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High rates of serum selenium deficiency among HIV- and HCV-infected and uninfected drug users in Buenos Aires, Argentina

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Abstract

Objective: To describe the prevalence of low serum Se and determine whether HIV, hepatitis C virus (HCV) and/or the types of drugs used are associated with serum Se in a cohort of infected and uninfected drug users.

Design: Independent correlates of low serum Se levels based on data collected from food recalls, physical examinations and clinical questionnaires were identified using multivariate regression analysis.

Setting: Buenos Aires, Argentina

Subjects: A total of 205 (twenty-five female and 180 male) former and current drug users.

Results: Drug users had an average serum Se level of 69·8 (SD 32·8) μg/dl, and 82 % were considered deficient (<85 μg/dl). Multivariate analyses found that HIV- and/or HCV-infected individuals had lower mean Se compared with healthy, uninfected drug users (HIV/HCV co-infection: −25·3 μg/l (SE 7·6), $P = 0·001$; HIV alone: −28·9 μg/l (SE 6·9), $P < 0·001$; HCV alone: −19·4 μg/l (SE 7·1), $P = 0·006$). Current and previous drug use was associated with higher serum Se. Cigarette smoking and heavy alcohol consumption were not found to be associated with Se status.

Conclusions: Low serum Se levels are highly prevalent among drug users in Buenos Aires, Argentina. Se supplementation and/or dietary interventions may be warranted in drug users who are at high risk for HIV and/or HCV infection.

Keywords
Selenium
HIV
Illicit drug use
Hepatitis
Depression

The trace mineral Se is essential for immune function and for defence against oxidative stress. Low serum Se levels are associated with more rapid HIV disease progression and mortality[1–3], decreased immune function[4,5], increased oxidative stress markers[6], cancers associated with hepatitis C virus (HCV) infection[7] and increased HIV viral shedding suggestive of increased transmission[8,9]. Se supplementation trials have shown that supplementation improves HIV-related outcomes such as CD4+ cell counts and HIV viral load[10], decreases respiratory opportunistic infections[11] and decreases hospitalizations[12].

Drug users have increased vulnerability to both nutritional deficiencies and to infection of HIV and HCV. Nutritional deficiencies in drug users could be attributed to poor diet, poverty, increased metabolic rate, malabsorption or increased oxidative stress[13–16]. Se-deficient drug users may transmit or contract more infectious diseases because of increased viral replication and decreased immune function[16,17]. Se-deficient drug users who are already infected by HIV and/or HCV may have increased disease progression to AIDS, increased susceptibility to opportunistic infections such as tuberculosis[11] or increased hepato-cellular carcinoma[7].

To our knowledge, the present study is the first to examine the Se status of drug users (with or without HIV or HCV infection) in Argentina. The present study aimed to describe the prevalence and correlates of low serum Se status in this population. In particular, we were interested in whether HIV, HCV and/or the types of drugs used were associated with Se status in this population. Effective dietary intervention or recommendations for supplementation cannot be made without first assessing the prevalence and correlates in this high-risk substance-using population. The ability to report the independent effects of HIV, HCV and drug use on Se status while controlling for dietary intake, nutritional status and other sociodemographic characteristics makes the present study unique.

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Experimental methods

Participants and data collection

We enrolled 205 former and current drug users into a cross-sectional study to examine the nutritional status of HIV+ and HIV− drug users in Buenos Aires, Argentina. We excluded two participants without serum micronutrient results from the present analysis. From November 2005 to November 2006, men and women were recruited from CENARESO (Centro Nacional de Reeducación Social), a government-run drug rehabilitation centre, and from FUNDAI (Fundación de Ayuda al Inmunodeficiente), an HIV/AIDS clinic located within the Muñiz Hospital for infectious diseases. The inclusion criteria for the study were as follows: age 18–65 years; should have injected, smoked or snorted cocaine or coca paste in the past 5 years; and women not pregnant at the time of study visit. Written informed consent was obtained from each participant and the protocol was approved by the Institutional Review Boards of Tufts Medical Center, CENARESO and FUNDAI.

Body composition measurements, including height and weight, were obtained from all participants. Each participant completed a demographic and food security questionnaire, a questionnaire on medical history, a 24 h dietary recall and also underwent a fasting blood draw. Dietary intake data were analysed using the Nutrition Data System for Research software version 2005, developed by the Nutrition Coordinating Center, University of Minnesota (Minneapolis, MN, USA)[18]. When available from a local food composition book[19], the nutritional content of Argentinean foods was compared with that of similar foods from the Minnesota Nutrient Database or from the US Department of Agriculture National Nutrient Database, until a close match was made between nutrients using the method of Merchant and Dehghan[20]. Since limited mineral content was available in the local food composition book, the Se content of foods is based predominantly on the US version of foods. A standard Argentinean cookbook[21] or the Internet was used for developing the user-recipe file for the sixty-two mixed dishes in these dietary recalls.

Depression was assessed using the Center for Epidemiologic Studies Depression Scale-20 questionnaire[22]. Participants were categorized as depressed if their score exceeded 20 on this scale. Food security was assessed using a modified version of the short form of the Household Food Security Scale developed by the National Center for Health Statistics[23]. A 30 d reference period was used for the food security scale and the resulting classifications were: food secure; food insecurity without hunger; and food insecurity with hunger. Participants reported whether the following symptoms had occurred in the previous 6 months: abdominal pain; diarrhoea; fever, sweats or chills; loss of appetite or nausea; mouth sores or white patches; pain in the mouth, lips or gums; and/or vomiting. Symptom severity was determined by answering the question 'How much did it bother you?' with 'not at all', 'very little', 'moderately', 'quite a bit' or 'extremely'. In our analyses, the presence of a symptom with a severity rating of 'moderately' or greater was coded as 'yes'; otherwise, no symptom occurrence or symptoms with 'very little' or less severity were coded as 'no'. The frequency and amount of alcohol intake over the past 30 d were assessed. Responses were categorized as hazardous or non-hazardous using the National Institute on Alcohol Abuse and Alcoholism guidelines[24]. Participants were classified as housing secure if they lived in any of the following: their own house; rented house; parent's house; relative's house; friend's house; hotel; church; or work place. Participants who were squatting, homeless or living in a shelter were considered housing insecure. Participants who reported living at the hospital or at the drug treatment centre were classified as institutionalized.

Micronutrient and other laboratory assays

Fasting blood (at least 5 h) was drawn and aliquoted in trace element-free conditions. Sera were stored at −70°C and shipped in one batch to Tufts Medical Center (Boston, MA, USA) for analysis of micronutrients. Serum Se was quantified by graphite furnace atomic absorption spectrometry using a Perkin Elmer AAnalyst 800 with Zeeman background correction (Perkin Elmer, Shelton, CT, USA). Samples and standard concentrations were read in duplicate. Serum Se was considered low if the level was <85 μg/l (1·08 μmol/l), which was the cut-off point associated with increased mortality in a population of HIV-infected drug users in the USA[2]. C-reactive protein was quantified by PCR-latex (Wiener Laboratory, Rosario, Argentina), which qualitatively detects levels above 6 mg/l as reactive. Our statistical models therefore included C-reactive protein as a dichotomous reactive/non-reactive variable. Participants were considered to have chronic hepatitis B when their hepatitis B surface antigen (HBsAg), detected by IMx-HbsAg (V2; Abbott, Buenos Aires, Argentina), was positive. Hepatitis C antibody was detected using IMx-HCV (version 3·0; Abbott). HIV-1 status was determined by ELISA (IMx EIA HIV-1/HIV-2 III Plus; Abbott), with confirmation by Western blot (HIV Blot 2·2, Genelabs Diagnostics, Singapore Science Park, Singapore). HIV-1 viral load copies were quantified by RT-PCR using the AMPLICOR HIV-1 Monitor 1·5 (Roche, Indianapolis, IN, USA). Viral load <1000 copies/ml were considered undetectable.

Statistical analyses

Participants were classified into one of four infected groups according to their HIV and HCV status: HIV+/HCV+; HIV+/HCV−; HIV−/HCV+; or HIV−/HCV−. Mean and SD were calculated for all continuous variables by HIV/HCV-infected group. To compare means between the four study groups, the ANOVA F test was used. Categorical variables were compared between the four

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study groups using an overall χ^2 or Fisher's exact test when expected cell counts were less than five. In order to adjust for potential confounding, GEE (generalized estimating equations) models with robust standard errors were fit using the normal distribution and identity link (PROC GENMOD in SAS). Se level as a continuous variable was the outcome for these models and HIV/HCV infection status (entered as three indicator variables, with HIV−/HCV− as the reference group) was the exposure of interest. We assessed for potential confounding by recruitment site, gender, age, BMI, chronic hepatitis B, housing security, institutionalization status, food security, self-reported symptoms, percentage of body fat, cigarette smoking, depression, vitamin supplements, dietary intakes of protein and Se, C-reactive protein, injection drug use (IDU) and non-IDU and alcohol use. The missing indicator method[25] was used for the variables depression and self-reported white patches in the mouth, each of which was missing for five participants.

We began our model-building strategy with a full model and then used backward elimination to determine our final model. Our full model included all variables that were predictors of serum Se at $P<0{\cdot}2$ or were confounders of the association between HIV/HCV and serum Se (changed any of the β coefficients of the HIV/HCV indicator variables by ≥15 %). Our final model included variables that were either independent predictors of Se at $P<0{\cdot}05$ or confounders. From the final model, we computed least squares means of serum Se for each level of the exposures of interest (HIV and HCV infection).

Analyses were conducted using the SAS statistical software package version 9·2 (SAS Institute, Cary, NC, USA).

Results

Table 1 provides the demographic, nutritional, drug use and clinical characteristics of the 203 participants, stratified by HIV and HCV infection status. Gender, housing security, education and incarceration history were not significantly different between groups. However, because of study design, recruitment site and institutionalization rates differed significantly between groups, whereby uninfected participants were more likely to be recruited at the drug rehabilitation centre than at the HIV clinic in a hospital setting. However, all infected groups included at least some participants from each recruitment site. Age, ethnicity and sexual orientation were also statistically different between groups. HIV+ participants had a lower percentage of body fat compared with those uninfected with HIV. Those with HCV alone or uninfected with either HIV or HCV had higher BMI. Energy, fat, carbohydrate, and fibre intakes analysed from 24 h dietary recalls were not statistically different between groups (not all data shown). However, the percentage of energy from protein was higher in uninfected drug users and food insecurity was more common in those infected with HIV. HIV+ participants were more likely to have C-reactive protein reactivity, chronic hepatitis B, fever and mouth sores or white patches. Bothersome nausea was most prevalent in those with HIV alone. There were no significant differences between groups with regard to depression levels, alcohol consumption or cigarette usage. Although all groups had similarly high numbers of participants using illicit drugs in the previous 6 months (87 to 100 %), those with HCV (with or without HIV) were more likely to have used injection drugs in their lifetime and within the past 6 months. Coca paste, snorted cocaine and marijuana were the most commonly used illicit drugs in the 6 months before clinic visit. Injected cocaine was the only illicit drug with a statistically significant difference between groups, and those infected with HCV (with or without HIV infection) were most likely to be injecting cocaine.

Overall, HIV+ participants (*n* 69, 34 % of the cohort) had mean CD4 levels of 239 (cells/mm^3) and viral load levels of 152 817 copies/ml. Only 35 % of HIV-infected participants reported being on anti-retroviral medications, and 68 % of HIV-infected participants were co-infected with hepatitis C. HIV-infected participants without HCV infection were less likely to be on anti-retroviral medications (14 % *v.* 46 %, $P=0{\cdot}014$) and were less likely to have viral load suppression compared with those with HIV/HCV co-infection (0 % *v.* 33 %, $P=0{\cdot}003$). HIV-infected participants were recruited from both the drug rehabilitation centre (*n* 24, 35 %) and the HIV/AIDS clinic at the hospital (*n* 45, 65 %).

Overall prevalence of low serum Se (<85 μg/l) was 82 % in this cohort. Table 2 provides the unadjusted mean and median serum Se levels by infection status. Unadjusted mean serum Se levels were not significantly different between groups and ranged from 62 (SD 19) μg/l in the HIV-only group to 73 (SD 37) μg/l in the HIV/HCV co-infected group. However, mean Se dietary intake was lowest in the HIV/HCV co-infected group (117 (SD 54) μg), although it did not reach statistical significance.

Table 3 shows the final multivariate model examining the association between HIV/HCV-infected groups and other variables with Se levels. All three HIV- and/or HCV-infected groups were associated with lower serum Se compared with the healthy, uninfected group. HIV/HCV co-infected participants had a mean Se level that was 25·3 (SE 7·6) μg/l ($P=0{\cdot}001$) lower than that of the healthy, uninfected group. Having HIV infection alone was associated with a 28·9 (SE 6·9) μg/l ($P<0{\cdot}001$) lower Se level, and those with HCV infection alone had 19·4 (SE 7·1) μg/l ($P=0{\cdot}006$) lower serum Se level compared with the reference group. Figure 1 depicts the final model's adjusted least squares mean and SE of serum Se values by HIV/HCV-infected group.

The final multivariate model also indicated that depression and recruitment from CENARESO (the drug rehabilitation centre) were independently associated with lower serum Se levels ($\beta=-9{\cdot}3$ μg/l, SE 4·0, $P=0{\cdot}02$;

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Table 1 Sociodemographic, nutritional, drug use and clinical characteristics of the 203 participants of the TANGO Argentinean cohort, by HIV and HCV status

	Uninfected (*n* 120)		HCV alone (*n* 14)		HIV alone (*n* 22)		HIV and HCV (*n* 47)		
Characteristic	*n* or mean	% or SD	*n* or mean	% or SD	*n* or mean	% or SD	*n* or mean	% or SD	*P* value†
Sociodemographic									
Female	16	13	2	14	5	23	2	4	0·11*
Age (years)‡	28·5	6·5	35·5	8·1	31·3	5·5	36·3	5·2	<0·001
Caucasian (all other Amerindios)	97	82	10	71	12	55	32	68	0·03
Heterosexual	114	96	14	100	18	82	39	83	0·01
Recruitment site									
Drug treatment centre, CENARESO	105	88	9	64	7	32	17	36	<0·001
HIV clinic, Muniz Hospital	15	22	5	36	15	68	30	64	
Currently living in an institution	89	74	8	57	10	45	21	45	<0·001
Housing insecure	1	1	0	0	1	5	3	6	0·13*
Education (≥8 years)	22	18	4	29	4	18	7	15	0·69*
Incarcerated during lifetime	103	86	13	93	21	95	43	91	0·46
Nutritional and dietary assessment									
BMI (kg/m^2)‡	24·8	4·1	23·9	3·8	22·1	2·4	23·1	3·0	0·003
<20	7	6	0	0	4	18	4	9	0·02*
20 to <25	66	55	11	79	15	68	35	74	
25 to <30	36	30	1	7	3	14	5	11	
≥30	11	9	2	14	0	0	3	6	
% Body fat‡	21·0	8·4	22·2	6·6	18·8	6·2	18·5	5·8	0·14
Food secure	81	69	10	71	12	55	20	43	0·01*
Food insecure/no hunger	26	22	2	14	9	41	15	32	
Food insecure/with hunger	11	9	2	14	1	5	12	26	
Regular vitamin or supplement use	14	12	2	14	5	23	10	22	0·25*
Protein intake (g/10 kg weight)‡	15·1	6·6	16·7	6·7	14·6	5·0	13·2	5·7	0·19
% Fat intake‡	31·7	8·3	28·2	5·3	29·3	10·5	29·0	9·7	0·19
% Carbohydrate intake‡	53·1	9·9	52·9	11·9	53·0	14·8	55·8	12·9	0·54
% Protein intake‡	15·4	4·9	13·8	3·3	13·4	4·8	13·3	4·7	0·03
Clinical									
C-reactive protein >6 mg/l	24	20	3	21	9	43	18	38	0·03*
Chronic hepatitis B (HBsAg)	0	0	0	0	2	10	2	4	0·02*
Symptoms§									
Fever, sweats or chills	34	28	5	36	17	77	26	55	<0·001
Abdominal pain	55	47	6	43	15	68	16	34	0·07
Diarrhoea	45	38	3	21	8	36	13	28	0·47*
Mouth sores or white patches	4	3	1	7	5	24	6	13	0·01*
Pain in mouth, lips or gums	50	42	4	29	9	43	14	30	0·44*
Nausea	32	27	3	21	13	59	14	30	0·03*
Vomiting	26	22	2	14	9	41	13	28	0·20*
Depression (CESD-20 ≥21)	67	56	9	64	12	55	20	43	0·36
Drug use									
Hazardous alcohol consumption	59	50	9	64	14	64	28	60	0·40
Cigarette smoking	109	91	11	79	16	73	39	85	0·09
Injection drug use									
Never	94	78	3	21	15	68	4	9	<0·001*
Previously	19	16	9	64	6	27	32	68	
In the past 6 months	7	6	2	14	1	5	11	23	
Any illicit drug use in the past 6 months	111	93	14	100	20	91	40	87	0·44
Specific drugs used in the past 6 months									
Marijuana	84	70	9	64	14	64	32	68	0·92
Cocaine injected	3	3	1	7	0	0	11	23	<0·001*
Coca paste	87	73	10	71	17	77	30	64	0·63
Cocaine snorted	82	68	9	64	14	64	30	65	0·96
Sedatives	60	50	11	79	8	36	22	47	0·09
Amphetamines	8	7	3	21	2	9	1	2	0·08*
HIV-specific									
HAART use	N/A	N/A	N/A	N/A	3	14	21	46	0·01*
CD4 absolute (cells/μl)‡	N/A	N/A	N/A	N/A	202	167	255	166	0·24
CD4 <200 cells/μl	N/A	N/A	N/A	N/A	11	55	19	41	0·42*
Log HIV viral load copies‡	N/A	N/A	N/A	N/A	5·2	0·7	3·9	1·2	<0·001
VL suppression (<1000 copies)	N/A	N/A	N/A	N/A	0	0	15	33	0·003*

HCV, hepatitis C virus; CENARESO, Centro Nacional de Reeducación Social; HBsAg, hepatitis B surface antigen; CESD, Center for Epidemiologic Studies Depression Scale; HAART, highly active anti-retroviral therapy; VL, HIV viral load; N/A, not applicable.
†*P* value for ANOVA *F* test for continuous variables. For differences in proportions, *P* value is for the χ^2 or Fisher's exact test when denoted by an asterisk (*).
‡Data are presented as mean and SD.
§Self-reported symptoms in the past 6 months and affecting at least moderately.

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Table 2 Unadjusted serum selenium and selenium intakes of 203 drug users in the TANGO Argentinean cohort

	Overall (*n* 203)	Uninfected drug users (*n* 120)	HCV alone (*n* 14)	HIV alone (*n* 22)	HIV and HCV (*n* 47)	*P* value
Serum Se (unadjusted; μg/l)						
Mean	69·8	70·5	64·4	62·2	73·1	0·56*
SD	32·8	33·9	25·6	18·8	36·7	
Median	60·9	60·7	59·6	57·3	64·7	
IQR	51·5, 78·8	54·2, 76·6	42·2, 92·1	50·5, 72·0	52·8, 81·0	
Low Se (<85 μg/l)						
n	167	99	10	20	38	0·51†
%	82	83	71	91	81	
Se intake from food (μg)						
Mean	132	137	151	123	117	0·09*
SD	56	57	55	51	54	

HCV, hepatitis C virus; IQR, interquartile range.
*F test, ANOVA, P value between the four study groups.
†The χ^2 test, for differences in proportions, P value between the four study groups.

Table 3 Multivariate model for correlates of serum selenium (μg/l) in 203 participants of the TANGO Argentinean cohort

	Final model		
	β Estimate	SE	*P* value
HIV/HCV infection status			
Uninfected	Ref.	Ref.	Ref.
HCV only	−19·4	7·1	0·006
HIV only	−28·9	6·9	<0·001
HIV/HCV co-infection	−25·3	7·6	0·001
Recruited from the drug rehabilitation centre, CENARESO	−35·8	6·5	<0·001
Age (years)	−0·6	0·3	0·10
Injection drug use			
Never	Ref.	Ref.	Ref.
Past	13·5	5·9	0·02
Current (last 6 months)	26·1	9·2	0·004
Symptoms†			
Mouth, lip and gum pain	−11·5	3·9	0·003
Nausea	12·0	5·3	0·02
Depression (CESD-20 score ≥ 21)	−9·3	4·0	0·02
Chronic hepatitis B (HBsAg)	−23·7	10·1	0·02

HCV, hepatitis C virus; CENARESO, Centro Nacional de Reeducación Social; CESD, Center for Epidemiologic Studies Depression Scale; HBsAg, hepatitis B surface antigen; Ref., reference category.
†Self-reported symptoms in the past 6 months and affecting at least moderately.

and $\beta = -35{\cdot}8$ μg/l, SE 6·5, $P \leq 0{\cdot}001$, respectively). Current IDU and previous IDU were both independently associated with higher serum Se levels ($\beta = 26{\cdot}1$ μg/l, SE 9·2, $P = 0{\cdot}004$; and $\beta = 13{\cdot}5$ μg/l, SE 5·9, $P = 0{\cdot}02$, respectively) compared with never having injected drugs. Patients with self-reported symptoms such as mouth, lips or gum pain had lower serum Se levels ($\beta = -11{\cdot}5$ μg/l, SE 3·9, $P = 0{\cdot}003$), although those who reported nausea had higher levels ($\beta = 12{\cdot}0$ μg/l, SE 5·3, $P = 0{\cdot}02$). Chronic hepatitis B was associated with lower serum Se levels ($\beta = -23{\cdot}7$ μg/l, SE 10·1, $P = 0{\cdot}02$). Age was used in the final model as a potential confounder of the association between HIV/HCV status and Se levels.

Discussion

The present study reveals an 82% prevalence of low serum Se in drug users recruited from Buenos Aires, Argentina. Yet, it is notable that the cohort did not have a high prevalence of overall malnutrition/wasting, with only 0·9% of the participants (two out of 203) having a BMI <18·5 kg/m^2 (underweight). High rates of low serum Se were found in all infected groups, including in those without either HIV or HCV. In contrast, using data analysed in the same micronutrient laboratory by the same technicians, using the same equipment and standards, two other Boston-based cohort studies found low Se (<85 μg/l) to be much less common. One study found 3·4–7·7% prevalence in mixed-ethnicity HIV-infected adult patients[3] and the other reported 16·1% prevalence in Hispanic drug users with and without HIV and/or HCV[26]. Internationally, higher Se-deficiency rates (38%) were found in 100 newly diagnosed Iranian HIV+ patients, 72% of whom were injection drug users[27]. Interestingly, two other Argentinean studies of HIV patients found a high prevalence of low Se levels similar to those of our cohort. Stambullian *et al.*[28] found that roughly 70% of forty-three

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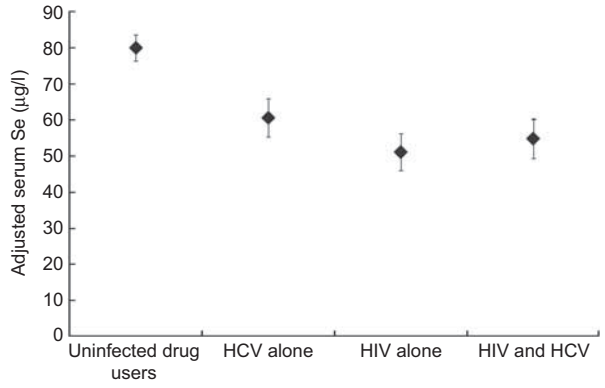

Fig. 1 Adjusted serum selenium (mean and SE for serum selenium after adjusting for: recruitment site, age, injection drug use (never, past and current), symptoms (mouth/lip/gum pain and nausea), depression (Center for Epidemiologic Studies Depression Scale-20 ≥ 21) and chronic hepatitis B) by HIV and hepatitis C virus (HCV) status in 203 drug users from the TANGO Argentinean cohort

adult HIV patients had plasma Se levels <60 μg/l, whereas all eight paediatric HIV patients were found to have plasma Se levels <60 μg/l[29].

Multivariate analyses revealed that uninfected drug users had significantly higher mean serum Se levels compared with any of the infected groups, controlling for age, recruitment site, nausea, pain in the mouth, lips or gum, chronic hepatitis B, IDU and depression. Differences between the other HIV/HCV-infected groups were not statistically significant. Other published studies have found differences in Se status among HIV/HCV-infected groups. One study found lower Se levels in HCV-infected patients and in HIV/HCV-co-infected patients compared with patients infected with HIV only[30]. Discrepancies exist between Se studies of patients with HCV alone and those of healthy controls. At least two studies found reduced serum Se in patients with HCV[6,31], whereas another study did not[32]. One possible explanation for these discrepancies is the multiple influences on homeostatic Se levels in serum. Dietary intake, disease progression (i.e. HCV or HIV viral load) and other sources of oxidative stress (such as other infections and usage of drugs, tobacco and alcohol) could contribute to serum Se status. Loguercio *et al.*[32], for instance, found no differences between healthy controls and those with HCV, but ensured that participants in all groups were non-drug users, non-smokers and non-drinkers. Jain *et al.*[31] matched only on the basis of age and gender, whereas Look *et al.*[30] analysed results by clinical HIV stage and hospitalization but did not control for other sources of oxidative stress. None controlled for dietary intake of Se.

There are several biochemical pathways through which Se interacts with HIV and HCV. The first is as an essential trace mineral cofactor for antioxidant enzymes that ameliorate oxidative stress due to HIV, HCV, drug abuse and ageing[33]. Second, it has been theorized that HIV uses Se by encoding its own selenoproteins that control gene regulation[34]. Therefore, Se levels may decrease as HIV viral replication uses and sequesters Se. Improved virological control through highly active anti-retroviral therapy (HAART) was shown to improve Se status in a study by Rousseau *et al.*[35], in which 77 % of participants were intravenous drug users. Rousseau *et al.* followed thirty persons over time, from before HAART to after HAART, and found a dramatic reduction in the proportion that had low Se levels: 77 % before HAART to only 10 % at 3 years after HAART. Chronic HCV is also associated with increased oxidative stress and lower Se levels[6,31,36].

In addition to being associated with HIV and HCV, serum Se was associated with IDU, recruitment site, depression, chronic hepatitis B and symptoms such as nausea and pain in the mouth, lips or gums. Low Se status has been previously correlated with HIV-related dementia in drug users[37] and with increased susceptibility to depressed moods in healthy men[38]. An Se supplementation trial in healthy adults found decreased anxiety and improved mood after 5 weeks of Se supplementation[39]. Interestingly, in our study, current and previous IDU was associated with higher serum Se levels. The impact of IDU on serum Se deserves further investigation and confirmation. Recruitment into the study from the drug treatment centre, CENARESO, was associated with lower serum Se levels. Since 63 % of the participants are currently living at either CENARESO or at the Muniz Hospital Clinic, differences in standard meals and menus in these two institutional settings need further exploration. Analysing the institutional diets and developing menu suggestions to improve Se intake at CENARESO were beyond the scope of the present study. Several self-reported symptoms were associated with Se. Bothersome mouth, lips and gum pain was associated with lower Se status, possibly from a decrease in dietary intake as a result of discomfort. However self-reported nausea was associated with higher Se status. Chronic hepatitis B was found to be negatively associated with Se status; however, a larger study will be needed to confirm these findings since we had only four participants with chronic hepatitis B.

Our study has a few limitations. First, serum Se is not a true measure of functional Se deficiency or of Se stores. Quantification of the activity of an Se-dependent enzyme may be a more accurate detection of Se deficiency[40]. Second, a single dietary 24 h recall is not considered representative of an individual's typical intake. However, by using a 24 h dietary recall we were able to have some estimate of dietary intake and comparisons of mean intakes by group are generally accepted. We were limited to one 24 h dietary recall because of the instability of the drug-using population. In addition, because of the lack of a local or South American-based nutrient content database, our assessment of Se intake based on a US nutrient composition database led to our intake data having some degree of measurement error.

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The lack of published studies regarding the Se status of healthy, non-drug users in Argentina precludes an inference of whether the low Se status in drug users is specific to this population or indicative of a more general public health issue yet to be uncovered. Two studies found high rates of Se deficiency in HIV patients in Argentina[28,29]; however, to our knowledge, our study is the first to include non-HIV patients. Unlike other noted geographical areas of deficiency (such as China and Russia), Argentina is not known to have Se-deficient soils. However, a high prevalence of several other vitamin and mineral imbalances in cattle, such as Cu deficiency (hypocuprosis)[41] and excessive vitamin D (toxic hypercalcinosis)[42], has been recognized in the main cattle breeding areas of Buenos Aires province. Bovine diseases associated with these nutritional imbalances have prompted cattle and forage studies. One such Argentinean study of cattle suffering from vitamin D toxicity found low Se content in bovine serum and in their fresh forage originating from the fields of low lands of Buenos Aires province[43]. International comparison studies of the Se content of wheat[44] and non-fat dry milk[45] have shown at least average levels of Se content in Argentinean wheat and milk. Although we cannot rule out that low serum Se is a larger population issue in the general Buenos Aires population, our study documents a high prevalence of low serum Se in the drug-using population beyond those infected with HIV.

Conclusions

Our results indicate some of the first evidence of high rates of low serum Se in Argentinean current and former drug users. After controlling for nutrition, drug use and sociodemographic characteristics, multivariate analyses have concluded that HIV- and/or HCV-infected individuals have significantly lower serum Se levels compared with those without either infection.

The association of lower serum Se levels with HIV and/or HCV infection suggests that these populations may particularly benefit from intervention. The high prevalence of low serum Se would make drug users a great target for an Se supplementation intervention to both prevent HIV transmission and slow HIV progression in those with HIV.

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