

## Hepatitis C, B, and Human Immunodeficiency Virus Infections in Illicit Drug Users in Israel: Prevalence and Risk Factors

Ronen Loebstein MD<sup>1\*</sup>, Rafae Mahagna MD<sup>2\*</sup>, Yasmin Maor MD<sup>3</sup>, Daniel Kurnik MD<sup>1,2</sup>, Eliyahu Elbaz PhD<sup>4</sup>, Hillel Halkin MD<sup>1</sup>, David Olchovsky MD<sup>2</sup>, David Ezra MD<sup>2</sup> and Shlomo Almog PhD<sup>1</sup>

<sup>1</sup>Institute of Clinical Pharmacology and Toxicology, and Departments of <sup>2</sup>Medicine and <sup>3</sup>Infectious Diseases, Sheba Medical Center, Tel Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

<sup>4</sup>National Center for Diagnosis and Follow up of Drug Addicts, Tel Aviv-Jaffa, Israel

**Key words:** hepatitis C, illicit drug users, risk factors

### Abstract

**Background:** Infections with blood-borne viruses are a major health problem among illicit drug users. There is little information about infection rates and risk factors for hepatitis virus B, C or the human immunodeficiency virus in drug users in Israel.

**Objectives:** To determine the prevalence of HCV, HBV and HIV infections in a large cohort of drug users in Israel; to compare rates of HCV, HBV and HIV between injecting versus non-injecting drug users and between different countries of origin; and to identify risk factors for HCV among illicit drug users.

**Methods:** We conducted a cross-sectional study using an interviewer-administered questionnaire and serological screening for HCV, HBV and HIV in 1443 consecutive drug users diagnosed at the Israeli National Center for Diagnosis of Drug Addicts between January 2003 and December 2005.

**Results:** Fourteen (0.9%), 51 (3.5%) and 515 (35.7%) subjects tested positive for HIV, HBV and HCV, respectively. All three infections (HIV, HBV and HCV) were significantly more common among injecting drug users and immigrants from the former Soviet Union and other East European countries compared to native Israelis. Multivariate analysis showed that HCV infection was associated with age (> 40 years) (OR=2.06, 95% CI 1.40–3.03), immigration from East European countries and the former Soviet Union (OR=4.54, 95% CI 3.28–6.28), and injecting drug use (OR=16.44, 95% CI 10.79–25.05).

**Conclusions:** HIV, HBV and HCV prevalence among drug users in Israel is significantly lower than in North America and West Europe. Risk factors for HCV infection in this population include injecting drug use, older age, and immigration from the former Soviet Union.

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Hepatitis B, human immunodeficiency virus and especially hepatitis C are major health issues among drug users [1-7]. Current HCV prevalence among injecting drug users worldwide averages 70%, but there are marked geographic differences (5%–95%), with Asia and North America having the highest prevalence [2]. The major determinants associated with HCV infection in injecting

drug users include age, duration of injecting career, country of origin, and ethnicity [4-9]. Although reliable HCV testing has been available since 1989, its implementation among injecting drug users has been minimal and most are unaware of their HCV status [10]. In addition, there are many other barriers to treatment of HCV infection in this population [11,12]. Thus, hepatitis C contributes substantially to morbidity and mortality in drug users. Little is known about the prevalence of HCV, HBV and HIV infections in Israeli drug users.

The Israeli population is a mix of different ethnic groups originating from many countries. In the early 1990s, the former Soviet Union together with East European countries relaxed their emigration policies, allowing the immigration of an estimated one million new immigrants to Israel. Patterns of drug use (e.g., alcohol and IDU) in these countries differ from those in Israel, and the prevalence of some chronic infectious diseases (including HBV and HCV) is higher [6,8]. Accordingly, a higher rate of intravenous drug use and self-reported chronic medical conditions, including HCV infection, has been reported among immigrants from the former Soviet Union and other East European countries compared to native Israelis [8,13]. However, the relationship between patterns of drug use, country of origin, and infections with HCV, HBV and HIV has been poorly characterized.

The National Center for Diagnosis and Follow up of Drug Addicts was founded in 1988. Its main goals are to provide a comprehensive and standardized diagnosis for the entire population of drug addicts in Israel and to set criteria for the National Insurance Institute for granting financial support. Presently, this is the largest database of drug addicts in Israel, with approximately 10,000 individuals on its roster.

Using this large-scale source, our objectives were to determine the prevalence of hepatitis B and C and HIV among drug users in Israel, to compare the rates of these infections between injecting and non-injecting drug addicts and between immigrants from different countries of origin and native Israelis, and to identify risk factors for HCV infection.

### Subjects and Methods

This was a retrospective chart review study of consecutive drug users attending the National Center for Diagnosis of Drug Addicts

\* The first two authors contributed equally to this work

HCV = hepatitis C virus

HBV = hepatitis B virus

HIV = human immunodeficiency virus

IDU = injecting drug use

between January 2003 and December 2005. A visit to the center involves an examination by a physician (including a full medical history with special focus on drug use habits, recorded on an interviewer-administered structured questionnaire, and physical examination), an intake by either a social worker or a psychologist, blood sampling for complete blood count, serum chemistry, and HCV, HBV and HIV serology. Chart data recorded for each individual included age, gender, country of origin, year of immigration to Israel, medical history including sexually transmitted diseases, history of illicit drug use, drugs used at present, route of drug administration (smoking, snorting, injection), cigarette smoking, and alcohol consumption.

### HBV, HCV and HIV testing

Testing for HBsAg and antibodies against HBV and HCV was performed at the Blood Bank, Sheba Medical Center, using a microparticle-based enzyme linked immunoassay (AxSYM, HBV, HCV, Abbot Laboratories, USA). HIV testing was performed using a sandwich qualitative microparticle-based enzyme-linked immunoassay (AxSYM, HIV 1/2 gO Abbot Laboratories) at the Department of Infectious Diseases, Sheba Medical Center [14]. For positive HIV tests, results were confirmed on a repeat serum sample, and Western blot testing was performed at the National HIV Reference Laboratory, Sheba Medical Center.

### Statistical analysis

Data are presented as mean  $\pm$  standard deviation. Pre-specified subgroups stratified by route of drug use (injecting vs. non-injecting users) and by country of origin were compared using chi-square test for categorical variables and Student *t*-test for continuous variables. Logistic regression analysis was used to determine risk factors associated with hepatitis C infection, using age categories (20–29 reference group) 30–39 and 40–49 years, intravenous drug use and country of origin as covariates. Analyses were performed with the statistical software SAS. All analyses were two-sided, and *P* value < 0.05 was considered significant.

### Results

Charts of 1443 drug users were reviewed and included in the analysis. The majority (86.8%) were male. Two-thirds (927, 64.2%) were native Israelis, 441 (30.6%) were immigrants from the former Soviet Union, and 46 (3.2%) and 30 (2.1%) had immigrated from other East European and Mediterranean countries, respectively. The most commonly used drug was heroin with or without methadone (96%), followed by benzodiazepines (64%), marijuana (44%), cocaine (36%), and amphetamines (including metamphetamines) (12%). Approximately half the drug users (*n*=743, 51.4%) reported either current or past IDU [Table 1]. Reported duration of drug use was  $12.2 \pm 7.6$  years for non-IV drug use and  $0.7 \pm 1.0$  years for IV drug use. Table 1 summarizes demographic characteristics of injecting versus non-injecting drug users. Compared to native Israelis, IDU was significantly more common among immigrants from the former Soviet Union and other East European and Mediterranean countries.

**Table 1.** Demographic and clinical characteristics of 1443 drug users and route of drug use

	Total ( <i>n</i> =1443)	IV drug use ( <i>n</i> =743)	Non-IV drug use ( <i>n</i> =700)	<i>P</i>
Male (%)	1252 (86.8%)	629 (84.7%)	623 (89.0%)	0.02
Age (yrs) (range)		33.8 $\pm$ 8.0 (18–59)	37.3 $\pm$ 7.6 (19–63)	< 0.001
Country of origin				
Israel	927	329 (35.5%)	598 (64.5%)	< 0.001
Former Soviet Union	441	396 (89.8%)	45 (10.2%)	< 0.001
Other East Europe	46	32 (69.6%)	14 (30.4%)	< 0.001
Mediterranean	30	21 (70.0%)	9 (30.0%)	0.005
Years of education (range)		9.7 $\pm$ 2.8 (0–22)	8.7 $\pm$ 2.7 (0–20)	< 0.001
Marital status				
Single		361 (48.7%)	201 (28.9%)	< 0.001
Married		162 (21.9)	270 (38.8%)	< 0.001
Other		218 (29.4%)	225 (32.3%)	NS
Religion				
Jewish		577 (77.8%)	507 (72.6%)	0.003
Christian		85 (11.5%)	15 (2.2%)	< 0.001
Moslem		75 (10.1%)	172 (24.6%)	< 0.001
Other		4 (0.5%)	4 (0.5%)	NS

\* Injecting drug use includes both former and present IV drug use.

**Table 2.** Demographic and clinical characteristics of 1443 drug users according to HCV status

	HCV positive <i>n</i> =515 (35.7%)	HCV negative <i>n</i> =928 (64.3%)	<i>P</i>
Male	436 (84.7%)	816 (87.9%)	0.08
Age (yrs) (range)	34.3 $\pm$ 7.9 (20–58)	36.1 $\pm$ 7.9 (18–63)	< 0.001
Country of origin			
Israel	182 (19.6%)	745 (80.4%)	< 0.001
Former Soviet Union	315 (71.4%)	126 (28.6%)	< 0.001
Other East Europe	34 (73.9%)	12 (26.1%)	< 0.001
Mediterranean	12 (40.0%)	18 (60.0%)	NS
Years of education (range)	9.8 $\pm$ 2.9 (0–22)	8.9 $\pm$ 2.7 (0–18)	< 0.001
Religion			
Jewish	406 (79%)	678 (73.3)	< 0.001
Christian	67 (13%)	33 (3.6%)	< 0.001
Moslem	39 (7.6%)	208 (22.5%)	< 0.001
Other	2 (0.4%)	6 (0.7%)	NS
IV drug use	461 (62.0%)	282 (38.0%)	< 0.001
Non-IV drug use	54 (7.7%)	646 (92.3%)	< 0.001

Anti-HCV antibodies were detected in 515 subjects (35%), 461 of whom reported IDU while the remaining 54 reported smoking/snorting (chi-square=640.1, *P* < 0.001) [Table 2]. The majority of immigrants from the former Soviet Union (71.4%) and East Europe (73.9%), but only 19.6% of native Israelis tested positive for HCV. In a multivariate analysis, HCV infection was associated with IDU (odds ratio = 16.44; 95% confidence interval

**Table 3.** Association between different variables and HCV infection in illicit drug users

Variable	Odds ratio	95% CI
Age 30–39	1.55	1.09–2.21
Age > 40	2.06	1.40–3.03
Immigration from former Soviet Union/Eastern Europe	4.54	3.28–6.28
Injecting drug use	16.44	10.79–25.05

Age group 20–29 was the reference group.

10.79–25.05), immigration from the former Soviet Union (OR=4.54, 95% CI 3.28–6.28), and age (mainly above 40) (OR=2.06, 95% CI 1.40–3.03) [Table 3].

Fifty-one subjects (3.5%) tested positive for HBsAg, 32 of whom (62.7%) were IDU (chi-square 4.08,  $P = 0.04$ ). The majority of HBsAg-positive subjects immigrated from the former Soviet Union and East Europe (39/51) while 9 were native Israelis.

Fourteen subjects (0.9%) tested positive for anti-HIV antibodies, all of whom were injecting drug users, resulting in a rate of 1.9% HIV-positive subjects among the IDUs. Most of the HIV-infected subjects (11/14, 78.6%) immigrated from the former Soviet Union and other East European countries.

## Discussion

Using a large database, this is the first study to examine HCV, HBV and HIV infection rates in Israeli drug users based on serological testing. Our main findings were that the prevalence of HCV among drug users in Israel is lower than the mean reported rates in the United States and West and East Europe [1,2]. Native Israelis were characterized predominantly by non-IDU and low rates of HCV infection (approximately 20%), while 70–90% of immigrants from the former Soviet Union and other East European countries reported IDU and approximately 70% tested positive for HCV, reflecting drug use patterns and infection rates similar to those reported for their countries of origin [2,6]. Importantly, after adjustment for patterns of drug use (IDU vs. non-IDU), immigration from the former Soviet Union and other East Europe countries remained a significant risk factor for HCV infection, suggesting that the three- to fivefold higher rate of positive HCV serology was not completely explained by the higher rate of IDU. Reported higher rates of sexually transmitted diseases in this group may also contribute to this finding [6].

There is little previous information about hepatitis exposure among Israeli drug users. Isralowitz et al. [8] interviewed 572 drug addicts in Israel between 2002 and 2006. Based on the interviewees' self-report, HCV infection rates were estimated to be around 35–38% among native Israelis and 67–75% among immigrants from the former Soviet Union. Similar findings were reported by Peles et al. [13]. Our study corroborates these estimates by serological testing in a much larger cohort. These rates are significantly higher than the HCV rate of 0.1% among blood donors in Israel.

OR = odds ratio  
CI = confidence interval

HIV prevalence in our cohort (0.9%) and among injecting drug users (1.9%) was lower than that reported in the USA or West Europe [1]. HBV prevalence in our study group was comparable to the reported rates in the U.S. and West European countries [1,4].

Of all the blood-borne viruses, hepatitis C is becoming one of the most prominent health issues among drug users, especially injecting users. Efforts to promote widespread testing of HCV among high risk populations with special emphasis on drug users have been minimal and mostly unsuccessful. The importance of knowing one's HCV status especially among drug users cannot be overstated. Previous studies have shown that while 70% of injecting drug users were HCV positive only 61% were aware of their status [10]. Moreover, those who were aware of their status were less likely to engage in risk behaviors such as syringe sharing and unprotected sex than those who were unaware. In addition, many physicians are still hesitant to treat drug users and/or opioid dependants with hepatitis C, mainly due to concerns about adherence to chronic therapy, stability and psychiatric co-morbidity [12]. This approach is further supported by the U.S. National Institutes of Health and European Consensus Conference guidelines to avoid treatment with interferon in cases of alcohol or drug dependence and major psychiatric disorders. Although overall illicit drug use has been shown to be associated with HCV persistence, injecting drug use has been shown to be an independent predictor for spontaneous clearance of hepatitis C and that together with extra support, compliance and treatment outcomes in opioid dependants after 24 weeks of HCV treatment correspond to that of non-dependants [15,16]. Moreover, sustained virological response and adherence in HCV-infected methadone-substituted patients was shown in a systematic review to be comparable to control groups or to representative clinically controlled trials [17]. In addition, there is a low uptake of HCV treatment among illicit drug users despite their high willingness to receive treatment. The main factors associated with the gap between willingness to receive therapy and actual treatment are lack of knowledge about both HCV status and treatment availability [18].

Our study has several limitations: first, since the data were obtained from a single center they may not be representative of the entire drug user population in Israel, especially in light of the marked ethnic differences across different regions of the country. Secondly, behavioral data were obtained by self-report and therefore may be subject to recall bias. However, the large sample size and data validation by urine analysis for illicit drug screening in selected cases (data not shown) allowed us to use the reported data with a relatively high level of confidence.

The findings of this study call for improved access to HCV, HIV and HBV testing in drug addicts together with implementation of a program of long-term follow-up, since awareness of their positive blood-borne viruses status has been shown to limit their engagement in risk behaviors. Finally, the substantial improvement of sustained virological response rates to interferon treatment among drug users calls for more generous treatment options for these patients.

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**Correspondence:** Dr. R. Loebstein, Institute of Clinical Pharmacology & Toxicology, Sheba Medical Center, Tel Hashomer 52621, Israel.  
Phone: (972-3) 530-2358  
Fax: (972-3) 535-1596  
email: ronien.loebstein@sheba.health.gov.il