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Not All Injection Drug Users are Created Equal: Heterogeneity of HIV, Hepatitis C Virus, and Hepatitis B Virus Infection in Georgia

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Abstract

Injection drug users (IDU) are widely believed to have accelerated the looming HIV/AIDS epidemic now faced by the Russian Federation and countries of the former Soviet Union. However, IDUs may be heterogeneous with regard to risk behaviors and a sub-population may be responsible for the majority of blood-borne pathogen transmission. We studied 926 adult injection drug users (IDU) from the cities of Tbilisi, Batumi, and Poti in Georgia, a small country in the Caucasus region between the Black and Caspian Seas, between 1997 and 1998. Study participants were administered a confidential questionnaire and were tested for antibody to HIV, hepatitis C virus (HCV), hepatitis B virus surface antigen (HBsAg), and hepatitis B core antibody (anti-HBc). Five (0.5%) individuals were positive for HIV, 539 (58.2%) for HCV, 67 (7.2%) for HBsAg, and 475 for (51.3%) for anti-HBc. 88.7% of the surveyed individuals reported sharing needles with others, and needle sharing with more than ten other individuals versus no sharing was a highly significant predictor (OR: 278.12, 95% CI: 77.57, 997.20) of HCV seropositivity. In adjusted analysis, individuals who usually injected stolen medical/synthetic drugs had significantly lower odds of HCV (OR: 0.38, 95% CI: 0.22, 0.68) and HBV (OR: 0.58, 95% CI: 0.37, 0.90) than individuals most commonly injecting opium. Despite some limitations, these results suggest the presence of substantial heterogeneity between different injection drug-using groups in Georgia. Identification of high risk IDU sub-populations is vital to efficiently target risk reduction programs, and to prevent confounding by risk status in large HIV/AIDS behavioral intervention and vaccine trials.

Keywords

epidemiology; HIV; hepatitis C virus; hepatitis B virus; injection drug users; heroin; synthetic drugs; Georgia; Caucasus region; former Soviet Union

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Introduction

Injection drug users (IDU) are thought to contribute significantly to the introduction, maintenance, and spread of HIV and other blood-borne pathogens in populations (Alcabes & Friedland 1995; McMahon 2005; Shepard et al. 2005; Vu et al. 2002), and are widely believed to be at the center of the looming HIV/AIDS epidemic now faced by the Russian Federation and countries of the former Soviet Union (Kazionny et al. 2001; Kelly and Amirkhanian 2003; Rhodes et al. 2002; Rhodes et al. 2006; Sanchez et al. 2006). While these statements may be true in general, there is increasing consensus that IDUs are a heterogeneous group and risk behaviors differ significantly between sub-populations within the larger IDU population (Boileau et al. 2005; Diaz et al. 2001; Millson et al. 2003; Strathdee et al. 2001). Realization of this fact, and subsequent identification of IDU sub-populations, are vital steps to not only efficiently target risk reduction programs, but also to prevent confounding by risk status in large HIV/AIDS behavioral intervention and vaccine trials.

Georgia is situated south of the Russian Federation in the Caucasus region between the Black and Caspian Seas (see Figure 1). Georgia has approximately 4.5 million citizens, and is resource constrained by European standards. Following the collapse of the Soviet Union and the subsequent dismantling of previously stringent border controls, Georgia became a major transit point for the increasingly large poppy harvests trafficked out of Afghanistan (United Nations Office for Drug Control and Crime Prevention 2002). Domestic demand for illicit drugs in Georgia increased along with trafficking through the late 1990s and early 2000s. The United States State Department estimated that there were only 5,000 illicit drug users in 1996 but the number had grown to 275,000 in 2004 (United States Department of State 1996; United States Department of State 2005), although part of this increase may be attributed to changes in Georgian laws defining illicit drugs.

While Georgia has experienced a dramatic increase in illicit drug use during the past ten years, this rise has been far from homogeneous. Georgia has historically been a country of opium and cannabis users, but beginning in the mid to late 1990s, Afghani drug traffickers developed the capability to synthesize heroin within Afghanistan (United Nations Office for Drug Control and Crime Prevention 2002). Within a few years, inexpensive and high quality heroin was flooding Southern Asian markets and heroin use became increasingly prevalent (United Nations Office for Drug Control and Crime Prevention 2002; United States Drug Enforcement Administration 2003). Concurrently, abuse of synthetic and medical drugs was on the rise, and currently large amounts of amphetamines and buprenorphine are trafficked into the Caucasus from Europe (United Nations Office on Drugs and Crime 2005; Parfitt 2006).

Georgia is experiencing an emerging HIV/AIDS epidemic (Tkeshelashvili-Kessler et al. 2005; Stvilia et al. 2006), but absolute numbers of HIV infected individuals have remained low. In contrast, other blood-borne pathogens such as hepatitis C are very common (Butsashvili et al. 2001; Stvilia et al. 2006; Zaller et al. 2004). In order to better characterize the drug-using behaviors associated with HIV, HCV, and HBV we recruited and studied 926 IDUs from three cities in Georgia between 1997 and 1998.

Methods

Study Population

Between October 1997 and June 1998, we recruited individuals who admitted injecting illicit drugs within the last six months as part of a large HIV/AIDS surveillance project conducted by the Georgian AIDS and Clinical Immunology Research Center (Tkeshelashvili-Kessler et al. 2005). Recruited individuals were between the ages of 18 and 65 and resided in one of the Georgian cities of Tbilisi, Batumi, and Poti. The participants were enrolled in the study and

administered a questionnaire by trained health care professionals. Participants were primarily an out-of-treatment convenience sample of IDU recruited from the community. Recruitment was accomplished through word-of-mouth advertising, through advertisements at locales providing medical and social services to IDUs, and via participant referral and snowball sampling techniques. Most subjects who were approached for enrollment agreed to participate in the study.

Participants were not paid for their participation in the study, but received testing for hepatitis C, B, and HIV infection along with pre- and post-test counseling and referral for medical evaluation and therapy when indicated. The research protocol was reviewed and approved by the Institutional Review Boards at the AIDS and Clinical Immunology Research Center in Tbilisi, Georgia and the Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.

Behavioral Questionnaire

Recruited individuals who agreed to participate in the study were interviewed confidentially by trained health care professionals. We collected data on both drug use history and current patterns of drug use, as well as on demographic and sexual behavior characteristics. We asked participants about their early experiences with injection drugs, the duration and patterns of their injection drug use, the partners with whom they shared injection equipment, and the drugs they most commonly injected. Our questions were based upon reported risks for infectious disease transmission in Georgia, as well as upon our experiences with other injection drug using populations in the United States, Thailand, and elsewhere. We did not collect social network information from recruited participants. Data was collected using paper forms, and was transferred to a Microsoft Access database for archival following each interview.

Laboratory Methods

Blood samples drawn from participating individuals were assayed for antibody to HIV-1 with the Abbott Recombinant HIV-1 assay (Abbott Laboratories, Abbott Park, IL, USA). Blood samples reactive for HIV-1 were confirmed using a licensed Western Blot assay (DuPont Co, Wilmington, DE, USA). Antibody to HCV was assessed using the Ortho HCV Version 3.0 ELISA (Ortho Diagnostics Systems, Raritan, NJ, USA). Hepatitis B surface antigen (HBsAg) and core antibody (anti-HBc) were assessed using Auszyme Monoclonal and Corzyme assays (Abbott Laboratories, Abbott Park, IL, USA). All laboratory testing was conducted at the AIDS and Clinical Immunology Research Center in Tbilisi.

Statistical Methods

We calculated descriptive statistics for laboratory results and questionnaire variables. We used bivariate and multivariable logistic regression models to evaluate the association of demographic, drug use history, drug use behaviors, and sexual history variables with HCV and HBV seropositivity. We defined individuals testing positive for either anti-HBc or HBsAg to be HBV positive. We included age and city of residence in our multivariable models to control for potentially confounding by these factors, and additionally needle sharing behavior in select analyses to further evaluate significant findings in isolation. All analyses were conducted using SAS 9.1 (SAS Institute, Cary, NC, USA).

Results

Demographic information, drug use history and behaviors, and sexual history for the 926 study participants are listed in Table 1. As seen in the table, the study participants were almost all male, and the majority were in their late twenties and were recruited in Tbilisi. Most study participants reported initiation of injection drug use while in their teens or very early twenties,

and injected opium most commonly, heroin secondly, followed by home-processed poppy straw and stolen medical/synthetic drugs. Most individuals reported that their first sexual contact occurred in their late teens, and the majority of participants reported having five or fewer sexual partners in the last two years. The majority of study participants reported sharing needles with one to five other individuals, although some participants reported sharing with more than ten other individuals.

Table 2 shows the needle sharing behaviors of individuals most commonly injecting different drugs. As seen in the table, users of poppy straw shared needles most commonly (94.3%), followed by users of heroin (93.2%), users of opium (90.7%), and users of stolen medical/synthetic drugs (64.7%). The vast majority (89.2%) of individuals injecting medical/synthetic drugs reported sharing needles with five or fewer other individuals, in contrast to users of poppy straw (56.9%), heroin (60.6%), and opium (62.1%).

Of the 926 study participants, 5 (0.5%) were positive for HIV, 539 (58.2%) for HCV, 67 (7.2%) for HBsAg, and 475 for (51.3%) for anti-HBc; 483 (52.2%) individuals were positive for antibody to either HBsAg or anti-HBc. The five HIV positive individuals were on average 25 years old and all reported sharing needles with at least one other person. Four of the HIV infected individuals were HCV co-infected, and three were anti-HBc seropositive. No HIV infected individuals reported injecting medical/synthetic drugs as their preferred drug.

Table 3 shows the results of bivariate and multivariable logistic regression analysis examining risk factors for HCV and HBV seropositivity. As seen in the table, needle sharing was by far the dominant risk factor for the presence of HCV, and was also associated with an increased odds of HBV seropositivity. An individual who shared needles with more than 10 other individuals had close to a three hundred-fold higher odds of being HCV seropositive than an individual who reported not sharing needles.

Also highly significant in this analysis was the protection obtained against the presence of HCV and HBV from most commonly injecting stolen medical/synthetic drugs versus opium. These associations remained significant even after adjustment for needle sharing behavior in addition to city and age (OR: 0.38, 95% CI: 0.22, 0.68 and OR: 0.58, 95% CI: 0.37, 0.90 for HCV and HBV respectively). Injecting poppy straw and heroin versus opium were significant risk factors for HCV, and also retained significance after adjustment for needle sharing behavior (OR: 2.54, 95% CI: 1.47, 4.41 and OR: 1.63, 95% CI: 1.03, 2.60 for poppy straw and heroin respectively). In contrast, injecting poppy straw was associated with a significantly reduced odds of HBV infection after adjusting for needle sharing behavior (OR: 0.51, 95% CI: 0.34, 0.78).

Additionally significant in this analysis were the associations between HCV and having been to prison, having multiple sexual partners in the last two years compared to only one partner, and having an age of first sexual contact of greater than 17 versus an age of 15 years or younger. After additional adjustment for needle sharing, only the associations between HCV and having been to prison (OR: 2.10, 95% CI: 1.38, 3.18) and having two sexual partners in the last two years versus one partner remained significant (OR: 1.89, 95% CI: 1.16, 3.07).

Discussion

Although countries such as Ukraine and Russia have recently seen HIV/AIDS transition from high-risk groups to the general population (DeBell & Carter 2005; Shakarishvili et al. 2005), many former Soviet republics, including Georgia, are at the earliest stages of the epidemic (Tkeshelashvili-Kessler et al. 2005) and thus have the opportunity to halt the disease before it becomes widespread. In this survey we found a relatively low prevalence of HIV infection among the IDUs tested, but high levels of needle sharing and infection with HCV and HBV. These data suggest that the risk behaviors for efficient transmission of HIV are common among

Georgian IDUs, but the virus- or host-associated factors that have thus far prevented HIV from making major inroads into Georgian IDU populations remain poorly understood.

An exception to the generally high prevalence of HCV and HBV among the studied IDUs was the low prevalence of these infections and lower reported needle sharing among IDUs who usually injected stolen medical/synthetic drugs. The wide disparity in risk of infectious diseases and risk taking behaviors between this group and the other IDU indicates that substantial differences between IDU sub-populations exist in Georgia. This heterogeneity could stem from drug-associated factors such as different procurement and drug preparation strategies employed by individuals using the different types of illicit drugs. Alternatively, the different types of illicit drugs could serve as proxies for other unknown factors associated with differential needle sharing and infection rates. Regardless of the root cause, recognition of sub-populations may suggest which IDU populations should be most targeted for intervention strategies, and should be taken into account during the conduct of epidemiologic studies. However, it is important to note that in countries such as Georgia illicit drug injection behavior can change markedly in a short period of time. Indeed, only two years after this survey was completed a survey of 583 IDU using similar recruitment strategies in the same three Georgian cities showed that heroin was the most commonly injected drug for 58.7% of the surveyed population (Shapatava et al. 2006).

Also of interest in this study was the magnitude of the association between needle sharing and HCV, and additionally the association between having been to prison and HCV. Although these findings are not novel (Delage et al. 1999; Girardi et al. 1990; Thomas et al. 1995), these results suggest that needle sharing is an especially efficient behavior for the transmission of HCV in Georgia, and that prisons are likely high risk environments for the transmission of HCV and possibly other parenterally-transmitted infections in this country. Georgian prisoners, like those in many other countries, may therefore constitute a group in special need of harm reduction interventions.

Although we found that individuals who reported increased needle sharing and younger age of first sexual contact were at increased risk of HBV infection, these increases were modest and did not attain statistical significance. Although HBV is readily transmissible by the injection of illicit drugs, it is also more effectively transmitted by perinatal or sexual contact than HCV. A recent study in Russia (Mikhailov et al. 2002) suggested that significant HBV transmission occurred during sexual contacts between teenagers. Our study would have limited power to detect this sexual risk factor.

The low prevalence of HIV infection among IDUs in Georgia found in this survey is consistent with other studies (Butsashvili et al. 2001; Shapatava et al. 2006; Stvilia et al. 2006; Zaller et al. 2004) and suggests that there is a window of opportunity to contain the transmission of HIV among this group. However, significant needle sharing and high prevalence of HCV and HBV suggest that Georgia, like many other former Soviet Republics, may be on the verge of an HIV/AIDS catastrophe. Containment of HIV/AIDS in Georgia will require the implementation of preventive measures directed to the sub-populations at highest risk, to reduce needle sharing behavior.

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Glossary

Amphetamines	Organic compound, prototype of a class of synthetic amphetamine drugs (e.g., Benzedrine, Dexedrine, methamphetamine), that stimulates the central nervous system. Amphetamines cause wakefulness, euphoria, decreased fatigue, and increased ability to concentrate. Undesirable effects include overstimulation, with paranoia, restlessness, insomnia, tremor, and irritability, and a deep depression when the drug wears off. This, along with rapid development of tolerance requiring increased doses, can lead to drug addiction.
Buprenorphine	Buprenorphine is an opioid drug primarily used for the treatment of opioid addiction.
Caucasus region	The Caucasus or Caucasia is a region in Eurasia bordered on the south by Turkey and Iran in Asia, on the west by the Black Sea, on the east by the Caspian Sea, and on the north by Russia. Caucasia includes the Caucasus Mountains and surrounding lowlands.
Poppy Straw	any part (other than the seeds) of the opium poppy (<i>Papaver Somniferum</i>).
Snowball Sampling	Snowball sampling relies on referrals from initial subjects to generate additional subjects. While this technique can dramatically lower search costs, it comes at the expense of introducing bias because the technique itself reduces the likelihood that the sample will represent a good cross section from the population.
Synthetic Drugs	are artificially produced substances for the illicit market which are almost wholly manufactured from chemical compounds in illicit laboratories (amphetamine, benzodiazepines).

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Figure 1.
Georgia

Table 1

Characteristics of the study participants (N=926)

	Number	Percent ^a
Male	922	99.6
Female	4	0.4
Age group		
18-24 years	320	34.6
25-30 years	327	35.3
> 30 years	279	30.1
City of residence		
Tbilisi	737	79.6
Batumi	113	12.2
Poti	76	8.2
Prison	179	19.3
Age at first injection drug use		
≤ 18 years	193	20.8
19 - 21 years	491	53.0
≥ 22 years	242	26.1
Most commonly injected drug		
Opium	582	62.9
Medical/synthetic drugs	102	11.0
Poppy straw	109	11.8
Heroin	132	14.3
Refused	1	0.1
Number people with whom shared needles		
0 people	105	11.3
1 - 5 people	490	52.9
6 - 10 people	205	22.1
> 10 people	126	13.6
Age at first sexual contact		
≤ 15 years	398	43.0
16 - 17 years	420	45.4
≥ 18 years	108	11.7
Number of sexual partners in last 2 years		
1 partner	198	21.4
2 partners	191	20.6
3 - 5 partners	286	30.9
> 5 partners	251	27.1
	Mean	SD^b
Age	27.6	6.3

^aPercentages are rounded to one decimal place

^bSD, Standard Deviation

Table 2

Needle sharing among individuals injecting different drugs (N=925)

Most commonly injected drug	Number of people with whom shared needles (%)			
	0	1 - 5	6 - 10	> 10
Opium	54 (9.3)	307 (52.8)	144 (24.7)	77 (13.2)
Medical/synthetic drugs	36 (35.3)	55 (53.9)	6 (5.9)	5 (4.9)
Poppy straw	6 (5.5)	56 (51.4)	25 (22.9)	22 (20.2)
Heroin	9 (6.8)	71 (53.8)	30 (22.7)	22 (16.7)

Table 3

Risk factors for HCV and HBV seropositivity among Georgian injection drug users (N=926)

Variable	HCV		HBV	
	OR	95% CI	OR	95% CI
City				
Tbilisi	1.0		1.0	
Batumi	0.81	0.54, 1.21	0.83	0.56, 1.23
Poti	0.85	0.53, 1.37	1.12	0.70, 1.80
Age group				
18-24 years	1.0		1.0	
25-30 years	0.94	0.69, 1.28	1.07	0.79, 1.46
> 30 years	0.96	0.69, 1.33	1.13	0.82, 1.56
	OR *	95% CI	OR *	95% CI
Prison				
No prison time	1.0		1.0	
Some prison time	2.34	1.63, 3.37	1.19	0.86, 1.66
Age at first injection drug use				
≤ 18 years	1.0		1.0	
19 - 21 years	0.72	0.51, 1.02	0.86	0.61, 1.21
≥ 22 years	0.97	0.65, 1.45	0.77	0.53, 1.14
Most commonly injected drug				
Opium	1.0		1.0	
Medical/synthetic drugs	0.21	0.13, 0.34	0.56	0.36, 0.86
Poppy straw	2.44	1.51, 3.93	0.53	0.35, 0.80
Heroin	1.58	1.06, 2.37	0.79	0.54, 1.15
Number people with whom shared needles				
0 people	1.0		1.0	
1 - 5 people	35.72	11.16, 114.29	1.20	0.79, 1.83
6 - 10 people	203.13	60.32, 683.97	1.37	0.71, 1.82
> 10 people	278.12	77.57, 997.20	1.57	0.93, 2.64
Age at first sexual contact				
≤ 15 years	1.0		1.0	
16 - 17 years	0.95	0.71, 1.26	0.86	0.65, 1.14
> 17 years	0.62	0.40, 0.96	0.81	0.53, 1.25
Number of sexual partners in last 2 years				
1 partner	1.0		1.0	
2 partners	2.07	1.37, 3.13	0.85	0.57, 1.26
3 - 5 partners	1.47	1.02, 2.12	0.94	0.65, 1.35
> 5 partners	1.48	1.02, 2.16	1.21	0.83, 1.76

* ORs are adjusted for city and age