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ORIGINAL ARTICLE

Hepatitis B Markers in Isfahan, Central Iran: A Population-Based Study

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Background and Aims: **Hepatitis B is the most frequent cause of chronic hepatitis and cirrhosis in Iran. To establish better preventive strategies, updating data on prevalence rates are needed. This study was conducted to determine the seroprevalence of hepatitis B virus (HBV) in Isfahan province, Central Iran, in 2006.**

Methods: **In a cross-sectional study in 2006, 816 subjects over 6 years old were selected through a systematic multi-stage cluster sampling from 32 urban and 9 rural areas of Isfahan province. Demographic data, HBV risk factors and blood samples were collected and hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb) and hepatitis B core antibody (HBcAb) were measured by enzyme-linked immunosorbent assay (ELISA) method. Chi-square test and Odds Ratio (95% CIs) and multistage logistic regression analysis were used for statistical analysis. A P<0.05 was considered statistically significant.**

Results: **The subjects of this study included 428 females (52.5%) and 388 males (47.5%). Of the 816 participants, 10 (1.3%) were positive for HBsAg, 98 (12.1%) for isolated HBsAb, 22 (2.9%) for isolated HBcAb and 11 (1.3%) for both HBsAb and HBcAb. The HBsAg seropositive rate ranged from 0 in 6-9-year-old to 1.9% in 40-49-year-old age groups. HBsAb and HBcAb were more frequently observed in 6-9-year-old and ≥50-year-old age groups, respectively. No subject vaccinated for HBV was found positive for HBsAg or HBcAb (age group 6-9 years old). According to the status of education, the highest HBcAb positivity rate was in non-educated group (P<0.001). There were no independent risk factors for any of HBV markers.**

Conclusions: **Isfahan province seems to have a low prevalence of HBV infection. However, as low HBcAb and HBsAb prevalence rates were seen in non-vaccinated at-risk age groups, improving the coverage of vaccination for HBV seems necessary.**

Keywords: **Hepatitis B, Epidemiology, Iran, Population Surveillance**

Introduction

Hepatitis B virus (HBV) infection is one of the major global health problems with two billion people infected worldwide, 75% of whom are Asians [(1)].

The main route of HBV transmission is via blood and blood products. Needle-stick injuries in health personnel, hemodialysis, shared needles in drug abusers, dental surgery, receiving blood or blood products, cupping, ear and nose piercing practices, tattooing, sexual contact and contact with body fluid

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or mucosa of HBV carriers (e.g., workers in clinical laboratories) have been associated with increased risk of transmission [2].

The prevalence of HBV infection and the predominant mode of transmission vary greatly depending on the geographical region from 0.1% to 20% in different parts of the world [3]. In areas of high endemicity, most people are infected early in life, and the prevalence of hepatitis B surface antigen (HBsAg) carriage is 8% to 20%. In most areas of the world (East and South Europe, South America, the Middle East, Middle Asia, Japan, and Turkey), HBV infection is of intermediate endemicity with HBsAg carriage rate of 2% to 7%. Areas with low endemicity (0.1% to 2%) include the United States, Canada, Western Europe, New Zealand and Australia, where only a minority of people come into contact with the virus, usually as a result of horizontal transmission among young adults [2, 4, 5].

In epidemiological studies so far conducted in the Islamic Republic of Iran, the prevalence of hepatitis B has been reported from as low as 1.7% in Fars (South of Iran) to as much as over 5% in Sistan and Bluchestan (Southeast of Iran). In Tehran, 3.6% of men and 1.6% of women were reported to be HBsAg positive and antibody to hepatitis B core antigen (anti-HBc Ab) was detected in 37% of this population [6].

To control the disease in the Islamic Republic of Iran, neonatal vaccination was included in expanded program of immunization for all newborns from 1993 onwards. To devise any further measures to control this disease more precise epidemiological information is required. There has been no definitive study about the prevalence rate of hepatitis B in Isfahan province, Central Iran. Therefore, in this study, we determined the prevalence of hepatitis B markers in Isfahan province and its associated risk factors.

Materials and Methods

In a cross-sectional study, 816 subjects over 6 years old of Isfahan province were collected using a multi-stage cluster sampling method in 2006. Twenty subjects were seleted from each of the 41 clusters which were selected proportionately to the population from the nine rural and 32 urban clusters. Then, families in each cluster were selected at random from the provincial health center census list; in the last stage, one person in each age group in a family was selected randomly. There were six age groups of 6-9, 10-19, 20-29, 30-39, 40-49 and ≥50 years old.

The subjects were given detailed information about the study and written informed consent was obtained. A questionnaire including demographic characteristics and exposure history to risk factors of hepatitis B was filled and coded by trained interviewers at the participants' homes. A 5-mL venous blood sample was taken from each subject and transferred to the healthcare centers within three hours. The whole blood samples were centrifuged at 3000 rpm for 15 min; the sera were frozen and transferred to Isfahan Infectious Diseases and Tropical Medicine Research Center by cold chain method and were stored at 70°C until used. All sera were screened for HBsAg using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Dia-Pro, Milan, Italy). Levels of antibodies to hepatitis B surface antigen (HBsAb) were measured through sandwich non-competitive ELISA (Radim, Italy). Hepatitis B core antibody (HBcAb) was also measured by competitive ELISA (Dia-Pro, Milan, Italy).

The study was approved by the regional bioethics committee. The subjects were informed in detail about the study and written consent was obtained from all participants or their parents according to national bioethics codes of practice of research.

Finally, the collected data were coded and analyzed using the Statistical Package for Social Sciences (SPSS®) for Windows® version 13. The maximum likelihood estimates of the odds ratio (OR) and exact corresponding 95% confidence intervals (CI) were calculated for each variable of interest. Bivariate and multivariate associations of seropositivity (as a dichotomous dependent variable) with other independent variables including risk factors and some of demographic data were examined by "enter model" of the logistic regression analysis to control for confounding variables. A $P \leq 0.05$ was considered statistically significant.

Results

The subjects in this study included 428 women (52.5%) and 388 men (47.5%), of whom, 77.7% were from urban and 22.3% from rural areas (Table 1). There were no statistically significant differences in the number of men and women. Of 816 participants, 10 (1.3%) were found positive for HBsAg, only one of whom was aware of having hepatitis. Among the studied subjects, 98 (12.1%) were positive for HBsAb, 22 (2.9%) were positive for HBcAb and 11 (1.3%) were positive for both HBsAb and HBcAb. None of the 6-9-year-old participants i.e. the age group that was covered fully

by neonatal vaccination were found positive for HBsAg or HBcAb; wheras, in this age group, we had the highest seroprevalence rate of HBsAb (48.2%) (Fig. 1). There was significant difference in age groups according to HBsAb and HBcAb levels (P<0.001). The least HBsAb levels were seen in 30-39-year-old and the most HBcAb levels in ≥50-year-old age groups. Moreover, the highest HBcAb positive rate was observed in non-educated persons (P<0.001). Other demographic data had no correlation with hepatitis B markers. Surgery, familial history of hepatitis, curetage, tattooing, and cupping were the main risk factors for developing a positive HBcAb (Table 2). Logistic regression analysis was used to find the independent risk factors. When all risk factors entered in a single model, there was no independent risk factor for hepatitis B markers (Table 3).

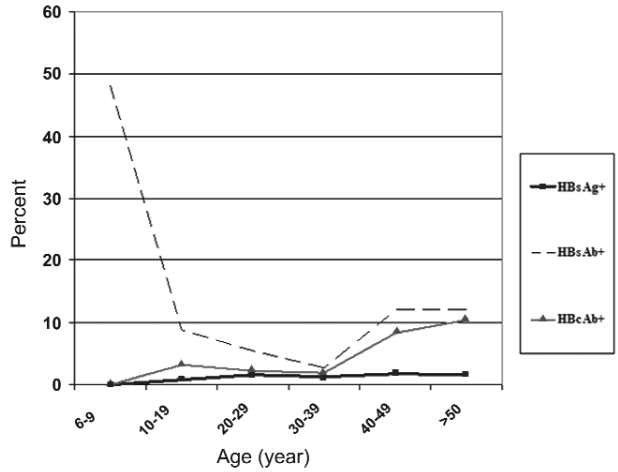

Figure 1. Prevalence of HBV markers in various age groups.

Table 1. Seoprevalence of HBV markers according to demographic characteristics in Isfahan, Iran.

Demographic characteristics		Total population (% of total)	HBsAg positive (% of the row)	HBcAb positive (% of the row)	HBsAb positive (% of the row)
Sex	Female	428 (52.5)	3 (0.7)	17(4)	55 (12)
	Male	388(47.5)	7 (1.8)	17(4.4)	53 (13.7)
Inhabitation	Urban	634(77.7)	9 (1.4)	25 (4)	89 (14)
	Rural	182 (22.3)	1 (0.5)	9 (4.9)	20 (11)
Household number	1-2	85 (10.9)	2 (2.4)	10 (11.7)	8 (9.4)
	3-4	402 (51.6)	5 (1.3)	17 (4.2)	61(15.2)
	5-6	230 (29.6)	2 (0.9)	5 (2.2)	33 (14.3)
	≥7	61 (7.8)	1 (1.6)	2 (3.2)	6 (9.8)
Age groups	6-9	110 (13.9)	0 (0)	0 (0)	53 (48.2)
	10-19	125 (15.8)	1 (0.8)	4 (3.2)	11 (8.8)
	20-29	180 (22.7)	3 (1.7)	4 (2.2)	10 (5.6)
	30-39	145 (18.3)	2 (1.4)	3 (2.1)	4 (3.7)
	40-49	108 (13.6)	2 (1.9)	9 (8.3)	14 (13)
	≥50	124 (15.7)	2 (1.6)	14 (11.3)	16 (13)
Education	None	98 (12.3)	1 (1)	12 (12.2)	15 (15.3)
	Primary	284 (35.5)	2 (0.7)	9 (3.2)	65 (22.9)
	High school	236 (28.9)	1 (0.4)	7 (3)	14 (5.9)
	≥Diploma	180 (22.5)	6 (3.3)	6 (3.3)	14 (7.8)
Marital status	Single	323 (40.2)	2 (0.6)	6 (1.9)	69 (21.3)
	Divorced	27 (3.4)	1 (3.7)	1 (3.7)	1 (3.7)
	Married	454 (56.5)	7 (1.5)	27 (5.9)	38 (8.4)

Discussion

This study demonstrated that the prevalence of hepatitis B in Isfahan province, Central Iran, is low according to definition. Chronic HBV infections in the Middle East countries have an intermediate prevalence of 2%-7% [4]. But, current studies have shown that the prevalence of HBV infection has decreased dramatically in Iran during the last decade; now Iran is classified as having "low prevalence" for hepatitis B infection [7]. Nowadays, in the Middle East, Bahrain, Iran, and Kuwait are areas of low endemicity. Iraq, Jordan, Oman, Palestine, Yemen and Saudi Arabia still seems to be of high endemicity [8]. The minimum rate of hepatitis B prevalence in the region was reported from Kuwait-the HBsAg seropositive rate was 1.5% [9].

In epidemiological studies in Islamic Republic of Iran, the prevalence of HBV infection has been reported in almost 1.7% of general population varying from 1.7% in Fars to over 5% in Sistan and Baluchestan provinces [6]. In Khorassan province, HBsAg+ rate was 2.9% in general population [10]. In a study conducted in 1993 on

Table 2. Risk Estimating for HBV markers.

Variables \ HBV Markers	HBsAg OR (95% CI)	HBcAb OR (95% CI)	HBsAb OR (95% CI)
**Surgery	2.8 (0.7-10.4)	*2.4 (1.2-5)	0.6 (0.4-1)
Transfusion	2.7 (0.5-13.4)	1.8 (0.7-4.8)	1.2 (0.6-2.3)
Transplantation	0.98 (0.98-0.99)	0.86 (0.84-0.89)	0.96 (0.94-0.97)
Familial History of hepatitis	3.38 (0.4-28)	*4.2 (1.3-12.9)	1.4 (0.5-3.8)
Extramarital sexual activity	0.98 (0.97-0.99)	1.57 (0.2-12.4)	0.4 (0.05-3.3)
Curettage	3.1(0.3-27.4)	*3.5 (1.2-9.7)	0.78 (0.3-2)
Dialysis	0.98 (0.98-0.99)	0.96 (0.94-0.97)	2.1 (0.2-21.2)
Dental Procedure	0.5 (0.1-2.2)	1.2 (0.6-2.5)	0.6 (0.4-0.9)
Tattooing	3.2 (0.4-27)	*4 (1.3-12.4)	0.2 (0.02-1.6)
Pearcing (ear, ..)	0.4 (0.1-1.8)	0.9 (0.5-2)	0.9 (0.6-1.4)
Cupping	2.5 (0.3-20.6)	*3 (1-9.1)	0.3 (0.08-1.5)
Drug Addiction	0.9 (0.98-0.99)	0.96 (0.94-0.97)	0.86 (0.84-0.89)
Place of Residance 1= urban 0= rural	2.2 (0.3-18.4)	0.8 (0.4-1.9)	1.3 (0.8-2.2)
Gender 0=female 1= male	2.2 (0.5-8.9)	0.97 (0.48-1.9)	1 (0.6-1.5)
Marrital Status 0=married 1= non married	0.6 (0.1-2.5)	0.28 (0.1-0.7)	*2.6 (1.7-4.1)

*Statistically Significant
** 0= NO 1= Yes

4930 subjects in Hamadan province, 2.49% were carriers of HBsAg; 18.09% were positive for HBsAb and 5.3% found positive for anti-HBc Ab alone [11].

It seems that contamination with HBV in Isfahan province is lower than that reported in limited studies performed in other parts of Iran. Improving public knowledge and practice about HBV risk factors including safe medical and healthcare team, barbers, and hair dresser practices, establishment of national vaccination program for all neonates and vaccination of high-risk groups in recent years could be the cause of this sharp decrease in the prevalence rate of the disease.

Our results also showed that there was no case of HBV infection in the 6-9-year-old age group which confirms that because of the national neonatal vaccination program all instances were protected against the infection effectively.

The HBV vaccination pilot program has started in infants in two provinces of Zanjan and Semnan in 1989. In 1993, the vaccination against HBV has been included in the National Expanded Program on Immunization. In two seroepidemiology surveys in Iran, it was shown that the overall HBV seropositivity rate has had significant decline from 1.3% to 0.8% in the age group of 2-14 years between 1991 and 1999 [12]. The epidemiology of infection is also changing from a vertical to horizontal transmission route and possibly from early childhood to adult age as indicated in current study.

However, in this study HBsAb, as the protective factor against HBV, was isolated from 13.4% of our total samples which most frequently was observed in 6-9 years age group within 48.2% of cases. As HBV vaccination of all newborns has begun 14 years before our study, all of the subjects in this age group have received HBV vaccine; national data showed near 95 percent neonatal vaccination coverage [7]. Why the antibody response in children seems to be inconsistent with our assumption? It could be assumed that antibody titer fall gradually within this age group and possibly some cases did not receive the first dose or the follow-up doses of the vaccine. HBsAb fell into 8.8%, 5.5% and 2.7% in 10-19, 20-29 and 30-39 years age groups, respectively. This may point that although the exposure may be increasing by age, the antibody may drop on time. Therefore, improving the coverage of vaccination seems necessary in all age groups especially in young adults.

Referring figure 1, and table 1, the trend of HBV chronic infection prevalence seems to be somehow constant after childhood, i.e. proportion of HBsAg positive cases of the age groups are similar thereafter. This finding may point to HBV transmission epidemiology in Iran; most of the transmission risk is before adulthood and since the chronicity rate decreases after childhood, the HBsAg positivity ratio does not change significantly. If we try to smooth the cure of HBV exposure (i.e. total sum up of all markers), a twice increase in prevalence is faced after 40 years old. This change in HBV epidemiology may be due to a change in life style and safer health and beauty practices in younger age groups throughout their life span, although this is just an assumption and further in depth analysis of the situation is needed. Other minor fluctuations in the data regarding HBV markers was neither statistically nor epidemiologically significant.

This study also showed that HBV infection and immunity was significantly correlated with the level of education. Health behaviors of educated people including safety percussions in their life style as well as immunization would affect HBV epidemiology in

Table 3. Multivariate Logistic regression of possible risk factors for HBV markers.

Variable	HBsAg		HBcAb		HBsAb	
	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)
Surgery	0.09	0.1 (0.01-1.3)	0.5	0.7 (0.4-1.5)	0.4	0.6 (0.2-1.7)
Transfusion	0.9	2 (0.0-.)	0.08	0.4 (0.1-1.1)	0.46	0.6(0.1-2.4)
Transplantation	1	6 (0.0-.)	1	4 (0.0-.)	1	8(0.0-.)
Familial history of hepatitis	0.9	2 (0.0-.)	0.2	0.1 (0.04-2)	0.07	0.2(0.05-1.1)
Extramarital sexual activity	0.9	1(0.0-.)	0.9	4(0.0-.)	0.9	1(0.0-.)
Curettage	0.6	0.5 (0.4-7.3)	0.6	0.7 (0.2-2.5)	0.06	0.1(0.07-1.1)
Dental procedure	0.4	2 (0.3-19.2)	0.8	2.8 (0.6-5.1)	0.6	1.2(0.4-3.4)
Tattooing	0.07	0.08 (0.007-1.2)	0.8	1.3 (0.1-12.3)	0.06	0.5(0.3-1.2)
Cupping	0.9	2(0.0-.)	0.3	3 (0.3-29)	0.3	0.4(0.01-18.3)
Not- married	0.9	2.8 (0.2-35)	0.08	0.2 (0.05-3)	0.07	2.9(0.8-9.4)
Being male	0.9	1.3 (0.001-1471)	0.9	0.9 (0.1-5.6)	0.09	9.2(0.7-118)

this group; also, the education of the people regarding the infection prevention and transmission especially of groups at risk of hepatitis exposure was reported to be the most cost effective way of infection control [7].

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