



# Epidemiology and Estimating the Risk Factors for the Transfer of Hepatitis B Virus Using Multivariate Analysis Model: A Retrospective Case-Control Study

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## Abstract

**Background and aims:** Hepatitis B virus (HBV) is one of the important public health diseases in Iran. Therefore, to control the prevalence of the disease, knowledge is required regarding the risk factor of HBV. Accordingly, the aim of this study was to determine the risk factors of HB transmission.

**Methods:** A retrospective case-control study was conducted on the possible risk factors of HBV transmission. To this end, a total of 171 patients with HBV infection and 171 controls from Rasoul-e-Akram hospital were investigated during 2015-2018. All subjects were directly evaluated using a face-to-face questionnaire about demographic aspects. Finally, HBV infection and its risk factors among the subjects were detected using hepatitis B surface antigen test.

**Results:** Overall, 171 HBV patients including 77 (42%) males and 93 (58%) females were evaluated. The mean age of the participants was  $40 \pm 13$  years. Univariate logistic analysis showed that HBV infection in these cases was associated with addiction injection (odds ratio [OR] = 4.08, CI: 1.3-9.57), family history (OR = 4.52, CI: 1.27-10.7), and having a history of blood transfusion (OR = 3.16, CI: 1.52-5.37). There were no significant relationships between the liver function tests, alcohol consumption, the history of dental visits, and HBV participants. In addition, the logistic-regression model proved that patients with a history of HBV-infected parents (At least one of them) and addiction injection were severely subject to HB infection. In other words, there was a significant association between a history of HBV-infected parents and addiction injection and HB infection.

**Conclusion:** In general, HBV infection was strongly related to having a family member infected with hepatitis B, suffering from addiction injection, and having blood injection.

**Keywords:** Epidemiology, Hepatitis B virus, Risk factors, Iran

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Received: 25 Sep. 2018  
Accepted: 4 May 2019  
ePublished: 10 June 2019



## Introduction

Hepatitis B is a kind of globally serious and contagious infection and over two billion people are exposed to its virus.<sup>1</sup> According to reports, up to 5% of the world population (350 million persons) are chronic carriers of this infection.<sup>2</sup> Moreover, patients infected with hepatitis B virus (HBV) can develop cirrhosis, hepatocellular carcinoma (HCC), and other hepatic dysfunctions. About 25% of those infected with HBV are at the risk of mortality due to chronic liver disease or HCC.<sup>3</sup> In addition, up to 1 million people die every year because of some serious consequences such as cirrhosis and HCC and clinical hepatic complications after initial HBV infection.<sup>4</sup>

Over three-quarters of HBV infections occur in Asia, Africa, and the Middle East. Further, Hepatitis B is more common in developing countries such as Iran and other

Middle East countries compared to developed countries.<sup>5</sup>

Although the effect of mass vaccination programs in some countries changed the direction of pattern towards intermediate or low endemicity, Asia and Africa are generally classified as the regions with high endemicity in terms of HBV risk.<sup>5-8</sup> Furthermore, although there is already an effective and safe vaccine for this virus, HBV continues to be a devastating health problem whose new cases are still being reported throughout the world.<sup>9</sup>

The prevalence of HBV is associated with the socio-cultural and economic climate in which Iran is considered as a region with low endemicity.<sup>10</sup> Neonates are exposed to contagious HBV infection vertically from mother or horizontally by means of blood products and body secretions. There are different prevalence rates of HBV infection in various countries.<sup>11</sup> The likelihood of exposure

to HBV infection in the area with a high prevalence rate (8% or more) is about 60%, which mostly occurs in infancy or childhood periods.<sup>12</sup>

According to Adibi et al,<sup>12</sup> mass national vaccination reduces the transmission rate of HBV infection from mothers with positive hepatitis B surface antigen up to 85.7% and it is argued that mass infant vaccination can decrease the risk of HBV infection up to 85% among the community. In developed countries, these infections mainly occur because of sexual relationships and drug injection or occupational exposure.<sup>5</sup> However, in developing countries, the causes of HBV infection transmission are related to household contact, vertical transmission hemodialysis, transmission from surgery, and the organ transplant or blood products.<sup>13</sup>

Given that HBV can be removed, finding the routes of its transmission seems to be one of the health priorities for detecting the risk factors responsible for finding the target population.<sup>14</sup> Identifying the routes of HBV transmission is vital for controlling the disease in any country, especially the regions where the virus is endemic. Moreover, considering Iran as a region of intermediate endemicity for HBV infection, the importance of the program for managing the transmission of this infection becomes further clear when most of the HBV-infected patients are the carriers of this virus in the community.<sup>15</sup>

Therefore, the present study aimed to identify the risk factors of HBV transmission and then compare these risk factors in case and control groups among patients with hepatitis B who referred to Rasoul-e-Akram hospital under the supervision of Iran University of Medical Sciences.

## Materials and Methods

The possible risk factors of hepatitis B transmission were evaluated in the present case-control study. Based on the aim of the study, a number of 170 HBV-infected patients and 170 controls from Rasoul-e-Akram hospital (Iran University of medical sciences) were examined during 2015-2018. All subjects (including 170 cases vs. 170 controls) were homogenized in terms of age, sex, and self-defined ethnicity. The case group including HBV-infected patients referred to gastroenterology and liver clinic in Rasoul-e-Akram hospital from March 2015 to December 2017.

These patients were from the urban and rural areas, which were periodically examined and/or treated in medical service clinics for chronic hepatitis B (i.e., all patients were hepatitis B surface antigen (HBsAg) and anti-HBc IgG positive). Additionally, the control group including hepatic and gastrointestinal patients (HBsAg negative) attended gastroenterology and liver clinic in Rasoul-e-Akram hospital during (March) 2015-(December) 2017. This case-control study evaluated HBV positive individuals who referred to Voluntary Counseling and Testing Center (for HBV) of Rasoul-e-Akram hospital.

The age range of HBV-infected cases was between 18 to 80 years and HBV infection was confirmed by ELISA (Hepanostika HBsAg Uniform 2 Micro Elisa System, Organon Technical and Holland). Positive samples were also rechecked by ELISA method. In addition, the active HBV infection was determined by HB polymerase chain reaction (HBV qualitative, Keyvan Lab, Tehran, Iran). Convenience sampling technique was used to collect the data from HB patients who referred to Rasoul-e-Akram hospital. After informing the patients about the stages and results of the study, informed consent was verbally obtained from the patients.

Then, data were collected using data collecting forms. The research demographic data in this study included gender, age, a history of imprisonment, prenatal transmission, the injection of drugs, blood group, blood and blood product transfusion, high-risk partner, partner with HBV, drug abuse, alcohol consumption, smoking, surgery, liver enzymes (left), fasting blood sugar, triglyceride, and cholesterol.

All subjects were examined for the serological status of HCV and HIV infection by using HCV Ab and HIV Ab levels. The blood samples were tested for HBsAg by ELISA, and then HBsAg seronegative patients were examined for HBs Ab and HBc Ab based on the same technique in Keyvan Laboratory.

The results were statistically described as mean  $\pm$ SD and the range of continuous variables and the frequency and percentage of categorical variables were reported as well. In addition, univariate logistic regression analysis was applied using a chi-square test with an odds ratio (OR) calculated for the risk factors. Similarly, multivariate logistic regression was performed for variables that were found to be significant in univariate analysis. The magnitudes of these associations were estimated as OR with 95% CI. Eventually, data were statistically analyzed using SPSS software, version 22. A *P* value of less than 0.05 was considered statistically significant.

## Results

Generally, 171 HBV-infected patients including 113 (67%) males and 57 females (33%) were diagnosed and enrolled in the present study. The mean age of the subjects was  $40 \pm 13$  years and they were within the age range of 18-77. Further, 151 (88%) cases were married and 82 (48%) of them were unemployed. The blood-type distribution among the subjects included 65 (35%) O, 21 (20%) A+, 15 (14%) A, and 13 (12%) B. Furthermore, HCV Ab was detected in 37 (22%) cases, in which the number of positive tests for males and females was 23 and 14, respectively. Cases and controls were within the same age range and up to 88% of the subjects were married (the ratio of male to female was 2). Additionally, there was a higher HBV positivity among foreign visitors (*P* value < 0.05).

Totally, 171 patients with a negative test for hepatitis B referring to gastroenterology and liver clinic in Rasoul-e-Akram hospital were evaluated in this study (Table 1).

Univariate analysis showed that a history of blood transfusion (OR=3.16, 95% CI: 1.52-5.37), injection addiction (OR=4.08, 95% CI: 1.3-9.57), and parents' history were significantly associated with HBV infection. However, there was no significant difference between HBV cases and controls regarding alcohol consumption, liver function test, fasting blood sugar, triglyceride, cholesterol (Table 2).

The multivariate logistic regression model including all variables was found significant in the univariate analysis in terms of blood transfusion (OR=3.1, 95% CI: 1.8-5.4), parents history (OR=4.76, 95% CI: 1.12-11.9), and addiction injection (OR=4.3, 95% CI: 1.8-9.32). Conversely, no significant difference was observed between case and control groups respecting the other variables in multivariate analysis (Table 3).

The logistic-regression model confirmed a positive correlation between a record of HBV-infected parents and addiction injection with HBV infection. In other words, patients who had parents (At least one of them) with HBV infection and were addicted to injection were highly susceptible to HB infection ( $P$  value <0.05), the details of which are provided in Table 3.

**Table 1.** Distribution of Demographic Characteristics of the Cases and Controls

Factors	Case (n=171)	Control (n=171)	P Value
Age	40±13	40±14	0.098
Gender, No. (%)			0.023
Male	113 (67%)	92 (54%)	
Female	57 (33%)	78 (46%)	
Occupation, No. (%)			0.22
Manual	36 (21%)	42 (24%)	
Military	23 (13%)	18 (11%)	
Unemployed	82 (48%)	74 (44%)	
Blood group, No. (%)			0.4
O	65 (35%)	72 (42%)	
A	32 (19%)	35 (21%)	
B	16 (10%)	19 (12%)	
AB	8 (3%)	7 (3%)	
Vaccination status, No. (%)			0.325
Vaccinated	32 (19%)	42 (24%)	
Non-vaccinated	101 (60%)	98 (58%)	
Smoke			0.092
Positive	92 (54%)	87 (52%)	
Negative	78 (46%)	83 (53%)	
Marital status, No. (%)			0.432
Married	151 (88%)	142 (83%)	
Unmarried	19 (22%)	28 (17%)	
Nationality, No. (%)			0.028
Native	119 (70%)	158 (92%)	
Foreigners	51 (30%)	12 (8%)	

## Discussion

The results demonstrated that injection addiction, having a hepatitis B-infected family member, and a history of blood transfusion factors put a person at the risk of HB infection transmission. All these risk factors should be addressed by public health professionals in order to formulate prevention and control measures. However, since injection addiction was found to be the most significant risk factor associated with HB infection, there is an important factor in controlling the transmission of the virus in this area and thus intervention can be vital in this respect. Overall, 22% of individuals were vaccinated.

Because of the long-term effects of HBV on liver function, the public health burden of this infection is a matter of investigation.<sup>16,17</sup> The worldwide HB carrier rate is reported from 0.1% to 20%.<sup>18</sup> and the Middle East, in particular, has the endemicity and intermediate status with carrier rate ranging from 2% to 7%.<sup>19</sup> It is estimated that over 35% of Iranians have been exposed to HBV and about 3% are the chronic carriers.<sup>20</sup> Based on the results of this study, male gender was predominant in the case group compared to the control group. Other similar studies in Turkey and Egypt reported that male gender was a risk factor in HB infection. In addition, the present outcomes proved that there was a higher HBV positivity among male gender, namely, the ratio of the number of males to that of the females was 2 to 1.

The age range of 15-45 was dominant among the patients. This may be attributed to the incising incidence of the risk factors of HB infection in the final stages of adolescence. This is also related to the allowed age range of blood donation, employment and the childbearing age of the females, which are considered as the three most common sources of HB case detection.

The findings of this research further showed that, in general, 22% of the individuals were vaccinated and the

**Table 2.** Univariate Analysis for HBV Risk Factors

Factors	Case (171)	Control (171)	P Value
History of blood transfusion, No. (%)	32 (18%)	12 (7%)	0.03
History of surgical operation, No. (%)	44 (26%)	31 (18%)	0.09
Injection addiction, No. (%)	38 (23%)	16 (9%)	0.001
History of dental visits, No. (%)	108 (63%)	114 (67%)	0.082
Alcohol consumption, No. (%)	32 (18%)	29 (17%)	0.23
AST (mean ±SD)	56±166	55±164	0.012
ALT (mean ±SD)	60±146	57±145	0.062
FBS (mean ±SD)	92±35	94±35	0.44
Cholesterol (mean ±SD)	93±44	92±45	0.09
HBV participants, No. (%)	16 (9%)	15 (9%)	0.32
Parents history (positive), No. (%)			0.0001
History of mother	81 (48%)	34 (20%)	
History of father	54 (32%)	19 (12%)	

HBV: Hepatitis B virus; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; FBS: Fasting blood sugar; SD: Standard deviation.

**Table 3.** Multivariate Analysis of Hepatitis B Risk Factors

Factors	Case (n=171) Frequency (%)	Control (n=171) Frequency (%)	P-value	OR (CI95%)
Nationality			0.089	2.8 (0.72-6.85)
Native	119 (70%)	158 (92%)		
Foreigners	51 (30%)	12 (8%)		
History of surgical operation	44 (26%)	31 (18%)	0.32	1.4 (0.7-4.1)
Injection addiction	38 (23%)	16 (9%)	0.0001	4.3 (1.8-9.32)
History of dental visits	108 (63%)	114 (67%)	0.23	1.5 (0.75-8.2)
Alcohol consumption	32 (18%)	29 (17%)	0.09	1.02 (0.32-3.80)
History of blood transfusion	32 (18%)	12 (7%)	0.022	3.1 (1.7-5.4)
Family history (positive)			0.012	4.76 (1.12-11.9)
History of mother	81 (48%)	34 (20%)		
History of father	54 (32%)	19 (12%)		

OR: Odds ratio; CI: Confidence interval.

rate of vaccination was 19% and 24% for case and control groups, respectively. This result is in agreement with that of a similar study in Egypt.<sup>21</sup> However, there are considerable variations in transmission mode across geographic areas and among populations.<sup>22</sup> Infections in endemic countries ( $\geq 8\%$  chronic HBV patients) mostly occur prenatally or during childhood through close household contacts.<sup>23</sup> Alternatively, infections in countries with a low HBV prevalence ( $\leq 2\%$  chronic HBV patients) mainly occur in adulthood.<sup>24</sup>

Univariate analysis revealed that, in terms of behavioral risk factors, there was a higher proportion of cases with a parent's history, as well as a history of surgical operation, dental visits, intravenous drug use, and blood transfusion. In Western countries, HBV positivity is attributed to a history of multiple sex partners, male homosexual activity, age, addiction injection, a history of blood transfusion, illicit drug use (IDU) and/or intranasal cocaine use.<sup>25</sup>

This research strongly corroborated IDU as an important way of HBV transmission. Sharing the syringes for IDU is common among Iranian addicted population, which justifies IDU as an independent risk factor. This is consistent with the results of a study conducted in Canada.<sup>26</sup>

Similarly, based on the results, a higher proportion of cases with a history of blood transfusion was observed, which is in agreement with the findings of several previous studies in developing countries.<sup>27,28</sup> Further, the family history of the patients in this study considered as the higher risk factor in comparison with Brazilian patients whereas other risk factors such as smoking and the history of alcohol consumption were higher risk factors among Brazilian patients.<sup>29</sup> According to research in China, the sociodemographic characteristics and HBV-transmission mode were not significantly correlated with the HBV route of transmission.<sup>30</sup>

Furthermore, in another study by Nasir et al sociodemographic variables were not significantly associated with hepatitis B surface antigen positivity, but sharing needles and injecting drugs in prison were found

as the main transmission modes.<sup>31</sup> Moreover, Bani et al reported that the recent history of hospitalization was a risk factor for HBV transmission.<sup>32</sup> Based on the reports of a similar study in Rasoul-e-Akram hospital, the history of surgical operation and dental visits were detected the higher risk factors, which is contrary to the results of the present study.

The logistic regression analysis of cases and controls showed that a family history of HBV infection and injection addiction were two independent risk factors for HB transmission. About 23% of HBV cases suffered addiction injection whereas only 9% of the control subjects had a similar history, thus the difference between the two groups was found to be statistically significant. The other similar studies in Iran and Jordan reported that HB infection was associated with addiction injection.<sup>33, 34</sup> Unlike the previous studies, the findings of this research indicated that a family history of HBV infection and injection addiction were regarded as the higher risk factors. Consequently, some key data may be lost concerning HBV factors. Moreover, the patient's medical records were incomplete because of the retrospective nature of the study, which is considered as another limitation of this study. Despite the above-mentioned limitations, the results of this study may be helpful in identifying the epidemiological surveillance of transmission routes since it produces asymptomatic infections in numerous population.

## Conclusion

HBV infection frequently occurs due to the common route of transmission. In this study, HBV infection was strongly associated with having a family member infected with hepatitis B, addiction injection, and blood injection and injecting drug addiction was the most important risk factor for HBV transmission. Therefore, medical authorities should consider proper attention to mass vaccination against HBV infection in high-risk individuals and attempt to treat HBV infection.

Finally, it is highly recommended to focus on HBV infection, including screening and managing this infection



in order to prepare a clinical guideline.

### Ethical Approval

This study was approved by the Iran National Science Foundation under the ethical number of 90007743.

### Conflict of Interest Disclosures

None.

### Acknowledgments

The authors would like to thank the participants for their contributions.

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**How to cite the article:** Bahardoust M, Mokhtare M, Sarveazad A, Karimi S, Talebi A, Chaharmahali A, Agah S. Epidemiology and estimating the risk factors for the transfer of hepatitis B virus using multivariate analysis model: a retrospective case-control study. *Int J Epidemiol Res*. 2019;6(2):70-75. doi: 10.15171/ijer.2019.13.