et al., 2012), and gender-related factors (Tapp et al., 2011) should be a public health priority in this setting.

This study has several limitations. Participants were not randomly selected, and therefore not representative of all HIV-positive drug users in BC. The cross-sectional study design limits ability to infer causation and temporality. Responder bias, and potentially social desirability bias, may have led to nondifferential misclassification of hunger, biasing our estimates toward the null. Self-reported nutritional estimates are less reliable than clinical nutrition markers (Gorber, Tremblay, Moher, & Gorber,2007); future studies should apply dietary intake assessment methods validated for use among HIV-positive illicit drug users (Sahni, Forrester, & Tucker, 2007; Smit & Tang, 2000).

In summary, we found that hunger was common among HIV-positive illicit drug users in this setting. Although, there was an association between hunger and lower likelihood of plasma HIV RNA suppression, this did not persist in multivariate analyses. Further research is required to describe the relationships between hunger, adherence, and HIV treatment outcomes among illicit drug users. Research is additionally warranted to understand the social-structural, policy, and physical factors shaping the health outcomes of individual drug

users in this setting. Public health efforts should evaluate the possible role of nutritional support within existing harm reduction and HIV services.

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Table 1

Univariate analysis off actors associated with self-reported hunger among HIV-positive illicit drug users receiving antiretroviral therapy in Vancouver, Canada (n = 375).

Characteristic	Hunger 235 (63.7%)	No hunger 140 (37.3%)	Odds Ratio (95% CI)[a]	p – value
Age				
Median, interquartile range [IQR]	43.5 (38.7–48.0)	45.2 (39.6–49.9)	0.75 (0.56–0.99)	0.045
Gender				
Male	159 (67.7%)	97 (69.3%)	0.93 (0.59–1.46)	0.744
Female	76 (32.3%)	43 (30.7%)		
Aboriginal ancestry				
Yes	94 (40.0%)	50 (35.7%)	1.20 (0.78–1.85)	0.409
No	141 (60.0%)	90 (64.3%)		
Homelessness				
Yes	31 (13.2%)	7 (5.0%)	2.89 (1.24–6.75)	0.014
No	204 (86.8%)	133 (95.0%)		
Education status				
High school or greater	205 (91.9%)	126 (93.3%)	0.81 (0.36–1.87)	0.626
Other	18 (8.1%)	9 (6.7%)		
Monthly income[b]				
≥ $1,050	110 (50.0%)	75 (57.7%)	0.73 (0.47–1.14)	0.164
< $1,050	110 (50.0%)	55 (42.3%)		
Money spent on drugs per day[b]				
≥ $60	138 (62.7%)	55 (43.0%)	2.23 (1.43–3.48)	< 0.001
< $60	82 (37.3%)	73 (57.0%)		
Incarceration[c]				
Yes	193 (82.1%)	102 (72.9%)	1.71 (1.04–2.82)	0.035
No	42 (17.9%)	38 (27.1%)		
Symptoms of depression[d]				
Yes	176 (76.2%)	66 (47.5%)	3.54 (2.26–5.55)	< 0.001
No	55 (23.8%)	73 (52.5%)		
Daily injection heroin[c]				
Yes	28 (11.9%)	12 (8.6%)	1.44 (0.71–2.94)	0.312
No	207 (88.1%)	128 (91.4%)		
Daily non-injection crack[c]				
Yes	37 (15.7%)	17 (12.1%)	1.35 (0.73–2.51)	0.338
No	198 (84.3%)	123 (87.9%)		
Daily injection cocaine[c]				
Yes	21 (8.9%)	13 (9.3%)	0.96 (0.46–1.98)	0.909
No	214 (91.1%)	127 (90.7%)		
Any drug binge[c]				
Yes	104 (44.3%)	52 (37.1%)	1.34 (0.88–2.06)	0.177

Characteristic	Hunger 235 (63.7%)	No hunger 140 (37.3%)	Odds Ratio (95% CI)[a]	p – value
No	131 (55.7%)	88 (62.9%)		
Daily alcohol use[b,c]				
≥ 4 drinks	58 (24.7%)	33 (23.6%)	1.06 (0.65–1.74)	0.809
< 4 drinks	177 (75.3%)	107 (76.4%)		
Adherence to ART[d]				
≥95%	79 (33.6%)	52 (37.1%)	0.86 (0.55–1.33)	0.489
<95%	156 (66.4%)	88 (62.9%)		
CD4 cell count (per 100 cell increase)				
Median, IQR	2.66 (1.59–4.14)	3.10 (2.01–4.63)	0.93 (0.83–1.04)	0.190
Plasma HIV RNA (per Log $_{10}$ increase)				
Median, IQR	2.73 (1.65–4.42)	1.83 (1.65–4.39)	1.10 (0.95–1.28)	0.198
Plasma HIV RNA suppression				
Yes	84 (55.3%)	68 (44.7%)	0.59 (0.39–0.90)	0.015
No	151 (67.7%)	72 (32.3%)		

Notes:

[a] Confidence interval.

[b] Based on median split.

[c] Within last six months of interview.

[d] Within last week of interview.

[e] Within last 12 months of interview.

Table 2

Multivariate analysis off actors associated with plasma HIV RNA suppression among HIV-positive illicit drug users receiving antiretroviral therapy in Vancouver, Canada (n = 406).

Variable	AOR[a]	95% CI[b]	p – value
Self-reported hunger			
Yes vs. no	0.64	037–1.10	0.105
Age			
Per 10 year increase	1.65	1.13–2.41	0.010
Homelessness			
Yes vs. no	0.39	0.15–1.02	0.055
Monthly income			
≥ $1,050 vs. < $1,050[c]	0.72	0.42–1.21	0.216
Average spent on drugs per day[c]			
≥ $60 vs. < $60	0.82	0.49–1.39	0.467
Adherence to ART[d]			
≥ 95% vs. < 95%	7.30	4.26–12.49	< 0.001

Notes:

[a] Adjusted Odds Ratio.

[b] 95% Confidence Interval.

[c] Based on median split.

[d] Within last 12 months of interview.