

Co-infection of human immunodeficiency virus, hepatitis C and hepatitis B virus among injection drug users in Drop in centers

Abbasali Javadi, Behrooz Ataei¹, Nazila Kassaian¹, Zary Nokhodian¹, Majid Yaran²

Nosocomial Infection Research Center, ¹Infectious Diseases and Tropical Medicine Research Center, ²Acquired Immunodeficiency Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are the three prevalent viral and bloodborne infections worldwide. Considering the similar route of transmission in these infections, their co-infections would be more challenging for health care professionals. Therefore, we investigated the rate of HIV/HBV/HCV co-infection among injection drug users (IDUs) referred to Drop in centers (DICs). **Materials and Methods:** In this cross-sectional study (2008-2009), IDUs referred to DICs in Isfahan province were evaluated. Venous blood samples were obtained and HBsAg, HBcAb, HCVAb, and HIVAb measured by using enzyme linked immunosorbent assay method. Demographic data and risk factors in patients with HBV/HCV, HIV/HCV, and HIV/HBV co-infections were obtained by a trained social worker using a structured checklist. Data were analyzed using Chi-square test, *t*-test, and multiple logistic regressions. **Results:** Totally, 539 IDUs with mean (standard deviation [SD]) age of 35.3 (7.9) were studied. HBV/HCV, HCV/HIV, and HBV/HIV co-infections were presented in 65 (12.1%), 6 (1.1%), and 0 (0%) of IDUs, respectively. All HIV infected IDUs were infected with HCV as well. There was a significant association between HBV/HCV co-infection and behaviors related to sharing needle (odds ratio [OR] = 2.06, 95% confidence interval [CI]; 1.23-3.45) and imprisonment (OR = 1.01, 95% CI; 1.04-1.06). **Conclusion:** According to the results of this study, history of imprisonment and needle sharing were the only adjusted risk factors for HCV/HBV co-infection in IDUs. This might be a warning for national health system and needs to urgent paying attention. It seems that expanded harm reduction strategies can be useful to reduce this co-infection and its mortality and morbidity rate among IDUs.

Key words: Co-infection, Drop in center, hepatitis B virus, hepatitis C virus, human immunodeficiency virus

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INTRODUCTION

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are the three prevalent viral and bloodborne infections worldwide.^[1] They are considered as important public health concerns due to their related health, social and economic consequences.^[2] Moreover considering the similar route of transmission in these infections, their co-infections would be more challenging for health care professionals.

The prevalence of HBV, HCV, and HIV among Iranian general population have been estimated to be <5%, <1%, and <0.2%, respectively.^[3-5] Iran is a country with low endemicity for HBV and HCV infections and concentrated epidemic for HIV infection.^[5-7] Current evidences indicated that the most common causes of these blood-borne infections in Iran are injection drug use (IDU) and its related high risk behaviors.^[8]

Injection drug users have potential risk for acquiring mentioned infections. They are considered as an

important reservoir for the infections. In addition, there are evidences that HIV, HBV, and HCV co-infections are more prevalent among IDUs.^[9-11]

It is estimated that 11-21 million people are IDUs worldwide.^[12] The rate is estimated to be 260,000 in Iran. Recent studies reported that the rate had more increasing trend in Iran in the past decade.^[13]

Co-infections of mentioned three viral infections are an important issue for the health authorities, because the co-infections are associated with increased risk of disease related morbidity and mortality due to changes in the natural history of each infection, increased risk of progression to severe hepatic injury, and hepatotoxicity due to antiretroviral therapy.^[14]

Several studies have investigated the prevalence of HIV/HBV/HCV co-infection among IDUs and its subgroups in Iran and other countries.^[15-17] In a study in Tehran, the prevalence of HIV/HCV, HIV/HBV, and HBV/HCV co-infections among IDUs was reported to be 8.7%, 7.8%,

Address for correspondence: Dr. Behrooz Ataei, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Science, Isfahan, Iran. E-mail: ataei@med.mui.ac.ir

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and 21.0%, respectively. According to the finding of that study in order to reduce the burden of these blood-borne infections, more comprehensive strategies are needed.^[15]

One of these strategies is harm reduction program which was first introduced in 2002 in Iran. Though the first report, 5 years after initiating of the program, was not satisfactory,^[18] but a recent study indicated its effectiveness in this regard.^[19]

It seems that determining the rate of co-infections would help us for better understanding of the epidemiological specifications of mentioned infections, especially in high risk populations such as IDUs. Considering that IDUs referred to Drop in centers (DICs) are the most available and appropriate population in this field, in the current study we investigated the rate of HIV/HBV/HCV co-infection among this subgroup of IDUs, 10 years after initiation of harm reduction program in Iran.

MATERIALS AND METHODS

In a cross-sectional study from November 2008 to February 2009, IDUs referred to seven health and social care DICs in Isfahan province, four affiliated to Isfahan University of Medical Sciences and three affiliated to welfare organization were evaluated. Included population was selected by simple sampling method.

The protocol of the study was designed and approved by the Institutional Review Board of Isfahan Infectious and Tropical Disease Research Center and Medical Ethics Committee of Isfahan University of Medical Sciences (Research project numbers: 290331, 291073, and 287167). After being informed about the goal and process of the study, written informed consent was obtained from all participants with the assurance that all obtained information would be just for research purposes and would be remained confidential.

The study included an interview and blood testing. The interview was done by an expert and trained social worker who had been working with IDUs, using a structured checklist. The checklist contained demographic data and risk factors for HBV/HCV/HIV infections. The demographic and risk factors of studied blood-borne infections including gender, age, marital status, job, education, surgical history, dentistry history, sex behaviors, history of sharing needle, history of imprisonment, multiple partners, tattooing, cupping, piercing, and transfusion.

A volume of 5 ml venous blood sample was obtained from IDUs and serum samples were transferred to the Isfahan infectious Diseases Research Center laboratory and stored at -20°C for analyzing. Blood samples were tested for HBsAg, HBcAb,

HCVAb, and HIVAb using enzyme linked immunosorbent assay (ELISA) method by DIAPRO kits (Diagnostic Bio probes s.r.l, Italy). Positive HIV ELISA results confirmed by western blot test to exclude false positive results.^[20]

Participants with positive HBsAg and/or positive HBcAb classified as those with current HBV infection.^[21] A positive test for anti-HCV antibodies was defined as past or ongoing HCV infection.^[21] The prevalence of HIV/HCV, HIV/HBV and HCV/HBV co-infections and related risk factors in each group was determined.

Obtained data were analyzed using SPSS version 18 (SPSS Inc., Chicago, IL, U.S.A.) software. Bivariate associations between risk factors and co-infections were assessed by using Chi-square test and *t*-test. Multiple logistic regression was used for the significant variables in the bivariate analysis and it was applied to calculate adjusted odds ratio for risk factors related to co-infections.

RESULTS

In this study, 539 IDUs were studied. Mean age \pm SD of the studied population was 35.3 ± 7.9 . The majority of participants were male (94.8%), Iranian (99.8%), urban population (99.4%) with an education level of junior high school or less (66.1%). 47.9% and 43.6% of them were married and jobless respectively. HBV/HCV, HCV/HIV and HBV/HIV co-infections were identified in 65 (12.1%), 6 (1.1%), and 0 (0%) IDUs, respectively. All HIV infected IDUs were infected with HCV as well.

Demographic characteristics and frequency of studied risk factors of IDUs with HBV/HCV, HCV/HIV co-infections are presented in Table 1. History of cupping ($P = 0.03$), history of having sex with IDUs ($P = 0.02$), history of sharing needle ($P < 0.001$), history of imprisonment ($P < 0.001$), duration of being IDU ($P < 0.001$) and frequency of imprisonment ($P < 0.001$) were significantly higher in IDUs with HBV/HCV co-infection than those without mentioned co-infection. Duration of being IDUs ($P < 0.001$) were significantly higher in IDUs with HCV/HIV co-infection than those without mentioned co-infection.

Multiple logistic regression analysis of potential risk factors for HBV/HCV, HCV/HIV co-infections are presented in Table 2. History of sharing needle and history of imprisonment were the most potent risk factors for HBV/HCV co-infection.

DISCUSSION

In this study, the prevalence of HIV/HCV/HBV co-infections among IDUs attending to DICs in Isfahan province was

studied. The findings indicated that the most common type of co-infection was HBV/HCV co-infection, there was not

any case of HIV/HBV co-infection and all HIV patients were HCV positive also. Behaviors related to unsafe IDU and history of imprisonment was the most important risk factors for HBV/HCV co-infection. Though related risk factors for HIV/HCV co-infection was determined, but considering the lower rate of patients in this group the results were not conclusive.

Table 1: Demographic characteristics and frequency of studied risk factors of injection drug users with HBV/HCV, HCV/HIV co-infections

Demographic characteristics	HBV/HCV	HCV/HIV
	co-infection n = 65 (%)	co-infection n = 6 (%)
Age (year)	35.8±8.5	35.2±8.5
Sex		
Male	62 (95.4)	6 (100)
Female	3 (5.6)	0 (0)
Residence		
Urban	61 (98.4)	6 (100)
Rural	1 (1.6)	0 (0)
Employment status		
Employment	26 (41.9)	2 (33.3)
Unemployment	36 (58.1)	4 (66.7)
Marital status		
Married	33 (50.8)	3 (50)
Single	32 (49.2)	3 (50)
Nationality		
Iranian	65 (100)	6 (100)
Non Iranian	0 (0)	0 (0)
Education		
Junior high school or less	49 (80.3)	3 (50)
High school graduated	10 (16.4)	1 (16.7)
University education	2 (7.3)	2 (33.3)
Risk factors		
Tattooing	41/65 (63.1)	5/6 (83.3)
Cupping	28/65 (43.1)	3/6 (50.0)
Ear piercing	36/65 (55.4)	1/6 (16.7)
Surgery	12/65 (18.5)	5/6 (83.3)
Blood transfusion	60/65 (92.3)	1/6 (16.7)
Dental work	9/63 (14.3)	5/6 (83.3)
Endoscopy	51/65 (91.1)	2/6 (33.3)
Illegal sex	15/60 (25)	2/6 (33.3)
Having sex with IDUs	31/60 (51.7)	0/6 (0)
Sharing needle	56/65 (86.1)	3/3 (50.0)
Imprisonment	53/65 (80.9)	6/6 (100)
Duration of being IDU (mean±SD)	15.6±8.2	15.5±11.5
Frequency of imprisonment (mean±SD)	8.4±7.7	5.2±5.3
Duration of being in prison (months)	56.9±51.7	55.2±73.3

HBV = Hepatitis B virus; HCV = Hepatitis C virus; HIV = Human immunodeficiency virus; IDUs = Injection drug users; SD = Standard deviation

There are some studies which assessed the prevalence of HIV/HCV, HIV/HBV and HBV/HCV co-infection and their related risk factors among IDUs in Iran and worldwide, however studies among different subgroups of IDUs such as those attending to DICs are sparse. We selected this subgroup of IDUs because: First they are considered as the most available group, and second we could evaluate the effect of harm reduction and other intervention in DICs, a decade after initiating in Iran.

In the epidemiological studies, data regarding the co-infection of mentioned three blood-borne infections would be helpful for determining the correlation between these infection and risk factors and transmission route of them. Moreover, evidences indicated that co-infection of HBV and HCV with HIV is important clinically. HIV infection in patients with HBV infection could alter the natural history of the disease. Immune suppression by HIV infection leading to some consequences such as increasing HBV viral load due to decreasing HBsAg clearance, faster progression to cirrhosis, earlier development and aggressive presentation of hepatocellular carcinoma.^[22-24] Similarly, simultaneous infection of HCV infection with HIV is an important public health issue. It could reduce the spontaneous clearance of HCV; increase its viral load which results in severe presentation of the disease and faster progression to liver failure.^[25] On the other hand, some studies revealed that HBV and HCV co-infection with HIV could faster HIV/AIDS progression and its related morbidity and mortality.^[26,27]

Rahimi-Movaghar *et al.*^[15] investigated the HIV/HCV/HBV co-infection among IDUs in Tehran, the prevalence of HIV/HCV, HIV/HBV, and HBV/HCV co-infections was reported to be in 8.7%, 7.8%, and 21.0% respectively.

Table 2: Multiple logistic regressions of potential risk factors for HBV/HCV and HCV/HIV co-infections

Risk factors	HBV/HCV co-infection n = 65			HCV/HIV co-infection n = 6		
	OR	95% CI	P value	OR	95% CI	P value
Cupping	1.16	0.69-1.96	0.56	0.77	0.13-4.32	0.76
Sharing needle	2.06	1.23-3.45	0.006	2.61	0.56-12.16	0.22
Imprisonment	1.01	1.04-1.06	0.000	1.00	0.99-1.02	0.27
Having sex with IDUs	1.16	0.64-2.07	0.61	1.00	0.32-1.86	0.99
Duration of being IDU	1.03	0.99-1.07	0.07	0.67	0.96-1.15	0.23
Frequency of imprisonment	1.00	0.97-1.02	0.915	0.94	0.83-1.05	0.30

OR = Odds ratio; CI = Confidence interval; HBV = Hepatitis B virus; HCV = Hepatitis C virus; HIV = Human immunodeficiency virus; IDUs = Injection drug users; Variables shown in this table are controlled for basic demographic characteristics including age, levels of education, job

In a study in Tehran, SeyedAlinaghi *et al.*^[16] determined the prevalence of HBV/HIV and HCV/HIV prevalence among patients referred to main referral center in Iran. According to their results, the prevalence of HBV/HIV and HCV/HIV co-infection among HIV positive IDUs were higher than other groups of HIV/AIDS patients with a prevalence rate of 61.2% and 85.1%, respectively.

In another study in Tehran, Mir-Nasseri *et al.* have reported that the prevalence of positive HBsAg/HCVAb, HBsAg/HIVAb and HCVAb/HIVAb in IDUs attending to drug rehabilitation centers were 0%, 0% and 1.5%, respectively.^[28]

In a study in India, the co-infection of HIV, HBV and HCV among IDUs attending to the addiction center was investigated. According to their results HIV/HCV/HBV, HBV/HCV and HIV/HCV co-infections were presented in 6%, 4.8%, and 52.4%, respectively.^[17]

In our study, the rates were 1.1%, 0%, and 12.1% for HIV/HCV, HBV/HIV, and HBV/HCV co-infection, respectively. To the best of our knowledge, there are not any baseline data in this field from our studied population before initiation of harm reduction program in Iran for comparing the results.^[19]

Considering the dynamic interaction between community and IDUs, it seems that the prevalence of mentioned co-infections depend on their rates in the community. As we assessed, we have not any reports regarding co-infection of these infection among the general population of Isfahan, but the rate of both HBV and HIV infection in Isfahan have been reported to be lower than other large cities in Iran. Hence, this could be another explanation for obtained results.^[29]

In this study, the most common type of co-infection was HBV/HCV infection. It was similar to other national and international reports.^[23,30,31] The related risk factors are those related to unsafe drug use and imprisonment, which was in line with other studies.^[15]

Considering the similar route of transmission, HCV/HIV co-infection is common according to that reported by several studies.^[32,33] In a review study Hegan *et al.* indicated that the rate of HIV/HCV co-infection is high among IDUs with an estimated rate of 52-92%.^[31] In our study, all HIV positive patients have co-infection with HCV. The results are consistent with other studies in this field both in Iran and other countries.^[34-36]

In our study, all of the HIV infected subjects were HCV infected as well which may be due to the fact that HIV is commonly transmitted by the same route as HCV. It seems that more comprehensive interventional and educational programs are still needed for eliminate the burden of the infections.

There are different reports regarding HBV/HIV co-infection. Though the route of transmission in HBV and HIV is similar, but evidences indicated that the correlation between HBV and HIV infection mainly depends on the characteristics of studied population and mode of transmission. There are controversies in this regard.^[37] Some studies reported an average rate of 10% HBV and HIV co-infection,^[38] whereas others showed no significant relationship between them. In Iran most of the HBV infected patients were HIV negative.^[39,40] In this study, there was not any case of HBV/HIV co-infection. It may be due to the lower prevalence of both HIV and HBV infection among studied group of population. In addition, related risk factors in HBV and HIV patients were not similar (unpublished data).

The limitations of this study were as follows; cross-sectional design of the study, data collection which was based on self-report questionnaire through interview and unsatisfactory results regarding sexual activity due to religious beliefs of the participants.

In sum, the results of this study intend that it is urgent paying attention on needle sharing and imprisonment as risk factors of HCV/HBV co-infection in IDUs. It seems that expanded harm reduction strategies can be useful to reduce this co-infection and its mortality and morbidity rate among IDUs.

AUTHORS' CONTRIBUTION

All authors have contributed in designing and conducting the study. ZN, NK, and MY collected the data and AJ, and BA did the analysis. All authors have assisted in preparation of the first draft of the manuscript or revising it critically for important intellectual content. All authors have read and approved the content of the manuscript and are accountable for all aspects of the work.

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