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Epidemiology of Hepatitis C Virus Infection Among High-risk Populations in Northeastern Iran

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Abstract

Background: Chronic hepatitis C virus (HCV) infection affects 58 million people globally. The frequency of HCV infection in the general Iranian population is less than 0.5%; however, a concentrated epidemic was reported among people who use drugs, particularly those with a history of drug injection.
Objectives: This cross-sectional study was performed to assess the prevalence of HCV infection among high-risk groups outside of prison in northeastern Iran.
Methods: A total of 962 participants in Razavi Khorasan province were enrolled from 2018 to 2022. They included drug users referred to drug treatment and harm reduction centers and individuals with a history of crimes such as drug use or imprisonment who worked in a private industrial unit. Serum anti-HCV antibodies were assessed using a rapid or ELISA kit, and seroreactive samples were confirmed by single-step reverse transcriptase or qualitative real-time polymerase chain reactions. A P-value < 0.05 was considered statistically significant.
Results: The mean age of 707 males and 255 females was 39.8 ± 10.2 years. Anti-HCV antibodies were detected from 129 samples (13.41%), of which 117 were available for polymerase chain reaction testing. HCV RNA was detected in 88 cases (75.2%); the total viremia rate was calculated as 9.26% (88/950). Logistic regression analysis revealed that HCV infection among drug users was significantly associated with older age ($P = 0.002$), being single ($P = 0.009$), and history of drug injection ($P < 0.001$) or incarceration ($P = 0.04$).
Conclusions: The findings showed a considerably high prevalence of HCV infection among people who use drugs in northeastern Iran. To achieve the global goal of viral hepatitis elimination by 2030, we strongly recommend stricter screening and treatment of this infection among such hard-to-access populations in Iran.

Keywords: Hepatitis C, Drug Users, Prevalence, Iran

1. Background

According to the World Health Organization (WHO) estimation, 58 million people are chronically infected with Hepatitis C virus (HCV). Approximately 1.5 million persons are infected with this virus every year, and 290,000 persons die from hepatitis C complications such as cirrhosis and liver cancer (1). The highest HCV infection prevalence has been reported among the general population of the WHO Eastern Mediterranean Region (2.3%) and European Region (1.5%) (2).

Compared to other countries in the Eastern Mediterranean Region and the world, Iran is considered a country with a very low anti-HCV seropositivity (0.3 - 0.6%) among the general population (3, 4). It is assumed that strict HCV screening of donated blood units since 1996, performing harm reduction programs for people who inject drugs (PWID), the early finding of HCV-seropositive individuals, and treatment of the patients with the low-cost generic direct-acting antiviral drugs are the most critical factors associated with the lower rate of this infection in Iran (3). On the other hand, much higher rates of HCV infection were estimated among Iranian populations at intermediate to high risk of exposures such as PWID (41 - 47%) (5-7), prisoners (22 - 28%) (6, 8, 9), hemodialysis patients (11%) (10), people who use but not inject drugs (8%) (6, 7), female sex workers (8%) (6), and homeless children (2%) (11).

Previously, we demonstrated a low HCV infection prevalence (0.4%) among the general population of Mashhad, the capital city of the Razavi Khorasan province, northeastern Iran (12). However, evidence regarding the epidemiology of this infection among the HCV at-risk population is limited in this region. In a recent brief survey, we detected 12.8% of HCV viremia among 390 persons referred to drug treatment centers in Mashhad (13).

2. Objectives

To assess HCV infection prevalence and the related risk factors among high-risk populations, especially people who use drugs (PWUD) outside of prison in northeastern Iran.

3. Methods

In this cross-sectional study, 962 persons in Razavi Khorasan province were recruited from August 2018 to the end of January 2022. They included PWUDs referred to eight drug treatment and harm reduction centers in Mashhad and Gonabad cities, and individuals with a history of crimes such as drug use or imprisonment who worked in a private industrial unit in Mashhad. All these centers were selected based on a non-random sampling method.

The demographic characteristics and risky medical history and behaviors were evaluated. The presence of serum anti-HCV antibodies was assessed using rapid test kits (SD Bioline HCV, South Korea). HCV viral genomes were extracted from seropositive samples (DynaBio, Takapouzist, Iran or RNJia Virus Kit, ROJETechnologies, Iran), and single-step reverse transcriptase or qualitative real-time polymerase chain reactions (Novin Gene, AmitisGen, Iran) was used to confirm the infection. The serum levels of alanine transaminase (ALT) and aspartate transaminase (AST) were measured using an autoanalyzer (Mindray, USA) among HCV RNA-positive samples.

Data were analyzed using chi-square and *t*-test and SPSS Windows software (version 19.0, IBM Corp., Armonk, NY, USA). Besides, logistic regression analysis was used to discover variables that predicted the existence of HCV RNA in the serum samples. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated, and P-values of less than 0.05 was statistically significant.

4. Results

A total of 707 males and 255 females with a mean age of 39.8 $\pm$ 10.2 years were enrolled. Anti-HCV antibodies were detected in 13.41% (129/962, 95% CI 11.26 - 15.56%), of which 117 samples were available for polymerase chain reaction (PCR) testing. HCV viral genome was detected in 88 cases (75.2%); the total HCV viremia rate was calculated as 9.26% (88/950, 95% CI 7.42 - 11.11%). The elevated serum concentrations of the enzymes aspartate transaminase and alanine transaminase (> 40 IU/mL) were identified in 31.33% (26/83) and 48.19% (40/83) of the HCV RNA positive patients, respectively.

The variables associated with HCV infection were evaluated among some people who were referred to the drug treatment centers. At the time of the survey, most responders were employed (61%, 332/544), married (44.9%, 244/544), and illiterate or with an education level of elementary school (45.7%, 236/516). Furthermore, history of imprisonment, tattooing, drug injection, and blood transfusion was declared by 65.42% (314/480), 41.88% (227/542), 17.44% (116/665), and 13.90% (73/525) of responders, respectively. As Table 1 shows, HCV viremia was significantly associated with the older age ($P < 0.001$), male sex ($P = 0.03$), being unemployed ($P = 0.009$) or single ($P < 0.001$), and a history of blood transfusion ($P = 0.003$), tattooing ($P < 0.0001$), drug injection ($P < 0.0001$), and incarceration ($P < 0.0001$). Logistic regression analysis showed that HCV viremia was significantly associated with the older age ($P = 0.002$), being single ($P = 0.009$, OR = 2.50, CI 95%: 1.25 - 4.99), and history of drug injection ($P < 0.001$, OR = 5.05, CI 95%: 2.60 - 9.80) or incarceration ($P = 0.04$, OR = 2.74, CI 95%: 1.04 - 7.19). On the other hand, no significant association was observed between HCV infection and participant's gender ($P = 0.49$, OR = 0.75, CI 95%: 0.33 - 1.71), employment status ($P = 0.49$, OR = 1.27, CI 95%: 0.65 - 2.48), and a history of blood transfusion ($P = 0.20$, OR = 1.70, CI 95%: 0.76 - 3.80), or tattooing ($P = 0.06$, OR = 1.90, CI 95%: 0.99 - 3.67).

5. Discussion

The present study shows that 13.4% of the individuals with a history of drug use in northeastern Iran have serological markers of HCV exposure, 9.3% have detectable HCV RNA, and are currently infected with this virus. Furthermore, the HCV viremia rate among the population with drug injection history (44.0%) was significantly higher than that among those without such a history (6.2%). These proportions are much higher than reported previously for anti-HCV seropositivity and viremia (0.67% and 0.42%, respectively) among the general population in this area (12).

The findings of HCV prevalence among people who use or inject drugs were consistent with the earlier data estimated at the national level in Iran. Malekinejad et al. systematically reviewed 24 eligible reports on the prevalence of HCV infection among drug-dependent people outside of prison in Iran. They estimated that the overall HCV

Table 1. Demographic Characteristics and Risky Medical History or Behaviors Associated with HCV Infection in People Who Were Referred to Drug Treatment Centers in Northeastern Iran [a]

Variables	HCV-Positive	HCV-Negative	Odds Ratio	95% CI	P-Value [b]
Age (y), mean ± SD	45.2 ± 9.8	39.0 ± 10.2	-	-	< 0.001
Gender (n = 912)			1.88	1.06 - 3.34	0.030
Male	72 (10.8)	593 (89.2)			
Female	15 (6.1)	232 (93.9)			
Marital status (n = 534)			-	-	< 0.001
Single	24 (15.2)	134 (84.8)			
Married	22 (9.2)	218 (90.8)			
Divorced/Widowed	38 (27.9)	98 (72.1)			
Education (n = 506)			-	-	0.358
Illiterate	6 (10.0)	54 (90.0)			
Elementary school	30 (17.5)	141 (82.5)			
Secondary school	19 (12.6)	132 (87.4)			
High school/ academic education	15 (12.1)	109 (87.9)			
Employment (n = 534)			0.54	0.34 - 0.86	0.009
Employed	41 (12.6)	284 (87.4)			
Unemployed	44 (21.1)	165 (78.9)			
History of blood transfusion (n = 515)			2.39	1.32 - 4.33	0.003
Yes	19 (27.1)	51 (72.9)			
No	60 (13.5)	385 (86.5)			
History of tattooing (n = 532)			3.5	2.1 - 5.7	< 0.001
Yes	57 (25.8)	164 (74.2)			
No	28 (9.0)	283 (91.0)			
History of drug injection (n = 655)			11.9	7.1 - 19.8	< 0.001
Yes	48 (44.0)	61 (56.0)			
No	34 (6.2)	512 (93.8)			
History of imprisonment (n = 470)			7.1	3.0 - 16.8	< 0.001
Yes	64 (21.1)	240 (78.9)			
No	6 (3.6)	160 (96.4)			

Abbreviation: SD, standard deviation.
[a] Values are expressed as No (%) unless otherwise indicated.
[b] Chi-square test

seropositivity was 8% among persons who reported no history of drug injection and 45% among participants with such a history (7). Another systematic review estimated an HCV prevalence of 16.2% among substance-dependent individuals and 41.3% among PWID in Iran (6). Individuals who use drugs, especially those with a history of injection, are generally considered populations at high risk of HCV exposure. It is expected that using a piece of shared equipment for the injection is associated with a higher risk of HCV acquisition among PWID (5). The higher HCV prevalence rates among non-injecting PWUD might be attributable partly to misclassification of PWID as non-injecting PWUD (14, 15); however, sharing of non-injection equipment as well as other risky behaviors such as tattooing and unsafe sex could be a possible route of the virus transmission in this population (15).

It is estimated that the serological markers of HCV infection are detectable on average in 60% of PWID in the world (16). Furthermore, Scheinmann et al. systematically reviewed 28 published studies and identified that HCV prevalence in self-reported non-injecting PWUD ranged from 2.3 to 35.3%, with a median of 14%. They concluded

that HCV prevalence among this group was larger than in a population who did not use drugs (15). Correspondingly, nearly half of PWID in the Middle East and North Africa have ever been exposed to this virus (17, 18). However, the prevalence rates broadly varied (22–94%) in different countries in this region (18). A high burden of HCV infection has also been estimated in other regions of the world. In Latin America and the Caribbean, pooled regional anti-HCV seropositivity was reported as 49.0% in PWID; however, a much lower rate (3.6%) was estimated in non-injecting PWUD (19). Likewise, a systematic review of 40 reports estimated the high rates of anti-HCV seropositivity in both PWID (67.0%) and non-injecting PWUD (18.3%) in China (20).

The findings suggested that HCV infection prevalence among PWUD with a history of imprisonment was higher than those who did not report such a history (21.1% and 3.6%, respectively). Similarly, recent systematic reviews estimated higher pooled rates of HCV prevalence among PWID who resided some time in prison (52 - 58%) versus those who had no history of incarceration (44 - 45%) (5, 7). On the other hand, we could not find a significant association between HCV infection and tattooing in regression analysis; however, the probability value was close to the statistical significance level. Many researchers in Iran and other countries concluded that unsafe skin-piercing procedures such as tattooing effectively transmit HCV infection. This transmission can occur particularly among HIV-infected individuals, PWID, substance-dependent people who do not report drug injection, prisoners, and even low-risk populations such as the general population and blood donors (4, 21). Behzadifar et al. estimated that prisoners with a history of tattooing had a significantly higher HCV risk than other inmates (OR = 2.6) (8). Likewise, Jafari et al. estimated higher HCV frequency among non-injecting drug-dependent people with a history of tattooing than those without such a history (OR = 5.7) (22).

One of our study limitations is that we assessed the serum levels of liver enzymes only among patients with confirmed HCV infection, and therefore, we could not compare these results between HCV RNA-positive and HCV RNA-negative groups.

5.1. Conclusions

The findings revealed a high prevalence of HCV infection among persons who use drugs in northeastern Iran. To achieve the global goal of viral hepatitis elimination by 2030, we strongly recommend stricter screening and treatment of HCV infection among hard-to-access populations such as drug-dependent people in Iran.

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Footnotes

Authors' Contribution: M. R. H.-M. developed the original idea and the protocol, collected the clinical data, performed the statistical analysis, and drafted and revised the manuscript. M. D. contributed to the development of the protocol and collected the clinical data. H. S. , S. A. V., A. M., M. S. and A. S. collected the clinical data.

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