Hepatitis C Virus Prevalence, Medical Status Awareness and Treatment Engagement among Homeless People Who use Drugs: Results of a Street Outreach Study

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ABSTRACT

BACKGROUND: Hepatitis C virus (HCV) infection is a primary health concern among people who use drugs (PWUDs). Homeless PWUDs that constitute a key population for HCV transmission remain underrepresented in many surveys.

OBJECTIVES: We performed a proactive street outreach to evaluate HCV infection prevalence among homeless PWUDs in Tel Aviv, identify risk factors associated with HCV infection, awareness of disease status and linkage to care rate.

RESULTS: Thirty-eight percent of approached PWUD were willing to participate in the study. Out of 53 subjects who got tested for anti HCV by rapid test, 29 (54.72%) had a positive result, 20 of 29 anti-HCV positive (69%) patients had positive HCV PCR. Risk factors were investigated using structured questionnaires. Heroin use was reported significantly more frequently in the HCV-positive group (P=.05, CI 95%), whereas other established risk factors did not reach significance in our cohort. While 21 of 29 (72%) HCV-positive participants were aware of their condition, only 4 of 21 (19%) received treatment in the past, and 2 of 4 (50%) failed to achieve treatment goals, as assessed by HCV PCR.

CONCLUSIONS: Our data indicate a high prevalence of HCV infection among homeless PWUDs. Importantly, despite relatively high awareness of HCV status in this population, we found strikingly low access to care. These findings motivate novel interventional approaches targeted at improving patient access, and compliance among homeless PWUDs, in an effort to reduce HCV transmission.

KEYWORDS: Hepatitis C virus, people who use drugs, awareness, access to care, treatment

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Introduction

Hepatitis C is a viral liver disease: the hepatitis C virus can cause both acute and chronic hepatitis and is a major cause of liver cancer. A significant number of those who are chronically infected will develop cirrhosis or liver cancer.1-3 HCV is a bloodborne virus, transmitted primarily through exposure to blood or blood products. The most common modes of infection are through intravenous drug use, unsanitary health care procedures, transfusion of unscreened blood and blood products, and sexual practices that lead to blood exposure.3,4,6 Globally, an estimated 71 million people have chronic hepatitis C virus infection.3,4

It is estimated that 12 million people worldwide inject drugs.4,5 Negative health outcomes of drug use can include drug use disorders, mental health disorders, Human Immunodeficiency Virus (HIV) infection, liver cancer and cirrhosis associated with hepatitis, overdose and premature

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death. The greatest harm to health is associated with opioid use, as it often involves drug injection, primarily due to the risk of acquiring HIV or HCV through unsafe injecting practices.^{6,7} In 2017, the joint UNODC, WHO and the UNAIDS estimated HCV prevalence among injecting drug users worldwide at 49.3%, which translates roughly to 5.6 million PWUDs living with HCV.^{3,4} In comparison, the prevalence of HCV in 2015 among the general population worldwide was estimated at 1.0% (range: 0.8%-1.1%).3

Advances in treatment have led to higher cure rates than prior therapeutic approaches, showing high potency, favorable tolerability profile, higher barrier to resistance, shortened treatment duration, fewer drug interactions and reduced pill burden.8-14 The recent availability of highly tolerable new direct-acting antiviral (DAA) therapies has led to the development of World Health Organization HCV elimination targets, which proposed an 80% reduction in HCV incidence and a 65% reduction in HCV-related mortality by 2030.15 Thus, lack of tolerable and effective treatment is currently not a barrier to HCV eradication. Current barriers to achieving ambitious targets for

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Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). global HCV control include low awareness of infection among key populations such as PWUD,¹⁶⁻²⁰ low treatment-seeking behavior among PWUD, lack of access to care, or low compliance with treatment regimens.

It should be noted that every Israeli resident is covered by health insurance which entitles him/her to the services established under the National Health Insurance Law. Lack of payment or delayed payment of health insurance fees does not affect the rights of a policyholder and does not exempt the health plan from providing the healthcare services included in The Healthcare Basket. Nevertheless, deductibles for insured patients may not be affordable for all strata of the population since the costs of Hepatitis C treatment is close to 300\$. This obstacle may be overcome by receiving sponsored treatment, but the bureaucratic process may be cumbersome.

HCV prevalence, risk factors, and barriers to infection control among homeless PWUDs in Tel Aviv, Israel are not well understood. We sought to characterize these factors among this local population, in an effort to identify key avenues of intervention to increase HCV eradication in this community.

Methods

Study population

Subjects were recruited through street outreach by members of the Israel Aids Task Force (IATF) team and volunteers, from October 3rd, 2018, to November 14th, 2019. The area of activity was in the south Tel Aviv region, Israel.

All subjects declared being homeless (eg, with no permanent housing for at least 3 weeks) and current drug users, not being treated at any drug and addiction clinic except 3 individuals, who continued to use illicit drugs despite current opioid substitution therapy.

Fifty-three out of 142 participants agreed to be tested for HCV and HIV and filled out questionnaires. Results were obtained for 52 of 53 participants, as one blood sample was not tested due to insufficient quantity for proper testing.

Study procedures

Israeli Aids Task Force provided an ambulance with first aid equipment, sterile syringes and needles, food and hot drinks. As the subjects arrived at the ambulance, they were offered free HCV and HIV testing. Once one accepted to be tested, IATF staff and volunteers used structured interview questionnaires assessing HCV and HIV risk behaviors including drug use and sexual practices. For each subject, gender, country of origin, emigration date, drugs in use, duration of drug use, alcohol consumption, sexual practices (including safe sex and number of partners), HCV status awareness and previous HCV treatment were recorded.

Medical equipment included HCV rapid tests (OraQuick rapid test to detect antibodies [OraSure Technologies,

Bethlehem, PA USA]) and HIV rapid tests (Chembio HIV 1/2 STAT-PAK [Chembio diagnostic systems, New-York, US]). Blood specimens were shipped to the Infectious Diseases Unit at Sheba Medical Center, quantitative HCV PCR and HCV Genotype detection tests (Abbott RealTime HCV assay) were performed in all blood samples. For HIV positive test results, Enzyme-Linked Fluorescent Assay (VIDAS DUO) was made on a repeat serum sample and HIV confirmation by Western Blot test.

Statistical analysis

All analyses were performed in SPSS version 25 (IBM SPSS Statistics, Chicago, IL, USA). The statistical analysis was carried out in several steps. First, a univariate exploration of study variables was done, and it included inspection of the normal distribution of continuous variables and error values and outliers. Overall patient characteristics were summarized by mean (standard deviation) for continuous variables and by frequency (%) for nominal variables. Next, characteristics were compared between the study groups by bivariate analysis. The student's t-test and Wilcoxon rank-sum test were performed for comparison of normally and non-normally distributed continuous variables, while nominal variables were compared with the Chi-square test. Alpha and beta parameters were set at 0.05 and 0.2, respectively. A *P*-value was used for a convenient representation of statistical significance.

Results

Of 142 subjects who voluntarily approached the IATF ambulance, 53 (38%) participants agreed to be tested for HCV infection and fill out questionnaires. 89 (62%) subjects who approached IATF ambulance but refused to be tested, did not fill out questionnaires. Hence, qualitative data for these subjects are missing. Demographic characteristics for the 53 individuals are summarized in Table 1. The median age of participants was 41 (range 26-68 years). The mean age of drug use was 16 years (range 0–35 years of drug use). 37 (69%) subjects reported intravenous drug use, 9 (17%) reported using drugs by other practices such as sniffing, smoking, drinking, or swallowing and 3 (0.06%) refused to share that kind of information (Figure 1A). Drug type, alcohol use and sexual behavior are depicted in Figure 1B to E.

Fifty-two rapid tests to detect HCV and HIV based on whole blood specimens were performed. The prevalence of HCV exposure among homeless PWUDs was 56%, as 29 of 52 rapid HCV antibodies tests were positive. Positive viral load was detected in 20 out of 29 (69%) exposed patients as assessed by HCV PCR. All 23 patients that were negative by rapid antibody test were HCV PCR negative (100% specificity). One HIV rapid test reacted.

Genotype characterization was performed in 18 samples. Genotype 1a and genotype 3 were most common: 7 patients, 39% of each genotype, followed by genotype 1b in 4 patients (22%).

	N=53 (%)
Sex	
Male	42 (79.3)
Female	11 (20.7)
Age	
20-30 years	2 (4)
30-50 years	36 (70.6)
>50 years	13 (25.5)
Country of birth	
Israel	21 (42)
Former Soviet Union	23 (46)
Other countries*	6 (12)
Native language	
Hebrew	15 (28.3)
Russian	23 (43.4)
Arabic	8 (15.1)
Immigration [†] >10 years	23 (79.3)

*Other countries include Jordan, Ethiopia, Sudan and Brazil.

[†]Twenty-nine immigrants in total.

When the denominator is less than the total n it is due to missing data.

To identify risk factors associated with HCV infection, we compared HCV positive vs negative participants (Table 2). Both Anti-HCV positive and Anti-HCV negative had a male majority, with no age differences between the groups (44.7 vs 43.7, P=.73) nor differences related to the country of birth, with an equal number of immigrants from the former Soviet Union in the HCV-positive and HCV-negative groups (52% vs 52.6% respectively, P=.96). Among the immigrant group, the proportion of people that immigrated before 2010 was higher in HCV-positive participants compared to the HCVnegative group (93.5% vs 61.5%, P=.06).

Regarding mode of use, intravenous drug use was extremely common in all examined populations. Despite a higher rate of IVDU in the HCV-positive group vs the HCV-negative group (82.2% vs 61.9%), this difference did not reach statistical significance. Heroin use was reported significantly more frequently in the HCV-positive group compared with the HCV-negative group (85.7% vs 61.9%, P=.05). Participation in an opioid substitution therapy program, having 1 partner, practicing safe sex, were reported at a similar frequency in both groups.

Medical status awareness and access to care

Forty-five of all 53 subjects had medical insurance (84.9%), 1 had no medical insurance and 4 were unable to report

insurance status. 23 out of 53 (43%), declared that they are aware of being carriers of hepatitis C (Figure 2). This selfreported HCV positive status was confirmed in 21 out of 23 subjects (91%) by positive results on a rapid HCV test. Based on PCR laboratory results, 14 out of these 21 subjects (67%), were HCV PCR positive, suggesting an active infection and the potential of disease transmission.

Out of 21 patients that claimed themselves as HCV infected and had an evidence of HCV exposure by a rapid test, only 4 (19%) subjects declared receiving trial of hepatitis C treatment (Figure 2). Two out of four treated patients (50%) were treated successfully as defined by a negative HCV PCR, while the other 2 failed to achieve treatment goals as defined by a positive HCV PCR result (Figure 2). Out of 29 patients that thought to be HCV negative or were unaware of their HCV status, 8 patients (27.5%) were diagnosed in the process of our research, based on anti-HCV rapid test, and 6 of them were HCV PCR positive based on laboratory tests.

In summary, out of 29 anti-HCV positive patients, 21 (70%) were aware while 8 (30%) were unaware of hepatitis C infection.

Linkage to care of diagnosed individuals

Despite a full explanation regarding advances in HCV treatment leading to more tolerable and efficient therapies, accompanied by a leaflet with phone numbers and an open invitation for a hepatology clinic and treatment (free of charge), only 2 of 29 HCV antibody-positive individuals sought treatment at the medical center that was made available to them. In both cases, sustained virological response was achieved.

Discussion

In our prospective study, we report for the first time in Israel the real prevalence of hepatitis C in the urban PWUD population that was approached on the streets and needle exchange stations. This population is under-investigated worldwide due to challenging outreach while most of the existing data are based on screening that is limited to prisoners and opioid substitution therapy participants.^{1,2,16-18,21} Although recruitment of PWUDs to participate in medical research is known to be challenging,²² the recruitment rate in our study was relatively high (40%) among this population, owing to professional and friendly communication by IATF volunteers and social workers. However, selection bias have be addressed, as further discussed in study limitation.

Our data indicate that HCV infection prevalence was 56%, similar to previous studies that were performed among PWUDs in the Middle East.²³ Considering all our participants are defined as very high-risk population (homelessness and active drug use),^{1-7,15,21} we can estimate that HCV prevalence amongst the general Israeli population is likely to be lower.

Predictors of HCV positivity among PWUDs worldwide generally include increasing age, male gender, frequent and



Figure 1. Behavioral characteristics: (A) pie chart depicting mode of drug consumption among study participants. IVDU = Intravenous Drug Use. (B) pie chart depicting drug type use as follows: *Schedule 1:* Heroin, Lysergic acid diethylamide (LSD), Marijuana, Cannabis, Methamphetamine, Bath salts, Psilocybin. *Schedule 2:* Morphine, Methadone, Oxycontin, Fentanyl, Phencyclidine (PCP), Cocaine, Methamphetamine. *Schedule 3:* Suboxone, Ketamine, Anabolic steroids. *Schedule 4:* Alprazolam, Clonazepam, Diazepam. (C) bar graph depicting alcohol consumption, "abuse" is defined as daily use. (D) Bar graph depicting frequency of condom use. (E) bar graph depicting number of partners.

	HCV AB-POSITIVE (N=29)	HCV AB-NEGATIVE (N=23)	P-VALUE
Male gender, n (%)	20/29 (69)	21/23 (91.3)	.08
Age, years, mean (±SD)	44.7 (±8.3)	43.7 (±11.2)	.73
Born in Israel, n (%)	12/27 (44.4)	9/23 (39.1)	.77
Immigrants from Former Soviet Union vs Israelis, n (%)	13/25 (52)	10/19 (52.6)	.96
Immigration Before 2010, n (%)	15/16 (93.8)	8/13 (61.5)	.06
Mean drug use, years (±SD)	19.1 (±9.5)	13.4 (±10.8)	.1
IV Drug Use, n (%)	23/28 (82.1)	13/21 (61.9)	.112
Heroin use, n (%)	24/28 (85.7)	13/21 (61.9)	.05
Methadone use, n (%)	3/29 (10.3)	2/23 (8.7)	>.999
One partner, n (%)	6/29 (20.7)	6/22 (27.3)	.58
Safe Sex, n (%)	4/28 (14.3)	5/21 (23.8)	.47
HIV positive, n (%)	0/29	1/22 (4.5)	.43

Table 2. Risk factors associated with HCV infection.

Abbreviations: Ab, Antibodies; HCV, Hepatitis C Virus; HIV; Human Immunodeficiency Virus; IV, Intravenous; SD, standard deviation. When the denominator is less than the total n it is due to missing data or subgroup analysis.



Figure 2. Medical status awareness and access to care. Pie charts depicting awareness of HCV exposure among study participants (left), treatment seeking among participants who reported HCV exposure (middle), and achievement of treatment goals as assessed by HCV-PCR among those who sought treatment for their condition (right). Abbreviations: Ab, antibody; SVR, sustained virological response.

longer duration of injection, use of shared injecting equipment, living in an urban area, history of arrest and more.^{2,18-20} In our study we did not find an association between participant's age or gender to HCV positivity, nor between duration of injection and HCV exposure.

Established risk factors for HCV positivity in the general population in Israel include a history of blood product transfusion before 1990, history of drug use and being an immigrant from the former Soviet Union.^{14,24} In contrast to significantly higher HCV seroprevalence in immigrants from the former Soviet Union in the general population, there was no difference between Israeli-born or immigrants in PWUDs emphasizing the high significance and robustness of HCV transmission in drug users. Indeed, heroin use was the only significant predictor of HCV positivity in this dis-privileged population.

In accordance with results from previous studies,^{21,25} the awareness of study participants to their HCV status was high (72%) with the concordance of 91% between self-reported HCV positivity to laboratory results. Despite a high level of awareness and receiving detailed instruction about the option of getting free anti-HCV treatment including an open invitation to hepatology clinic, only 7% of participants sought treatment. This reluctance to receive treatment is concordant with additional studies.^{21,26,27} The reasons vary and may include fear of treatment side effects, underestimation of hepatitis C impact on the health due to lack of symptoms and misunderstanding of access to treatment steps.^{6,22} Depression and other psychiatric conditions which are associated with injection drug use, pose additional obstacle and significant treatment challenge, and may lead to decreased attention to personal health, including treatment rejection or deferral.²⁸⁻³¹ Discrimination and stigmatization by medical staff toward actively PWUDs may also contribute to low treatment and recovery rates.^{6,22}

The main limitation of our study is its small sample size which may hinder accurate identification of risk factors for HCV infection. In addition, the fact that only 38% of those who approached IATF ambulance was tested may challenge the generalizability of the findings.

As the subjects who refused to be tested, did not fill out questionnaires, qualitative data for them are missing. Our observations suggest that the main reason for approaching the ambulance in subjects who refused testing was need for sterile needles and syringes. Thus, we can conclude that this group possessed the knowledge regarding blood-transmitted diseases and the ways of their prevention and still preferred to avoid HCV testing. We believe that the reasons for not seeking treatment in the subjects who refused undergo testing, may be different from these of tested subjects and may include fear or ambivalence regarding HCV status, unsecure immigration and legal status and mistrust in the medical system.³²

Information based on self-report may be unreliable, particularly when some participants were under illicit substance influence during questionnaire completion (hence were assisted by the IATF staff). In terms of reporting duration of drug use, types of drugs and mode of use, some participants were concerned that they could be identified by name or ID number, resulting in false or partial information being provided (for example, declaring an absence of drug use or marijuana as the primary substance rather than heroin use, respectively).

Conclusions

This study summarizes the results of proactive street HCV testing in the active PWUD population in Israel and demonstrates high HCV frequency and extremely low access to care in this population. Based on our results, awareness of HCV status is a contributing factor but not sufficient to lead to HCV eradication. Given our data, we believe that maximal efforts should be directed at improving understanding of therapeutic side effects, duration and outcomes, with an emphasis on comparison with outdated therapeutic approaches, to reduce stigma and misinformation regarding HCV treatment in individuals aware of HCV status or willing to engage with treatment. Additionally, further research should address the reasons for high level of avoiding HCV testing among this population and the ways to promote adapted and secure access to medical care for these individuals.

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Author Contributions

RL, OS, IB, MN and HK contributed to data acquisition. RL and HK contributed to writing the first draft, analysis of results and article revision. OS contributed to statistical analysis and article revision. AS and OM contributed to the article revision.

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