

Seroprevalence of Hepatitis B Infection and Associated Risk Factors among Drug Users in Drop-in Centers of Isfahan, Iran

Abstract

Background: Scientists perceive drug users (DUs) as a high-risk population for hepatitis B virus (HBV) infection. Effective strategies aiming at the reduction of HBV infection can be depicted when its epidemiological status is clearly defined. The present study provides new insight into associated risk factors of HBV infection and its seroepidemiological status among DUs attending drop-in centers (DICs). **Methods:** This was a cross-sectional study, which was implemented in 7 DICs of Isfahan province. The sample size included 539 participants. Demographic data and risk factors for HBV infection were obtained by a trained social worker using a self-made structured questionnaire. Venous blood sample was obtained and tested for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody, and total hepatitis B core antibody (HBcAb) using enzyme-linked immunosorbent assay. **Results:** Mean age of the participants was 31.76 ± 8.4 years. They were generally male, Iranian, urban, with an education level of high school or less. The prevalence of HBV infection (HBsAg and/or HBcAb) was 18% (88.490). Regression analysis showed that age, bloodletting, and drug injection, being the sexual partner of injecting DU (IDU), as well as frequency and duration of imprisonment positively correlated with HBV infection. **Conclusions:** Drug injection bloodletting, and being the sexual partner of IDU, as well as frequency and duration of imprisonment could be considered as contributing factors in HBV infection.

Keywords: Drug users, hepatitis B, hepatitis B surface antigens, prevalence

Introduction

Drug users (DUs) are considered as one of the paramount and complicated public health problems while United Nations Office on Drug and Crime estimates that about 200 million individuals globally use illicit drugs.^[1-3] In this context, developing countries are facing a rising tide of injecting DUs (IDUs), especially in Iran (260,000 DUs).^[4]

Although dissimilar risk factors exist among different groups of DUs, nevertheless, they share common high-risk behaviors which predispose these vulnerable part of society to viral infections such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV).^[1,5] By comparison with other blood-borne infections, HBV and HCV infections are more common; therefore, World Health Organization highlights DUs in depicting strategies aiming HBV control and prevention.^[6-8]

Epidemiological studies show that about 2 billion individuals have been infected

with HBV worldwide while about 240 million of them are considered as chronic carriers of the virus.^[9] HBV infection is relatively low among Iranian general population (<2%); nevertheless, high-risk behaviors of DUs (such as unsafe injection) lead to further rates of the virus transmission.^[10,11] Therefore, public health policies considering harm reduction programs as well as methadone, buprenorphine, and naltrexone maintenance treatments have been developed in the recent years.^[12] In this context, hundreds of community-based drop-in centers (DICs) have been founded in Iran, which aim to provide DUs with harm reduction services such as needle syringe exchange program, methadone maintenance treatment, and condom provision.^[12]

Different studies have assessed the seroprevalence of HBV infection among DUs.^[11,13,14] A study undertaken in French people who use drugs showed that about 1.4% of them had HBV infection.^[13] However, the prevalence of HBV infection among IDUs living in Tehran is relatively

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high (28%).^[11] Hence, the serological status of individuals attending DICs dramatically ranges. The present study was implemented to determine the markers and risk factors of hepatitis B infection (HBV) in DICs of Isfahan, Iran.

Methods

This cross-sectional study was conducted, in 2015, among DUs attended to seven Isfahan DICs (four of them were affiliated with Isfahan University of Medical Sciences [IUMS], and the remaining were under the supervision of welfare organization). Studied population was selected through convenience sampling method. We had to use the convenience sampling method since the managers of the DICs did not permit us to access to the lists of the DUs due to the ethical issues. Hence, the sampling methods based on probability, such as simple random sampling or systemic random sampling, could not be used.

The study design was approved by Ethics Committee of IUMS (project code: 291073). The study aims and protocols were described for the patients and written informed consent was acquired from them.

The information regarding demographic data (age, sex) and risk factors for HBV infection was collected through a self-made questionnaire. This questionnaire inquired about sexual behaviors as well as occupational, educational, and marital status, bloodletting, getting tattoos, piercing, going to prison, blood transfusion, history of surgical or dentistry operation, and abroad traveling of the infected individuals. Content validity and reliability of the questionnaire were approved by 10 experts and Cronbach's alpha (0.78), respectively. This questionnaire was filled by a trained social worker.

Venous blood samples (5 ml) of DUs were prepared and applied for serum isolation. Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and total hepatitis B core antibody (HBcAb) of the sera were measured through enzyme-linked immunosorbent assay using a commercial kit (DIA. PRO Srl, Milan, Italy).

We recruited all of the cases, who had acute (HBsAg⁺, total HBcAb⁺, IgM HBcAb⁺, and HBsAb⁻) or chronic (HBsAg⁺, total HBcAb⁺, IgM HBcAb⁻, and HBsAb⁺) forms of HBV infection. In addition, those who had past infection and were recovered were recruited (HBsAg⁻, HBsAb⁺, total HBcAb⁺, and IgM HBcAb⁻). Those who were previously vaccinated (HBsAg⁻, HBsAb⁺, total HBcAb⁻, and IgM HBcAb⁻) or never infected (HBsAg⁻, HBsAb⁻, HBcAb⁻, and IgM HBcAb) were excluded.

Statistical analysis

Missing data were corrected through multiple imputations, and sociodemographic variables were descriptively depicted. Categorical variables were presented by frequency and percentage and whereas continuous variables were demonstrated by mean and standard deviation. We applied

univariate logistic regression model to describe potential risk factors and their unadjusted odds ratio (OR) with 95% confidence interval (CI). The potential variables were assessed in univariate analysis. Afterward, the variables having a significant relationship ($P < 0.05$) with the HBV infection were entered in final multivariable logistic regression model. Goodness-of-fit of the final model was assessed through Hosmer–Lemeshow test.

Results

Univariate analysis

In the current study, 539 individuals meeting our inclusion criteria were recruited; however, 49 participants were excluded in our data analysis since they were previously immune against HBV infection. The mean age of the participants was 31.76 ± 8.48 years while their ages varied from 19 to 64. They were generally male (94.7%), Iranian (99.8%), unmarried (52.7%), and lived in urban areas (99.4%). Educational levels of the participants were for the most part senior high school or less (65.1%). The majority of them were employed (57.6%). HBV positive infection was found in 18% of the participants.

Sociodemographic factors

In general, the prevalence of HBV infection significantly increased by age ($P < 0.001$) [Table 1]. To elaborate, the probability of HBV infection rose by 7% for one year increase in the age of the participants. Compared with the first sextile, ORs of HBV infection in the third, fourth, and fifth sextiles were 0.28, 0.19, and 0.15 respectively, and all of these ORs were significant ($P = 0.028$, $P = 0.043$, and $P = 0.002$). However, in comparison with the first sextile, the ORs of second and sixth sextile of HBV infection were not significant. Association of marital and occupational status with HBV infection was not significant ($P = 0.051$, and 0.07 respectively). Neither gender nor place of living significantly correlated with HBV prevalence ($P = 0.86$ and $P = 0.49$ respectively).

Medical-related factors

Prevalence of HBV infection increased by 90% through bloodletting. Not only pulling teeth positively correlated with HBV infection (OR = 2.38, 95% CI: 1.52–4.955) but also endoscopic operation associated with HBV prevalence (OR = 2.16, 95% CI: 1.279–5.341). Association of dental treatment and blood transfusion with HBV infection was not significant ($P = 0.055$, 0.064 and 0.057 respectively). Other medical risk factors, including dental filling, gum surgery, and suture application, did not significantly associate with HBV infection [Table 2] ($P \geq 0.05$).

Factors related to risky behaviors

Number of DUs applied illicit drugs just through inhalation, oral, or injection were 11.9%, 7.1%, and 59.4%, respectively.

Table 1: Univariate analysis showing the association of various sociodemographic factors with hepatitis B virus infection in drug users attended drop-in centers

Characteristics	Number of participants with HBV infection (%)	OR	95%CI	P
Age	N/A	1.07	1.04-1.10	<0.001**
Education level			-	-
Illiterate*	6 (6.8)	1.0	0.179-1.802	0.337
Primary school	26 (29.5)	0.568	0.092-0.870	0.028**
Junior high school	34 (38.6)	0.283	0.038-0.950	0.043
Senior high school	3 (3.5)	0.190	0.047-0.499	0.002**
High school diploma	16 (18.1)	0.153	0.060-1.589	0.159
University degree	3 (3.5)	0.308		
Marital status				
Never married*	38 (43.2)	1.0	-	0.051
Ever married	50 (56.8)	1.59	0.999-2.533	
Employment status			-	-
Employment*	45 (51.1)	1.0		0.07
Unemployment	43 (48.9)	0.652	0.410-1.035	
Gender				
Female*	5 (5.7)	1.0	-	0.862
Male	83 (94.3)	0.915	0.335-2.497	
Residence				
Rural*	1 (1.1)	1.0	-	0.499
Urban	87 (98.9)	0.435	0.039-4.851	

*Reference group. ***P* values indicating significant change. HBV=Hepatitis B virus, OR=Odds ratio, CI=Confidence interval, N/A=Not applicable

There were some DUs, who applied drugs through more than one method: inhalation and injection (7.1%), injection and oral (5.4%), oral and inhalation (2.6%), as well as oral, injection, inhalation (6.1%). Some levels of alcohol abuse were found in 81.6% of the participants.

In comparison with those who were not IDUs, OR of HBV infection in IDUs was three. However, the ORs for inhaled and oral DUs were not significant. Not only HBV infection was more prevalent in needle-sharing DUs (OR = 2.5, *P* < 0.001) but also this infection was more frequently found in individuals being the sexual partners of IDUs (OR = 2.73, *P* < 0.001). By comparison with those who never been kept in prison, individuals having the historical background of imprisonment were more infected with HBV (OR = 3.56, *P* < 0.001). The frequency of sex partners positively correlated with HBV infection. For example, ORs of HBV infection in those who had more than 9 sexual partners compared with participants having fewer (2-9) was 0.5 (*P* = 0.02). The OR of HBV infection in those who had one sexual partner compared with participant having more than 9 sexual partners was 1/3 (*P* = 0.02).

Frequency and duration of imprisonment significantly correlated with HBV prevalence (*P* < 0.001). For example, HBV prevalence in our participants, whose frequency of imprisonment was more than three times, was six times higher than individuals who was not being held in custody. On the other hand, the prevalence of HBV infection rose by 2% for every month of being kept in prison (OR = 1.019,

95% CI: 1.013–1.025). Comparing with non-IDUs, HBV infection increased 2.6 times in IDUs, whose frequency of drug injection (DI) was 30 times per month or further. Prevalence of HBV infection rose by 1.5% for every liter of hard drink use (OR = 1.015, 95% CI: 1.004–1.026, *P* = 0/007). HBV infection positively correlated with duration of drug abuse since HBV infection rose 8% for every year of drug abuse (*P* < 0.001). The relation between HBV infection and tattooing was not significant (*P* = 0.07). Neither body piercing nor different roots of drug abuse correlated with HBV infection [Table 3].

Multivariable analysis

Forward stepwise logistic regression was used to analyze the association of HBV infection with high-risk behaviors, as well as sociodemographic and medical-related factors (inclusion criteria: *P* < 0.05 on univariate analysis). Logistic regression analysis showed that age, drug injection, and being the sexual partner of IDU, as well as the duration of imprisonment positively correlated with HBV infection [Table 4]. According to the logistic regression, the prevalence of HBV infection rose by 7% for one year increase in the age of the participants. HBV infection in participant being sexual partners of IDUs rose by 2.35 times, compared with those who were not. In comparison with those who were not IDUs, OR of HBV infection in IDUs was 2.92. The prevalence of the HBV infection increased by 1.3% for one-month imprisonment. Drug injection was the strongest factor for HBV in the prediction of HBV infection.

Table 2: Univariate analysis showing the association of medical-related factors with hepatitis B virus infection in drug users attended drop-in centers

Characteristics	Number of participants with HBV infection (%)	OR	95% CI	P
Bloodletting				
No*	49 (55.7)	1.0	-	-
Yes	39 (44.3)	1.916	1.195-3.072	0.007**
Surgery				
No*	45 (51.1)	1.0	-	-
Yes	43 (48.9)	0.919	0.579-1.459	0.721
Suture				
No*	18 (20.4)	1.0	-	-
Yes	70 (79.6)	0.809	0.459-1.424	0.462
Therapeutic injection				
No*	31 (35.2)	1.0	-	-
Yes	57 (64.8)	1.521	0.942-2.457	0.086
Tooth pull				
No*	9 (10.2)	1.0	-	-
Yes	79 (89.8)	2.389	1.152-4.955	0.019**
Dental filling				
No*	59 (67.0)	1.0	-	-
Yes	29 (33.0)	0.644	0.396-1.047	0.076
Gum surgery				
No*	87 (98.9)	1.0	-	-
Yes	1 (1.1)	0.374	0.048-2.911	0.347
Endoscopy				
No*	75 (85.2)	1.0	-	-
Yes	13 (14.8)	2.614	1.279-5.341	0.008**
Blood transfusion				
No*	72 (81.8)	1.0	-	-
Yes	16 (18.9)	1.808	0.967-3.380	0.064

*Reference group. **P values indicating significant change. HBV=Hepatitis B virus, OR=Odds ratio, CI=Confidence interval

Discussion

In the current study, the seroprevalence of HBV infection among DUs attended Isfahan DICs was evaluated. According to our results and analysis, 18% of DUs were HBV infected, and it was noteworthy that age, and drug injection, being the sexual partner of IDU, as well as frequency and duration of imprisonment could be considered as contributing factors in HBV infection.

The prevalence of HBV infection in DUs widely differs between various communities. For example, a global systematic review, which was conducted by Nelson *et al.*, reported a various range of HBsAg in IDUs (from 5% to 10%).^[15] As such, HBV prevalence in different parts of Iran was enormously dissimilar. To elaborate, by comparison with IDUs living in Tehran (Iran), the prevalence of HBV infection in IDUs admitted to Razi Hospital (Ahvaz, Iran) was very low (50.7% vs. 3.6%).^[16,17] This discrepancy could be attributable to the age of the participants, HBV vaccination, route of drug administration, application of different methods resulting in various sensitivity and specificity, as well as, the various prevalence of HBV infection in general population, and attendance of IDUs at harm reduction programs implemented in DICs.^[9,18]

The present study showed that age independently correlated with HBV infection. In other words, the likelihood of HBV infection rose by 7% with every year of age increasing [Table 4]. In a different study, which was implemented in three different areas of Brazil, age was assumed as an independent predictive factor for HBV infection. It seems plausible that aging and initiation of sexual activity enhance predisposition towards viral exposure.^[19] In addition, in comparison with adults, children and young participants have faced compulsory vaccination program decreasing the load of infection. That is why majority of epidemiological studies found association between increased age of participants and HBV infection.^[20]

Our research indicated that sexual relation with IDUs predisposed the participants to HBV infection. In fact, by comparison with other participants, the likelihood of HBV infection increased more than two times when the DUs had a history of previous sexual relation with IDUs [Table 4]. Consistently, Alavian *et al.* showed that high-risk sexual behavior put people at risk for HBV infection.^[21]

We found that in comparison to other DUs, the probability of HBV infection increased about three times (2.9) among IDUs [Table 4]. Consistently, Nelson *et al.* documented

Table 3: Univariate analysis showing the association of different behavioral risk factors with hepatitis B virus infection in drug users attended drop-in centers

Characteristics	Number of participants with HBV infection (%)	OR	95% CI	P
Getting tattoos				
No*	34 (38.6)	1.0	-	-
Yes	54 (61.4)	1.542	0.962-2.470	0.072
Body piercing				
No*	73 (82.9)	1.0	-	-
Yes	15 (17.1)	1.153	0.627-2.119	0.647
Alcohol consumption				
No*	19 (21.6)	1.0	-	-
Yes	69 (78.4)	0.806	0.457-1.421	0.456
Casual sex				
No*	39 (44.3)	1.0	-	-
Yes	49 (55.7)	0.988	0.621-1.573	0.961
Previous sexual relationship with IDUS				
No*	63 (71.6)	1.0	-	-
Yes	25 (28.4)	2.731	1.578-4.728	<0.001**
Number of sexual partners				
0	39 (44.3)	0.627	0.366-1.08	0.094
1	5 (5.7)	0.304	0.110-0.840	0.022**
2-9	15 (17.1)	0.457	0.229-0.910	0.026**
>9*	29 (32.9)	1.0	-	-
History of imprisonment				
No*	15 (17.1)	1.0	-	-
Yes	73 (82.9)	3.566	1.977-6.432	<0.001**
Times of imprisonment				<0.001**
0*	15 (17.1)	1.0	-	-
1	9 (10.2)	1.386	0.581-3.310	0.462
2	6 (6.8)	1.555	0.570-4.239	0.389
≥3	58 (65.9)	5.851	3.162-10.828	<0.001**
Duration of imprisonment (months)	N/A	1.019	1.013-1.025	<0.001**
Inhaled drug user				
Yes*	70 (79.6)	1.0	-	-
No	18 (20.4)	0.59	0.337-1.033	0.65
Oral drug user				
No*	74 (84.1)	1.0	-	-
Yes	14 (15.9)	0.629	0.339-1.164	0.14
Injection drug user				
No*	9 (10.2)	1.0	-	-
Yes	79 (89.8)	3.024	1.465-6.243	0.003**
Frequency of drug injection per months				
0*	14 (15.9)	1.0	-	-
30 or less	14 (15.9)	2.000	0.899-4.448	0.089
31-90	34 (38.6)	2.612	1.336-5.108	0.005**
91 or more	26 (29.6)	2.612	1.293-5.277	0.007**
Needle sharing				
No*	53 (60.2)	1.0	-	-
Yes	35 (39.8)	2.500	1.532-4.081	<0.001**

*Reference group. **P values indicating significant change HBV=Hepatitis B virus, OR=Odds ratio, CI=Confidence interval, N/A=Not applicable. IDUS=Injecting drug users

high prevalence IDUs infected by HBV infection. In other words, they showed that 1.2 million individuals, out of

16 million DUs had HBV infection.^[15] Likewise, Matos *et al.* reported a high prevalence of HBV infection in IDUs

Table 4: The final multivariable logistic regression model of risk factors associated with hepatitis B virus infection in drug users attended drop-in centers

Variable	OR	95% CI*	P
Age	1.074	1.043-1.105	<0.001*
Previous sexual relationship with IDUS			
No	-	-	0.006*
Yes	2.358	1.275-4.161	
Injection drug user			
No	-	-	0.008*
Yes	2.925	1.324-6.461	
Duration of imprisonment	1.013	1.007-1.020	<0.001*

*P values indicating significant change. OR=Odds Ratio, CI=Confidence interval, IDUS=Injecting drug users

living in Central-West Region of Brazil.^[22] To elaborate, they showed that, in comparison with non-IDUs, the viral infection was more prevalent in IDUs (2/7% vs. 12/7%).^[22] The higher prevalence of HBV infection could indicate urgent need for more appropriate strategies aiming at reducing HBV infection.^[23]

Our study authenticated that duration of imprisonment associated with HBV infection. Indeed, according to multivariable analysis, the probability of HBV infection rose by 1% for every month of imprisonment [Table 4]. Consistently, Mohamed *et al.* demonstrated that duration of imprisonment being more than 10 years could be considered as a predictive factor for the positive titer of HBV infection.^[24] Moreover, a systematic review article conducted by Dolan *et al.* showed a higher prevalence of HBV infection in prisoners than their surrounding communities living across 196 countries of the world. In Iran, not only duration of imprisonment associated with the prevalence of HBV infection but also the frequency of incarceration correlated with HBV infection. Higher prevalence of HBV infection among prisoners could be attributable to the criminalization of drug use by incarcerated individuals.^[25,26]

Limitations

Cultural and religious beliefs regarding sexual relationship issues were considered as our study limitations. In fact, some of the DUs of DICs did not accept to participate in the study; therefore, the sample size did not thoroughly show the DIC population. The other limitation of this study derives from its cross-sectional nature, so we cannot exactly find the causal inference.

Conclusions

Altogether, drug injection as well as pervious sexual relationship with IDUs, duration of imprisonment, and bloodletting could potentially contribute to high prevalence of HBV infection. Therefore, further measures should be taken to raise the awareness of HBV transmission occurring

among IDUs or their family members. Moreover, the bloodletting centers warrant implementation of standard measures, which could efficiently prevent HBV transmission.

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Conflicts of interest

There are no conflicts of interest.

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