

## Intra-familial prevalence of hepatitis B virologic markers in HBsAg positive family members in Nahavand, Iran

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### Abstract

**AIM:** To determine the prevalence of hepatitis B in Nahavand and evaluate the HBsAg positive prevalence in families with a member who was confirmed to have HBV infection.

**METHODS:** This study was performed in two phases. In the first phase, 1 824 subjects in Nahavand city were selected. The interviewers visited the houses of chosen families to fill the questionnaire and take the blood samples. All subjects signed an informed consent before interviews and blood sampling. The samples were evaluated for HBV virologic markers. In the second phase, 115 HBsAg-positive cases were enrolled and evaluated for HBV virologic markers.

**RESULTS:** The prevalence of positive HBsAg in Nahavand was 2.3%. The most frequent relatives of index cases were sons and daughters (32.2% and 23.5% respectively). Twelve (11%) of all family members were HBsAg positive. Fifty (56.2%) were isolated HBsAb positive and only one person (2.5%) was isolated HBcAb positive. The higher rates of HBsAg marker were detected in the brothers (1-25%) and fathers (1-12.5%). The infection rate in husbands and wives of index cases was 10%. Only two (16.7%) of all HBsAg-positive participants reported previous HBV vaccination.

**CONCLUSION:** The prevalence of intra-familial HBV infection is lower in Nahavand of Iran compared to other studies. More attention should be paid to HBV vaccination and risk-lowering activities.

### INTRODUCTION

Middle East countries including Iran have an intermediate prevalence of hepatitis B. In Iran, hepatitis B prevalence is low as 1.07% in Shiraz and as high as 8.96% in Toiserkan<sup>[1]</sup>. There are three main routes of HBV transmission including blood, sexual contacts, and horizontal. In endemic regions of the world such as Africa, Greece, and Hong Kong, vertical transmission from mother to newborn infant and horizontal transmission among children play an important role in intra-familial transmission of HBV. In North America and Western Europe, however, the main route of transmission is intimate sexual contacts<sup>[2-4]</sup>.

A study of general population in Hamadan of Iran<sup>[5]</sup> reported that HBV infection is low in unmarried men and women (18.26%) and high in widows and divorcees (51.59%), suggesting that horizontal transmission is likely to be the primary mode of acquisition of HBV infection in children and young adults. Also, infection is partly transmitted before or soon after birth to babies of HBsAg-carrier mothers. Socio-economic and demographic variables have a greater impact on the prevalence of HBV infection than blood or medical care variables in this population.

In a study in Spain, 848 of family members of 285 HBsAg-positive patients were evaluated and reported that 33.5% of them were positive for at least one HBV virologic marker<sup>[6]</sup>. In the other study in Australia, family members of 145 HBV patients were studied and the results showed that 16% of them were HBsAg positive, and that HBV transmission within families is greater, if the index case has a HBsAg and HBeAg-positive mother rather than a HBeAg-negative one<sup>[7]</sup>.

The city of Nahavand in Hamedan Province (in west of Iran) has always been considered to have high prevalence of hepatitis B without any definitive study. This study aimed to determine the prevalence of hepatitis B in Nahavand and evaluate the HBsAg positive prevalence in families with a member who was confirmed to have HBV infection.

## MATERIALS AND METHODS

This cross-sectional study was conducted during a 2-mo period (February-March 2003) in people aged 6 years and over in the city of Nahavand, located in the western part of Iran with a population of 72 000. In Nahavand there are 5 health care centers and 1 health site, and 304 participations were randomly selected from each of them.

This research was carried out in two phases. First, we studied the prevalence of hepatitis B in population of Nahavand (2002) and after identifying the HBsAg-positive cases, all of their families were enrolled into the second phase. The population less than 5 years old was not included in our study because blood sampling was difficult.

A questionnaire including demographic data, marital status and history of vaccination was developed. After taking the approval of health authorities of the city and city council, the educational sessions for data collection teams and directors of health care centers were held to train them on the details of interviewing, questionnaire filling, and blood sampling. Demographic data on eligible families were obtained from 1999 health registry.

The selected families were contacted at their residence. The family members older than 5 years were interviewed and informed consent was obtained. For those under 15 the parents also signed the consent forms. The questionnaires were filled by interviewers, who also took blood samples. The blood samples were sent to the laboratory of research center for gastro-enterology and liver disease, Shaheed Beheshti University of Medical Sciences at the end of each day. The virologic markers of hepatitis B were assessed.

After revealing HBsAg-positive cases, we collected demographic data of their families. The selected families were contacted at their residence and given description of the second phase by the interviewers. After signing the consent forms by the family members, the interviewers took blood samples and sent them to the laboratory (as above mentioned). All the virologic markers of hepatitis B were assessed.

It should be explained that HBsAg detection was carried out by Diasorin kit with lot no. 0370790/1A through sandwiched

ELISA. HBsAb and HBcAb levels were measured by Diasorin kit with lot no. 9230320/A through sandwiched non-competitive ELISA and Diasorin kit with lot no. 8540480/1B through competitive ELISA, respectively. All data were fed into an access data bank. SPSS version 11 was used for the analysis of data.

## RESULTS

Of all subjects, 85 (4.6%) did not participate in study, 1 005 (55.1%) were married. The mean family population was  $4.8 \pm 1.9$ , the smallest family had 1 member while biggest family had 13 members. The prevalence of HBsAg-positive cases in Nahavand was 2.3%. The hepatitis B serologic markers in the study subjects are shown in Table 1.

One hundred and fifteen family members including 8 (7%) mothers, 8 (7%) fathers, 11 (9.6%) sisters, 4 (3.5%) brothers, 27 (23.5%) daughters, and 37 (32.2%) sons, 10 (8.7%) husbands, and 10 (8.7%) wives were enrolled. Seventy-one (61.7%) of them were married.

In the participants, 23 (20.2%) had the education of literacy, 19 (16.7%) diploma and 15 (13.2%) higher than diploma, 33 (28.9%) were students and 26 (22.8%) were housekeepers. Twelve (11%) of all family members were HBsAg positive. Fifty (56.2%) were isolated HBsAb positive and only one person (2.5%) was isolated HBcAb positive.

Table 2 shows the relevance of HBV virologic markers to the index case. Higher rates of HBsAg marker were detected in the brothers (1-25%) and fathers (1-12.5%). The prevalence of HBsAg-positive cases in sons and daughters was identical (1.1%). The infection rate in husbands and wives was 10%.

The most frequent relatives with HBsAb positive were husbands and wives (5-71.4%) and then daughters (17-70.8%). There was no positive HBsAb in fathers. Only one person (son) was HBcAb positive.

It should be mentioned that the HBsAg-positive family members were evaluated for HBeAg and HBeAb and all of them were HBeAg negative and HBeAb positive. Also

**Table 1** Frequency distribution of hepatitis B serologic markers in participants

	HBsAg positive	Isolated HBcAb positive	Isolated HBsAb positive	HBcAb and HBsAb positive
Number (%)	42 (2.3)	143 (7.84)	212 (11.62)	217 (11.9)
Sex (male%)	54.8	44.1	41.5	53.9
Age (mean $\pm$ SD)	40.2 $\pm$ 18	55.2 $\pm$ 16	37.3 $\pm$ 22	52.8 $\pm$ 17
Marriage (%)	66.7	71.3	51.4	80.2

**Table 2** Frequency distribution of hepatitis B virologic markers in family members of index cases, n (%)

	HBsAg positive	Isolated HBsAb positive	Isolated HBcAb positive
Mother	0 (0)	2/8 (25)	0 (0)
Father	1/8 (12.5)	0 (0)	0 (0)
Sister	1/8 (10)	5/8 (62.5)	0 (0)
Brother	1/4 (25)	1/4 (25)	0 (0)
Daughter	3/27 (1.1)	17/27 (63)	0 (0)
Son	4/37 (1.1)	15/37 (40.5)	1/37 (2.7)
Husband	1/10 (10)	5/10 (50)	0 (0)
Wife	1/10 (10)	5/10 (50)	0 (0)

they had normal liver function test.

Only 2 (16.7%) of the HBsAg-positive participants reported previous HBV vaccination, while 23 (46.9%) of the subjects with isolated HBsAb had previous HBV vaccination.

## DISCUSSION

Among the 115 family members studied, sons and daughters were the most frequent relatives. We had some limitations in categorizing the data for discussion, because the number of positive HBsAg cases in children was low (three daughters and four sons). Sex proportion was identical in HBsAg-positive cases and others. Single participants were about twice of married ones. The most frequent level of education of family members was illiteracy and the most frequent occupations were students and housekeepers. The population less than 5 years old was not included in our study because blood sampling was difficult. This can underestimate the true frequency of hepatitis B in our population.

The mean age of HBsAg-positive cases was  $40.2 \pm 18$  years. The phenomenon of e-seroconversion in this age group may be responsible for the low transmission rate of HBV in our study in comparison to some other regions because marriage age during recent years has increased in Iran. There is no population-based study about genotypes of HBV in Iran. In a limited study, genotype D is found to be the most common genotype in patients with chronic hepatitis B<sup>[8]</sup>.

In overall, 11% of family members were HBsAg positive. There are different studies about HBV intra-familial transmission in the world that in the strongest ones, phylogenetic sequence analysis and amino-acid variation of the HBV core gene were performed. It is obvious that this way is the only way to confirm HBV intra-familial transmission, but due to lack of sufficient resources in present study, this procedure was not possible<sup>[8-10]</sup>.

In a study in 2002 in Italy<sup>[9]</sup>, 49 individuals from 13 families with sibling clusters of positive HBsAg carriers are investigated, HBV isolates are genotyped following amplification of the surface gene region of the viral genome, thus providing convincing evidence that viral isolates within a family originate from the same source. It was reported that the prevalence of HBsAg is significantly higher in family members than in the control group ( $P < 0.001$ )<sup>[10]</sup>. A study in South Korea also reported that among 71 non-vaccinated HBsAg carriers, 10 are positive for HBsAg (14.1%), but none of the controls is positive for HBsAg<sup>[11]</sup>. In a study in Spain, among 330 relatives of 145 HBsAg carriers observed over a mean period of 20.1 mo, 284 were positive for at least one HBV marker<sup>[6]</sup>. It was reported that relatives of 26 positive HBsAg cases present an intra-familial prevalence of HBV infection of 28.8%<sup>[12]</sup>. In other countries, variable results have been reported<sup>[13-18]</sup>.

In this study, the highest prevalence of HBsAg was in the fathers and sons, and infection rate in the husbands and wives was identical. A Turkey study showed that the husbands had a higher rate of HBsAg than wives (70.0% *vs* 21.9%,  $P < 0.01$ )<sup>[10]</sup>. The high prevalence of HBsAg infection among spouses may be due to sexual transmission in menstrual period in other countries. In Iran, because of cultural and

religious aspects, this way of intra-familial transmission has a low prevalence. HBV transmission within families is greater, if they have a HBsAg positive mother rather than a HBsAg positive father<sup>[6]</sup>. The current results show that most of the family members are not vaccinated for HBV infection, so the necessity of HBV vaccination in HBsAg-positive family members must be considered. It has been shown that only half of the isolated HBsAb-positive persons have a history of HBV vaccination. Some people might have insufficient information about vaccines. Coexistence of HBsAg and hepatitis B surface antibody (anti-HBs) has been reported in approximately 24% of HBsAg-positive individuals<sup>[19]</sup> and low level of HBsAg in some of our people with isolated positive HBsAb may describe the above finding. We think that repeat testing for HBeAb in people with isolated positive HBsAb during a long time of follow-up may be helpful.

In conclusion, the prevalence of intra-familial HBV infection is low in Nahavand of Iran. More attention should be paid to HBV vaccination and risk-lowering activities.

## REFERENCES

- 1 **Zali MR**, Mohammad K, Farhadi A, Masjedi MR, Zargar A, Nowroozi A. Epidemiology of hepatitis B in the Islamic Republic of Iran. *East Mediterr Health J* 1996; **2**: 290-298
- 2 **Yeoh EK**. Hepatitis B virus infection in children. *Vaccine* 1990; **8** (Suppl): S29-S30
- 3 **Werner GT**, Frosner GG, Fresenius K. Prevalence of serological hepatitis A and B markers in a rural area of northern Zaire. *Am J Trop Med Hyg* 1985; **34**: 620-624
- 4 **Lionis C**, Frangoulis E, Koulentakis M, Biziagos E, Kouroumalis E. Prevalence of hepatitis A, B, and C markers in school children of a rural area of Crete, Greece. *Eur J Epidemiol* 1997; **13**: 417-420
- 5 **Amini S**, Mahmoodi MF, Andalibi S, Solati AA. Seroepidemiology of hepatitis B, delta and human immunodeficiency virus infections in Hamadan province, Iran: a population based study. *J Trop Med Hyg* 1993; **96**: 277-287
- 6 **Porres JC**, Carreno V, Bartolome J, Gutierrez J, Castillo I. A dynamic study of the intra-familial spread of hepatitis B virus infection: relation with the viral replication. *J Med Virol* 1989; **28**: 237-242
- 7 **Williams SJ**, Craig PI, Liddle C, Batey RG, Farrell GC. Hepatitis B in Australia: determinants of intrafamily spread. *Aust N Z J Med* 1987; **17**: 220-227
- 8 **Amini-Bavil-Olyaei S**, Sarrami-Forooshani R, Mahboudi F, Sabahi F, Adeli A, Noorinayer B, Azizi M, Reza Zali M. Genotype characterization and phylogenetic analysis of hepatitis B virus isolates from Iranian patients. *J Med Virol* 2005; **75**: 227-234
- 9 **Zampino R**, Lobello S, Chiaramonte M, Venturi-Pasini C, Dumpis U, Thursz M, Karayiannis P. Intra-familial transmission of hepatitis B virus in Italy: phylogenetic sequence analysis and amino-acid variation of the core gene. *J Hepatol* 2002; **36**: 248-253
- 10 **Erol S**, Ozkurt Z, Ertek M, Tasyaran MA. Intrafamilial transmission of hepatitis B virus in the eastern Anatolian region of Turkey. *Eur J Gastroenterol Hepatol* 2003; **15**: 345-349
- 11 **Kim YS**, Ahn YO, Kim DW. Familial clustering of hepatitis B and C viruses in Korea. *J Korean Med Sci* 1994; **9**: 444-449
- 12 **Aristegui J**, Perez A, Cisterna R, Suarez D, Delgado A. Characteristics of intra-familial transmission of the hepatitis B virus: a case load contribution and review of the literature [in Spanish]. *Enferm Infecc Microbiol Clin* 1989; **7**: 18-22
- 13 **Ordog K**, Szendroi A, Szarka K, Kugler Z, Csire M, Kapusinszky B, Xie J, Cszizmadia K, Brojnas J, Rusvai E, Tempfli A, Berencsi G. Perinatal and intrafamily transmis-

- sion of hepatitis B virus in three generations of a low-prevalence population. *J Med Virol* 2003; **70**: 194-204
- 14 **Pastore G**, Dentico P, Angarano G, Lapedota E, Schiraldi O. Infectivity markers in HBsAg chronic carriers and intrafamilial spread of hepatitis B virus infection. *Hepatogastroenterology* 1981; **28**: 20-22
- 15 **Thakur V**, Guptan RC, Malhotra V, Basir SF, Sarin SK. Prevalence of hepatitis B infection within family contacts of chronic liver disease patients-does HBeAg positivity really matter? *J Assoc Physicians India* 2002; **50**: 1386-1394
- 16 **Craxi A**, Tine F, Vinci M, Almasio P, Camma C, Garofalo G, Pagliaro L. Transmission of hepatitis B and hepatitis delta viruses in the households of chronic hepatitis B surface antigen carriers: a regression analysis of indicators of risk. *Am J Epidemiol* 1991; **134**: 641-650
- 17 **Dhorje SP**, Pavri KM, Prasad SR, Sehgal A, Phule DM. Horizontal transmission of hepatitis B virus infection in household contacts, Pune, India. *J Med Virol* 1985; **16**: 183-189
- 18 **Abdool Karim SS**, Thejpal R, Coovadia HM. Household clustering and intra-household transmission patterns of hepatitis B virus infection in South Africa. *Int J Epidemiol* 1991; **20**: 495-503
- 19 **Tsang TK**, Blei AT, O'Reilly DJ, Decker R. Clinical significance of concurrent hepatitis B surface antigen and antibody positivity. *Dig Dis Sci* 1986; **31**: 620-624

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