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HIV, hepatitis C virus, and hepatitis B virus co-infections among injecting drug users in Tehran, Iran

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Summary

Objectives: To assess the prevalence of HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections and co-infections among injecting drug users (IDUs) in Tehran.

Methods: A sample of 899 IDUs (861 male and 38 female) was recruited in Tehran from treatment and harm reduction facilities and from drug user hangouts in public areas in equal proportions. ELISA testing for HIV, HCV antibody (HCV-Ab), hepatitis B surface antigen (HBsAg), and hepatitis B core antibody (HBcAb) was carried out. Positive HIV tests were rechecked by Western blot.

Results: The prevalence of HIV was 10.7%, HCV infection was 34.5%, and past or current HBV infection was 50.7%. Infection with all three viruses was seen in 6.5% (95% confidence interval 4.9–8.2) of participants. HIV/HCV, HIV/HBV, and HBV/HCV co-infections were seen in 8.7%, 7.8%, and 21.0% of participants, respectively. The rate of HCV infection among HIV-positive cases was significantly higher than in HIV-negative IDUs (80.6% vs. 28.7%, $p < 0.0001$). There was no significant association between these infections and co-infections with gender and source of sampling.

Conclusion: In general, co-infection with these three blood-borne viruses is common among IDUs. Since co-infection increases the morbidity and mortality of all infections, the observed level of co-infection in the high number of IDUs in Iran necessitates a serious comprehensive response.

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Introduction

According to the current estimate for the year 2007, 15.9 million people are injecting drug users (IDUs) worldwide.¹ It has also been estimated that 180 000 IDUs live in Iran,¹ which

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is a very conservative estimate. Further, compared to non-injection drug use, it appears that injecting drug use has had a more rapidly increasing prevalence rate during the past decade.²

IDUs make up a population group that shows a high prevalence of blood-borne infections, mainly HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV).³ Co-infection with HIV and HCV has repeatedly been reported among IDUs. There is also evidence of HBV co-infection with other blood-borne infections.^{4,5}

In Iran, the prevalences of HIV, HCV, and HBV infections in the general population have been estimated to be <0.2%,⁶ <1%,⁷ and <5%,⁸ respectively. Iran is a country with a concentrated epidemic of HIV. The current data in Iran indicate that IDUs are the most affected population and have contributed to approximately 67% of identified cases of HIV/AIDS.⁶ Risk behaviors are quite common among IDUs, although different groups of IDUs have different risk profiles.⁹ Surveys have been conducted on various high-risk groups in the country, but so far there has been no study on co-infections with the three important blood-borne infections among IDUs. In addition, the data already available do not give a wide understanding of the epidemiological specifications of these diseases. Iran adopted a harm reduction policy in 2002. Expansion of the harm reduction interventions started after the design of the national five-year program (2002–2007) on harm reduction. In the year 2007, over a six-month period, 1 400 000 needles and syringes were distributed to IDUs through 120 drop-in centers (DICs) and 150 outreach teams. Also, around 22 000 drug users were on opioid substitution treatment in mid-2007.¹⁰ As rapid changes in the prevalence of blood-borne infections can occur among high-risk groups, continuous surveillance and repeated studies are needed to monitor trends and the effects of large-scale harm reduction interventions.

The research reported in this paper is a part of a larger study conducted on the characteristics, risk behaviors, infections and their risk factors, and service use of IDUs in Tehran, the capital city of Iran. We present herein the results of testing for HIV, HCV, HBV, and co-infections in this sample.

Methods

Study design and participants, and data collection

A cross-sectional study was carried out on 904 volunteer current IDUs who were selected from drug treatment centers and from the community during June 2006–March 2007. The study included an interview and blood testing. However, five of the interviewees refused participation in the blood testing. Therefore, 899 IDUs participated in both parts of the study. Drug users who had used drugs by the injection route in the last two months were regarded as current IDUs.

The community sample was selected from five areas of Tehran with high rates of drug-related risk behaviors, with purposive sampling using ethnographic observations in public places, peer referral, and snowballing. The other sample was selected from three drug treatment centers and two DICs located in different well-known areas with high rates of drug-

related risk behaviors in Tehran. The treatment centers provide methadone maintenance treatment (MMT) and DICs provide mainly other types of harm reduction interventions including a needle and syringe program (NSP). Cases were selected based on consecutive admission over the study time period. Apart from the current course of treatment, it was required that the subject should not have been in the same program or any other treatment program during the last six months.

Fieldwork, including interview and blood sampling, was carried out by experienced drug therapists and outreach workers after a short training course, which included training on the questionnaire and the transferring of blood samples to the laboratory.

The use of free-of-charge health services including drug treatment was offered as an incentive. IDUs could also receive the results of their tests on presentation of their code number. For those who received the results of their tests, post-test counseling was also offered.

Testing

Participant blood samples were tested for HIV (anti-HIV Tetra ELISA, Biotest Co., Germany), HCV antibody (HCV-Ab ELISA, DRG Co., Germany), hepatitis B core antibody (Anti-HBc EIA WELL, Radim, Italy), and hepatitis B surface antigen (HBsAg IEMA WELL, Radim, Italy), and also VDRL (venereal disease research laboratory; Immutrep VDRL Antigen, Omega Diagnostic, UK). Positive ELISA tests for HIV were confirmed using a Western blot test (HIV Blot 2.2, MP Biomedicals, France). A positive result either for hepatitis B surface antigen (HBsAg) or for hepatitis B core antibody (HBcAb) was considered as 'past or current HBV infection'. All positive and borderline samples for HBsAg, HBcAb, and HCV antibody (HCV-Ab) were retested by the same method. We excluded samples that showed a repeated borderline result. All tests were done at the Keyvan Laboratory, which is one of the few reference laboratories for Western blot testing authorized by the Ministry of Health.

Ethical issues

The research protocol was approved by the ethics committee of Tehran University of Medical Sciences in Iran. Participation in the study was on a voluntary basis after obtaining informed consent. All efforts were made to guarantee privacy during interviews and confidentiality. A de-linked method for testing was carried out. Instead of a block for the patient's name, each questionnaire had an identification code, which was used for laboratory results as well. For participants recruited from treatment centers, the option of refusing participation in the study or refusing to answer any question was offered, without affecting their service use.

Statistical analysis

Statistical analysis was done using SPSS for windows (version 16.0, 2007; SPSS Inc., Chicago, IL, USA). Univariate analysis using the Chi-square or Fisher's exact tests was done to assess the association between infection status, sex, and source of study sample.

Results

A total of 899 IDUs (861 male and 38 female) participated in the study. Study participant age ranged from 16 to 65 years, with a mean age (\pm standard deviation) of 33.87 (\pm 9.45) years. At the time of interview, more than a third (39.1%) of the respondents were homeless or resided in a room rented on a daily basis, residential community, drug treatment institution, or shelter. Around 64% of participants were unemployed.

The prevalence of HIV was 10.7%, HCV was 34.5%, and past or current HBV was 50.7%. The result of HBV testing was borderline or the sample was insufficient for HBV testing in 35 (3.5%) cases. HBsAg was detected in 30.9% and anti-HBc IgG in 29.1% of 864 cases. We also tested the sample by the VDRL test and found positive results in four (0.5%) of the participants, from whom three were also positive for HBV and one for HCV; none tested positive for HIV.

In 65% of tested participants, at least one of the three viral infections was seen (95% confidence interval (CI) 61.8–68.2) and 6.5% (95% CI 4.9–8.2) of cases were infected with all three viruses. HIV/HCV co-infection was seen in 8.7% (95% CI 6.9–10.6) of participants. HIV/HBV co-infection was seen in 7.8% (95% CI 6–9.6) and finally HBV/HCV co-infection affected 21.0% (95% CI 18.3–23.7) of cases.

The rate of HCV and HBV infections among HIV-positive cases was significantly higher than in HIV-negative IDUs (HCV 80.6% vs. 28.7%, $p < 0.0001$ and HBV 72% vs. 48.4%, $p < 0.0001$). The rate of HIV and HBV infections among HCV-positive cases was significantly higher than in HCV-negative IDUs as well (HIV 25.4% vs. 3.2%, $p < 0.0001$ and HBV 61.4% vs. 45.5%, $p < 0.0001$). Also, the rate of HIV and HCV infections among HBV-positive cases was significantly higher than in HBV-negative IDUs (HIV 15.3% vs. 6.2%, $p < 0.0001$ and HCV 41.3% vs. 27%, $p < 0.0001$). These results are shown in Figures 1–3. All other differences shown in Figures 1–3 are also statistically significant ($p < 0.0001$). Detailed results on the prevalences of the three infections in both sexes, as well as in the community and treatment/DIC samples are shown in Table 1. There was no significant association between these infections and co-infections with gender and source of sampling.

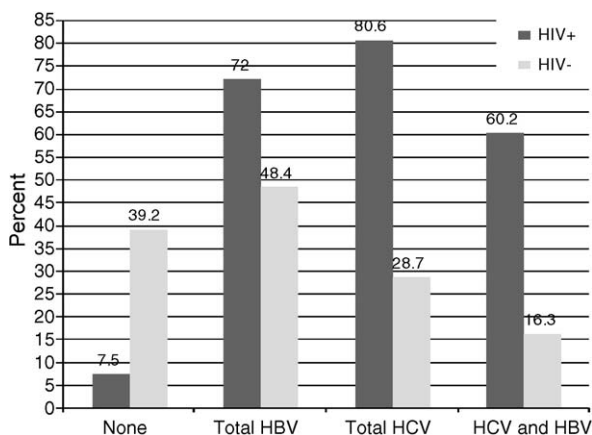


Figure 1 The prevalence of HCV, past or current HBV infections, and co-infections in IDUs by HIV infection status in Tehran (N = 860).

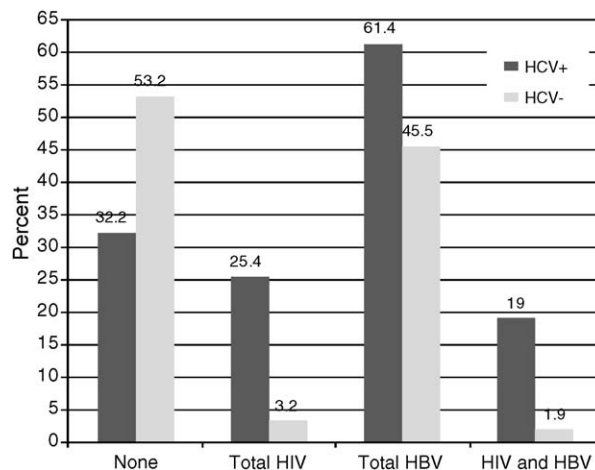


Figure 2 The prevalence of HIV, past or current HBV infections, and co-infections in IDUs by HCV infection status in Tehran (N = 860).

Discussion

A geographical and temporal variability is common in viral infections.¹¹ However, most previous studies on co-infections have been reported from only a few countries. Therefore, information from a variety of IDU populations would be useful in understanding the correlation between these infections, as well as the correlated factors in the transmission of each of them. To the best of our knowledge this study covers a wider spectrum of epidemiologic indicators of blood-borne co-infections among IDUs and has a relatively larger sample size than previous studies; it also presents the results from a developing country where a serious injection drug use problem exists.

Prevalence of HIV, HCV, and HBV infections

Since 1995, various studies on blood-borne infections have been conducted in Iran among IDUs in different cities and different settings, such as IDUs in drug treatment centers, prisons and in communities. The results have ranged from zero to 23.2% for HIV and from 11.2% to 89.5% for hepatitis C infections.^{12–24} Our study, with the highest ever sample size

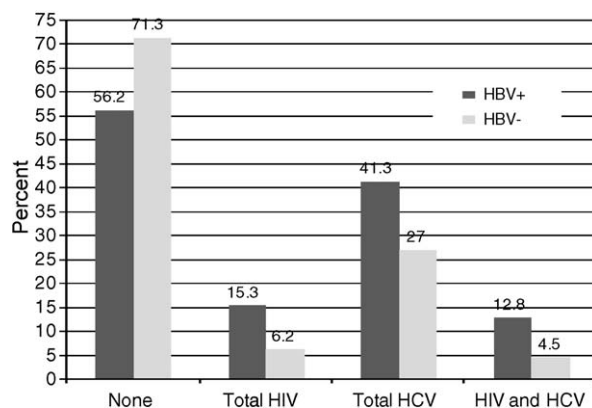


Figure 3 The prevalence of HIV, HCV infections, and co-infections in IDUs by HBV infection status in Tehran (N = 860).

Table 1 The prevalence of HIV, Hepatitis C, past or current Hepatitis B and Syphilis & viral co-infections in IDUs, by sex and source of sampling in Tehran

	Total		Male		Female		Community sample		Treatment/DIC sample	
	Number tested	Positive cases N (%)	Number tested	Positive cases N (%)	Number tested	Positive cases N (%)	Number tested	Positive cases N (%)	Number tested	Positive cases N (%)
HIV	899	96 (10.7)	861	92 (10.7)	38	4 (10.5)	448	52 (11.6)	451	44 (9.8)
HCV	895	309 (34.5)	859	293 (34.1)	36	16 (44.4)	445	160 (36)	450	149 (33.1)
HBV	864	438 (50.7)	827	421 (50.9)	37	17 (45.9)	429	217 (50.6)	435	221 (50.8)
VDRL	887	4 (0.5)	849	3 (0.4)	38	1 (2.6)	443	0 (0)	444	4 (0.9)
HIV/HCV	895	78 (8.7)	859	75 (8.7)	36	3 (8.3)	445	37 (8.3)	450	41 (9.1)
HIV/HBV	864	67 (7.8)	827	64 (7.7)	37	3 (8.1)	429	36 (8.4)	435	31 (7.1)
HCV/HBV	860	181 (21)	825	171 (20.7)	35	10 (28.6)	426	92 (21.6)	434	89 (20.5)
All three viruses	860	56 (6.5)	825	53 (6.4)	35	3 (8.6)	426	27 (6.3)	434	29 (6.7)

for research in Iran, shows relatively lower prevalences of HCV and HIV infections among IDUs compared to those found in studies conducted in recent years in Tehran.^{12,17,21–24} This finding is in line with the decreasing trend in newly identified HIV/AIDS cases by the National Surveillance System,²⁵ and might be a result of the scaling-up of harm reduction interventions including NSP and MMT in Tehran since 2003; this needs further investigation.

Diverse results have been reported on HBV infection in IDUs, perhaps due to the different serum markers used in the different studies. Some studies have reported the results of HBsAg testing and others have used different tests such as HBcAb, hepatitis B e antigen (HBeAg), and even HBV-DNA. Reported rates range from 6%²⁶ to 83.4%,⁴ depending on the markers tested as well as the settings from which the IDUs have been selected. To the best of our knowledge, in all studies reported from Iran so far the only tested marker has been HBsAg, with positive results ranging from 2.9% to 10%^{13,15,22,27} in IDUs, except for one study in which the infection rate in 28 prisoner IDUs was reported to be 25.9%.²⁰ However, the higher rate of past or current HBV infection found in our study necessitates further exploration. It should be noted that the specificity of the utilized tests for HBsAg and HBcAb have been reported to be 99.8% and 99.7%, respectively. An explanation for the high prevalence is that in Iran, in the nationwide health intervention, newborns have only been vaccinated against hepatitis B since 1992, and only 1.2% of IDUs in our sample were able to recall a history of three doses of hepatitis vaccination, on a voluntary basis.

Co-infections and the route of transmission

Hagan et al. have summarized a number of studies on the prevalence of co-infections in IDUs, most of which were on HIV-positive patients in clinical settings. In these samples, the prevalence of HCV infection has been high, at between 52% and 92%. A few other studies have examined HIV prevalence among HCV-positive IDUs and have reported results of from 8% to 50%.¹¹ Our study is consistent with these results, although in the medium to high range of the reported spectrum. A high rate of HCV co-infection (80.6%) among HIV-positive IDUs in our sample is an indicator that HIV is more probably being transmitted via infected injection equipment than by the sexual route. However, as 19.4% of HIV-positive IDUs were negative for HCV, and there is a high degree of

unsafe sex among Iranian IDUs,²⁸ it seems that sexual behavior is also contributing to the HIV epidemic among IDUs. This has been a concern in HIV epidemics among IDUs in other countries as well.^{29–31} However, the test for syphilis showed a very low rate compared to the rates of 1% to 13% among IDUs in other Asian countries,^{32–35} and is compatible with the result (zero from 19 IDUs) of the only study from Iran,¹³ although VDRL alone is not an adequate indicator for sexual transmission of HIV.

There are controversies surrounding the relationship between HBV infection with HIV and HCV infections, as it has been reported from several Asian and African countries,³⁶ as well as from Spain,^{4,5} and in a systematic review from China³⁷ that HBV infection has no significant relationship with HIV and HCV positivity. However, our study showed that HBV infection was significantly associated with HIV and HCV infections. Figure 4 schematically presents the high degree of association between these three infections.

Infections and co-infections among female IDUs

There is evidence that in Iran less than 3% of IDUs are female.³⁸ In our sample, 4.2% of the participants were

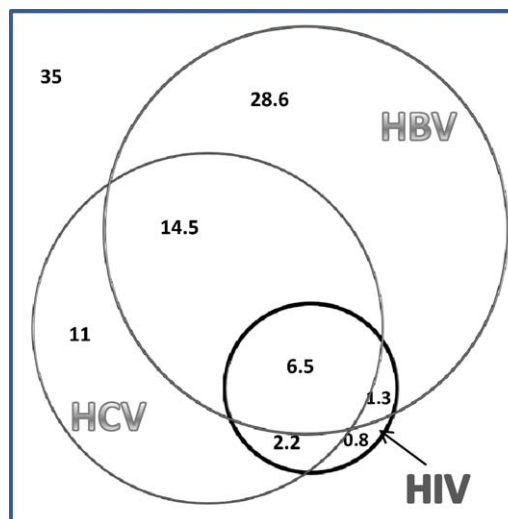


Figure 4 Venn diagram of HIV/HCV/HBV co-infections (%) among IDUs in Tehran, Iran (N = 860).

female. This is the first study in Iran reporting infections and co-infections among 38 female IDUs and comparing the prevalence of infections between male and female IDUs. A few studies have focused on HIV prevalence among female prisoners and found zero prevalence.^{18,39,40} This is why vulnerable groups of women have so far not been considered at high risk for HIV in Iran. However, our study showed no significant difference between the two sexes in infection with the studied viruses or co-infections, and suggests a similar degree of risk for women as for men. It appears that more studies are needed especially on HCV prevalence, which might be higher among female IDUs.

Infections and co-infections among different samples of IDUs

There is little evidence of differences in blood-borne infections and co-infections between community samples and other sources of sampling of IDUs such as treatment centers. Comparisons can only be made for different studies with various sources of sampling. There are various reports on HIV infection in IDUs showing a prevalence of from 0.5% in those receiving treatment and needle and syringes services²⁶ to 43.1% in those recruited from prisons.⁴ In studies from Iran, the lowest rate of zero²⁷ has repeatedly been reported in IDUs recruited from treatment centers in small cities. The highest rate of 23.2%, however, has been reported in IDUs recruited from the community¹² and harm reduction services in metropolitan Tehran.

In studies on HCV infection, the results from other countries also vary according to the source of sampling, from low rates such as 27% in new IDUs recruited from the community⁴¹ to 91.7% in prisoners.⁴ Similar results have been reported from Iran, with an HCV prevalence rate of 11–30% from those recruited from treatment centers^{15,17,27} to 80–90% in prisoner IDUs.^{13,14,17}

In our study, there was no significant difference between the prevalence of infections and co-infections from the community sample compared to the sample from the treatment and harm reduction services. This suggests that the two groups are not separated and have a dynamic interaction and might have a similar nature. Previous experiences and observations show that most drug users including IDUs enter treatment several times in their lifetime, and shift from one setting to another.²⁸

Limitations

This study was conducted in areas of Tehran that have been shown in previous studies to have a higher prevalence of drug-related high-risk behaviors. This selection was made in order to reach a higher number of IDUs and the results might not be representative of the average Iranian urban neighborhood.

Conclusions

In general, co-infection with the three blood-borne viruses (HIV, HBV and HCV) is common among IDUs and they are greatly at risk for all three infections and co-infections. Results of 65% prevalence of at least one of the three infec-

tions and 6.5% of infection with all three viruses show a critical risk profile for IDUs in Iran. Given the fact that co-infection of HIV with hepatitis C and B viruses increases the morbidity and mortality and changes the natural history of all infections, the observed magnitude necessitates a rapid and serious comprehensive response, addressing all infections simultaneously.

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Authors' contributions: EMR and ARM designed the study and were responsible for the overall study management. ESI directed the fieldwork and testing. MAE and ARM prepared the manuscript. All authors contributed to the final version of the manuscript.

Conflict of interest: No conflict of interest to declare.

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