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Hepatitis B Prevalence and Risk Factors in Blood Donors in Ghazvin, IR.Iran

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Background and Aims: **This study was done to find out the common routes of transmission of hepatitis B.**
Methods: **We assessed 39598 volunteer blood donors for hepatitis B and C. Risk factors were obtained from 186 patients and 186 healthy donors. Independent risk factors were determined using logistic regression analysis.**
Results: **Prevalence of HBV was 1.08%. Female sex, education level lower than secondary school, being married, and age more than 35 years old, were risk factors in univariate analysis. Logistic regression showed that only duration of marriage, close contact with an HBV infected person, extramarital sexual contact, history of sexually transmitted diseases and high risk jobs were independent risk factors for prediction of hepatitis B infection. Risk factors which were addressed in this study covered 95.7% of the patients.**
Conclusions: **Ghazvin is one of the low prevalent regions for hepatitis B in Iran. Prevalence of hepatitis B is decreasing in comparison with past decades. Horizontal mode is more important than vertical transmission in this region of Iran. Screening programs, education and vaccination, specifically in high risk groups are essential for prevention of new cases.**
Keywords: **HBV, Prevalence, Risk factor, STD**

Introduction

Hepatitis B is one of the most common viral infections worldwide. Hepatitis B carrier rate varies widely from 0.01 % to 20% through the world[(1)]. Over 2 billion of the world's population have been exposed to this virus. About 350 million of these, making 5% of the world's population, are chronic carriers[(2)]. Annually, up to 1 million of this population die due to the consequences of this infection such as cirrhosis and hepatocellular carcinoma (HCC)[(3)]. In the Middle East, the endemicity is intermediate, with a carrier rate of 2% to 7%[(2,4,5)]. It is estimated that over 35% of Iranians have been exposed to HBV and about 3% are chronic carriers[(6)], ranging from 1.07% in Fars Province[(7)] to over 5% in Sistan and Balouchestan[(8)]. Iran is an area of low endemicity for hepatitis B virus (HBV) in the Middle East[(9)]. Areas of high endemicity have the highest death rate due to HCC in comparison with other areas[(10)]. Similar studies suggest that HBV is the most common cause of cirrhosis and HCC in Iran[(11-12)]. Despite the availability of an effective vaccine, HBV still continues to be a major health problem. It is necessary to find the important routes of transmission of hepatitis for prevention of this disease in every country, specifically in endemic regions. The importance of programs to control risk factors becomes clearer when many patients who are infected with hepatitis are asymptomatic[(13)].

In an attempt to identify the risk factors for acquisition of HBV infection, we have surveyed volunteer blood donors in which donors with positive HBsAg were compared with control healthy donors. This study can particularly be of interest as it shows the prevalence of HBV infection among Iranian blood donors.

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mothers, nowadays it seems that we should pay more attention to horizontal way of HBV transmission in Iran.

Controls were selected from the same geographical area in our study and surveyed by the same surveillance system and the same blind interviewers. Anyhow, recall bias was inevitable especially about old exposures.

People with mentioned high-risk occupations, infected spouse, high-risk sexual behavior and STDs, especially individuals with multiple partners need to be trained, screened and vaccinated, if necessary. These measures could prevent the transmission of HBV infection to healthy people.

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Methods and Patients

An analytic cross-sectional study on 39598 volunteer blood donors admitted to Ghazvin Blood Transfusion Center in Iran was carried out from March 2000 to March 2002. For detection of HBV infection, hepatitis B surface antigen (HBsAg) was determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits (Hepanostika HBsAg Uni-Form II microelisa system, Organon Teknika, Holland). Positive samples were rechecked by confirmation tests. For HCV infection, anti-HCV antibody (Ab) was detected using a third-generation ELISA kit (ETI HCV K-3, DiaSorin, Spain). Positive results of anti-HCV Ab were confirmed with the recombinant immunoblot assay (RIBA-3 Chiron, New Jersey, USA). The serum samples were tested for anti-HIV antibody using ELISA kits (Genscreen HIV, Biso Rad, France). By assuming assumption that α equals 0.05, power equals 90%, the probability of being exposed to risk factors in control group equals to 30%, OR equals 2 (odds ratio) and using ratio comparison formula, sample size was calculated to be equal to 186 people in each group. After determining patients [positive for HBsAg but negative for HCV and HIV] and healthy blood donors [negative for HBV, HCV and HIV infection], simple randomization probability sampling was done in each group. Response rate was 85% among all persons who were invited for interview. All samples, who gave informed consent in writing, were then referred for a structured confidential interview consisting of sex, age, martial status and duration, education level, occupation, close contact with an HBV infected person, blood transfusion, gastrointestinal endoscopy, needle stick, extramarital sexual contact, dentist or experimental dental services, family history of hepatitis, smoking, alcohol consumption, non-IV drug use, icterus, tattooing, cupping, imprisonment, malaria, sexually transmitted diseases, minor and/or major surgery, war injury, foreign trip and hospitalization. If exposure time with risk factor was after detecting HBV infection or the person had a negative test at least 6-8 weeks after exposure, this variable was not assumed as a risk factor. Persons with a history of hemodialysis, hemophilia, major thalassemia, transplantation, and IDU (intravenous drug use) were not permitted to donate blood. Mean±SE (standard error), for description of quantitative variables, t-test for comparison of quantitative variables and chi-square test for comparison of categorical variables were used in analysis. Correlation coefficients such as eta, odds ratio, relative risk and their 95% confidence interval (CI) were also calculated to assess the strength of the differences. Wald logistic regression with adjustment for age for determination of the most principle independent risk factors for HBV infection and also for deletion of the confounders was used. Only variables which could significantly change the model chi-square were included in final logistic regression model. Differences or correlations with $P<0.05$ were considered statistically significant. SPSS 11.5 software (SPSS Inc. Chicago, Illinois, USA) was used in analysis. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Results

From 39598 blood donors, 454 persons had positive HBsAg test, out of whom 428 patients were HBsAg positive after confirmatory test. It means that HBV infection prevalence is 1.08 %. Five hundred and seven persons had a positive anti-HCV antibody test according to ELISA method, but it was confirmed with recombinant immunoblot assay only in 100 people. It means that HCV infection prevalence is 0.25% in this population.

Basic characteristics of cases and controls are shown in table 1. Patients were older than controls significantly ($P<0.001$, eta=0.257) (table 1). Female sex was a risk factor [P=0.005, OR=2.4(95% confidence interval (CI): 1.3-4.4)] even after deletion of confounder effect of age [P=.006, OR=2.44(95% CI: 1.29-4.6)]. Marriage was a risk factor [$P<0.001$, OR=3.1(95% CI: 1.9-4.8)] even after deletion of confounder effect of age [P=.014, OR=2(95% CI: 1.15-3.49)]. The ratio of married males to females was the same in both cases and controls. Duration of marriage in patients was significantly more than controls (P=0.002, eta=0.199) (Table 1). Patients had a lower education level in comparison with controls [$P<0.001$, OR=2.5(95% CI: 1.6-3.8)] (Table 1). Education level lower than secondary school was a risk factor

Table 1. Comparison of the basic characteristics of cases and controls.

	Cases (HBsAg positive donors)	Controls (HBsAg negative donors)	Sig.
Age (mean±SE)	36.69±0.82	30.88±0.8	< 0.001
Sex (male %)	80.6	90.0	0.005
Married (%)	79.3	55.9	< 0.001
Duration of marriage (mean±SE)	16.02±0.82	12.12±0.92	0.002
Education level (higher than secondary school %)	14.7	31.5	<0.001

even after deletion of confounder effect of age [P=.002, OR=2.03(95% CI: 1.3-3.2)]. Odds ratio of significant risk factors, without attention to other variables, is shown in table 2.

Table 2. Univariate analysis of significant risk factors.

Risk factor	OR (95% confidence interval)	Sig.
Sex (female/male)	2.4 (1.3-4.4)	0.005
Education level (lower than secondary school/secondary school and higher)	2.5 (1.6-3.8)	<0.001
Married	3.03 (1.9-4.8)	<0.001
Close contact with an HBV infected person	31.1 (7.4-130.3)	<0.001
Endoscopy	3.5 (1.6-7.6)	0.001
Extramarital sexual contact	17.4 (2.3-132.7)	<0.001
Dental services	1.8 (1.1-2.7)	0.009
Family history of hepatitis	12.9 (4.5-36.8)	<0.001
Alcohol consumption	2.4 (1.2-4.6)	0.01
Non-IV addiction	8.3 (1.03-67.2)	0.037
History of icterus	11.6 (1.5-91)	0.003
Tattooing	4.6 (1.5-13.9)	0.003
History of sexual transmitted diseases	8.2 (3.6-18.6)	<0.001
Age (>35 / <35)	2.7 (1.7-4.1)	<0.001
Duration of marriage (>10 / <10)	2.3 (1.3-3.8)	0.002
Jobs (High risk*/others)	1.83 (1.15-2.92)	<0.011

*: The term "high risk" jobs in this study refers to worker, unemployed, driver and barber.

Logistic regression analysis showed that only duration of marriage, close contact with an HBV infected person, extramarital sexual contact, history of sexually transmitted diseases and high risk jobs (simple worker, unemployed, driver and barber) are independent risk factors for prediction of hepatitis B infection. Significant level and odds ratio (with 95% CI) of these variables, with adjustment for age, is shown in table 3. The prevalence of mother's HBV infection was 7 (3.8%) in cases and zero in controls. History of HBV infection in mother multiplies the risk of HBV infection 1.04 (95% CI: 1.01-1.07) significantly (P=0.015).

Table 3. Independent risk factors using logistic regression model.

Risk factors	OR* (95% confidence interval)	Sig.
Duration of marriage	1.0412 (1.0085-1.0749)	0.013
Close contact with an HBV infected person	23.6227 (5.3181-104.9315)	<0.0001
Extramarital sexual contact	10.4611 (1.2758-85.7745)	0.0288
History of sexual transmitted diseases	5.3675 (2.0390-14.1297)	0.0007
High risk jobs	2.1982 (1.1879-4.0679)	0.0121

*: age-adjusted odds ratio

Forty-nine people had no risk factors; however, 8 of them were infected with HBV, which means that only 8 (4.3%) of these patients were not covered by our check list. Among the case group 33 patients (17.8%) had none, 67 patients (36%) had one, 64 patients (34.4%) had two, 20 patients (10.8%) had three, 1 patient (0.5%) had four and 1 patient (0.5%) had all of the five independent risk factors. In control group, these frequencies were 107 (57.9%), 60 (32.4%), 16 (8.6%), 2 (1.1%), 0 and 0, respectively.

Discussion

In 1979, the prevalence of hepatitis B surface antigen in Iran ranged between 2.5% and 7.2% [14]. It decreased to 1.7% in blood donors in 1987 [15]. In general population, this prevalence was 1.7% [4] and 2.49% [16] in 1992 and 1993, respectively. Another study showed that HBV prevalence is 1.07% in blood donors in Shiraz in 2000 [7], and it is 1.08% in present study. Therefore, HBV prevalence has decreased dramatically in Iranian population during the last decade. It is now considerably less than that seen in many developing countries and only slightly higher than that seen in developed countries such as the USA[1]. Improvement of the people's knowledge about HBV risk factors, national vaccination program from 1993 for all neonates, vaccination of high risk groups such as healthcare workers and the introduction of disposable syringes for use in vaccinations, hospitals and clinics might justify this decrease. However, it can be due to the nature of sampling. In most of these studies, blood donors have been the target population. This decrease can be virtual since high risk HBV infection volunteers are not usually permitted to donate blood. Therefore, we would have an underestimation of HBV prevalence in blood donors in comparison with general population.

Sexual transmission is the most important mode of spread of HBV in most developed countries [17]. In our study most of independent risk factors show the importance of sexual transmission. Although sexual transmission of HBV is shown in non-IV addicts [18], some studies have failed to show the relation between high-risk sexual behaviors and HBV [19]. Other studies have expressed that sexual acquisition of HBV is correlated with the duration of the sexual activity and the number of partners [20-

22). In the present study, duration of marriage (especially more that 10 years) was an independent risk factor for HBV infection. IDU is not a risk factor in Yemen (10) unlike Bangladesh (18) and Taiwan (23). Another study in the USA showed that HBV infection was positively associated with older age, longer duration of injection and heroin use (24). IDU was not a risk factor in our study due to recording the exact history before blood donation and not accepting IDUs for donation. However, non-IV addiction was found to be a risk factor.

Sexual contact is a known risk factor for HBV infection in Iran(4) and some other countries(21, 25, 26). A similar study in Iran indicated that the observed direct correlation between being married and HBV infection lost its statistical significance when age was eliminated as a confounding factor (4). The present study corresponds to the latter. Checking couples before marriage is advisable since it can be helpful in decreasing the prevalence of HBV infection.

The main goal in determining high-risk occupations is to implement measures to prevent HBV transmission among these groups. In the present study, those occupations that do not require higher education or level of skill were associated with higher rate of HBV infection. Other authors have also suggested a similar association for STD infection risk (27). It is necessary to evaluate the knowledge, attitude and practice (KAP survey) of workers, unemployed people, drivers and barbers in Iran. Barbers are a high-risk group for HBV infection in Turkey, as well (28). Significant potential factors, which might be related to HBV infection in barbers, are needle pricks or scissor cuts (28). Drivers are a high-risk group as shown in another study in Iran. However, in that study none of the independent variables were associated with being hepatitis B carrier (29). In addition, it seems that being unemployed or worker is a marker of other factors (such as low socioeconomic status) and not in itself a direct risk factor.

Known high-risk occupations such as physicians, dentists, nurses, paramedics and hospital personnel were not revealed as high-risk groups in the present study. It can be due to the sufficient knowledge of our medical personnel about how the virus spreads, acceptable vaccination coverage rate in this group as well as screening of donated blood products and screening of patients before surgery. Low number of cases in these occupations in our sample can be an alternative reason, as well.

The most important risk factors for HBV infection were contact with an infected person in the family (60%) and the work place (46%) in Romania (30). Contact with the infected family member was a risk factor in Thailand (31), as well as the present study. In our country, in addition to the sexual route, lasting contact with infected individuals in the family is an important mode of spread of HBV infection, as well. Hence, we should pay more attention to the education and vaccination of families who have an infected person.

Blood transfusion, hospitalization, surgery (10,32), IDU (24, 33, 34), sexual contact (18, 21, 25, 26) and contact with HBV infected people(30,31) have repeatedly been found by various studies all around the world to be independent risk factors of HBV infection although one study (10) failed to prove that IDU and hospitalization are risk factors. Improvement of knowledge in IDUs and hospital personnel, availability of sterile syringe for IDUs and observing sterility norms by hospital personnel could justify this result.

A cross-sectional study in Bangkok revealed that the family factors associated with HBV infection in children were older parents, low education in parents, low family income per month, low parents' knowledge and attitude about HBV infection and vaccination (35). Low education was a risk factor even after excluding the confounding effect of age in our study and another similar one in Iran (4).

Because there are often a large number of unknown causes regarding viral hepatitis, most of the studies were conducted to identify multiple risk factors for hepatitis (36). In the present study, our results showed that a person with more than three independent risk factors should not be considered as a healthy donor. Therefore, these people should be excluded from donation.

In this low prevalence condition, selecting people based on the presence of each single predictor appears to be an effective strategy for HBV infection screening in the context of the national vaccination program. According to this program, which started in March 1992, only neonates are vaccinated at 0, 45 and 180 days after birth.

HBV is transmitted via both vertical and horizontal routes (37). In this region (Ghazvin) it seems that horizontal route is more important because patients were older and had more HBsAg positive cases in their family in comparison with controls. In addition, predictors revealed by logistic regression show that horizontal route is a vital issue. On the other hand the odds ratio of these predictors is more than relative risk of the HBV infected mother. After focusing on the vertical route for many years, and implementing strategies such as vaccination and hepatitis B immunoglobulin (HBIG) injection to neonates of HBsAg positive

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