Epidemiology of Hepatitis B Virus Infection among Family Members of Chronic Carriers in Israel

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Abstract

Background: Hepatitis B is a major problem worldwide. Israel has intermediate endemicity for hepatitis B virus, and an annual carrier rate of 1–3%.

Objective: To evaluate both the prevalence of HBV infection among family members of HBV carriers and the competence of family practitioners in performing a comprehensive assessment.

Methods: A total of 152 HB surface antigen-positive blood donors were discovered in our subdistrict during the years 1993–97. Their family physicians were questioned regarding the patients' family members. Specific information on 85 spouses and 200 children was also obtained.

Results: Among the 85 married carriers, 5 of the spouses (5.9%) were found to be HBsAg positive. None of the 200 children was HBsAg positive. We found that in a third (n = 52) of the patients, the sexual partner had never been tested by a primary care physician. Patients were not routinely tested for HB e antigen or anti-HBe antibodies. Neither the parents nor the siblings had undergone any serological evaluation. However, most family members of the carriers had received an HBV vaccine from their family physicians.

Conclusions: Our findings show that horizontal transmission of HBV among spouses of HBV carriers still exists. We did not find any vertical transmission, probably due to male predominance and previous vaccination. Family physicians should be trained to perform an extensive serological evaluation of family members of patients with chronic HBV infection, including parents and siblings, and should vaccinate sero-negative family members.

Hepatitis B infection is one of the most common diseases in the

world. The virus has infected more than 40% of the world

population, and 350 million worldwide (two-thirds Asian) are

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chronic carriers of the virus. A quarter of the carriers will have a severe devastating liver disease, such as cirrhosis and hepatocellular carcinoma [1]. Two million HBV carriers die every year due to disease complications [2].

In Israel the prevalence of HBV infection is intermediate (1– 3%), with an estimated 80,000 carriers [3,4] and a variable rate among different ethnic groups. The Arab population is one of the ethnic groups with the highest rate of HBV infection in Israel. Nashef et al. [5] found a 47% rate of previous HBV infection among adult Arabs aged 30–50 years in Jerusalem. The rate of HBV carriers among pregnant Arab women was found to be 4.3% in one study [4] and 4.48% in another [6]. A variable rate of HBV infection was also found in different ethnic Israeli groups, whether living in urban or rural settlements [7].

Most cases of infection in Europe and North America occur during puberty and are attributed to sexual contact or belonging to a high risk population. In contrast, in Africa and the Middle East, infection is usually acquired in early childhood, either vertically from a carrier mother or horizontally from a family member carrier [4]. Children of HbeAg-positive mothers have a high risk of HBV infection (90%); 90% of them will become chronic carriers, of whom 25% will die from chronic liver disease in adulthood [8].

Since 1992, HBV vaccination is performed in every neonate in Israel. Efficacious vaccination is surprisingly successful in decreasing the rate of neonatal infection, even in children whose mothers are HBeAg positive. Although most neonates are vaccinated, there is still a possibility of horizontal transmission, as well as vertical transmission from the era prior to universal vaccination.

The aims of the present study were twofold: to evaluate the rate of transmission of HBV infection in families of asymptomatic HBV carriers, and to assess the competency of the family physician in confronting the problem by testing and vaccinating the entire family.

Patients and Methods

Population and study group

The population of the Hadera subdistrict numbers about 280,000 people of various ethnic origin, with Jews comprising

HBV = hepatitis B virus

HBsAg = hepatitis B surface antigen

HBeAg = hepatitis B e antigen

55% and Arabs 45%. About a third of the Jewish population are recent immigrants from the former USSR, mainly Asian republics.

All blood donors who were inhabitants of the subdistrict during the years 1993–97 were included in the study. The study design was a descriptive prevalence study.

The central blood bank in Israel reports all cases of HbsAgpositive donors to the relevant district health office. Using this information, the addresses and telephone numbers of all family physicians and subjects were obtained. All family physicians of the HbsAg-positive blood donors were interviewed regarding the patient's serological status, liver function tests, a possible source of infection, and the family's serological status, if known. Similar questions were posed to the patients. Further information was obtained from medical files by family physicians and the study team. All subjects were interviewed following informed consent to the study.

Data analysis

Demographic and laboratory data were collected using EXCEL 5 worksheets and then analyzed in SPSS for windows 5.0. Categorical variables were assessed by the chi-square test. Assessment of rate by ordinary variable was done using chi-square test for trend. The ANOVA test was used to compare means. Multivariate analysis was performed using logistic regression.

Results

During the years 1993–97 a total of 5,984 people in the district donated blood. Of these, 152 (2.54%) were found to be HBsAg positive. Their mean age was 37.1 ± 9.9 years, median age 36 years (range 20–63). The age distribution is demonstrated in Figure I. Patients' characteristics are presented in Table 1. Five of 80 known spouses were found to be HBsAg positive. None of the 200 offspring whose sera were sampled was HBsAg positive. Family details are presented in Table 2. The sera of most of the spouses and offspring were checked; however neither siblings nor parents were evaluated, nor were their sera checked.

Discussion

The pattern of HBV transmission varies in different parts of the world. In countries of high endemicity (e.g., South East Asia) the mode of transmission is mainly vertical and is acquired near birth [1–3]; in areas of intermediate endemicity most infections occur during childhood, while in countries of low endemicity transmission is horizontal and is acquired in adulthood through sexual transmission or drug abuse.

Given the high rate of sequelae and the 60–90% chronicity rate of neonatal infections in Israel, early childhood vaccination is considered an ideal and cost-effective option for preventive medicine [7]. Although Israel has a low endemicity of HBV infection and a low rate of early childhood transmission, universal

Table 1. General characteristics of HBV carriers

Gender	136 (89.5%) males	16 (10.5%) females
Religion	91 (59.2%) Jews	61 (40.13%) Arabs
Length of stay	39 (25.7%) new immigrants	113 (74.3%) Israeli born
Marital status	85 (55.9%) married	67 (44%) single
Liver function tests	150 (98.7%) normal	2 (1.3%) abnormal
HBeAg	150 (98.7%) negative	2 (1.3%) positive
Anti-HCV	148 (97.4%) negative	4 (2.6%)positive

 Table 2. Familial serological status

Relatives	HBsAg+	HbsAg-	Unknown/irrelevant
Spouses	5	80	67
Offspring	0	200	68

early childhood vaccination is recommended to prevent sequelae and chronicity, which are more common in childhood [7]. The Israeli HBV vaccination policy – which is similar to programs in the USA, West Europe, and South East Asia - is a universal immunization program that begins at birth. However, while our previous report [9] found the efficacy of this program to be optimal even in high risk patients in Israel, no other study has evaluated the rate of vertical and horizontal transmission among family members of HBV carriers in Israel. Two previous reports found a similar rate of HBV infection among family members of pregnant women with HBV infection [4,6]. The 6.25% rate of infected spouses is low, although significant, and is comparable to previous reports [10-14] showing higher secondary attack rates in spouses of acutely or chronically infected people than in other household contacts. The seropositivity of one spouse was significantly correlated with the seropositivity of the other, suggesting a role for heterosexual transmission of HBV infection [15]. Others concluded that horizontal, non-parenteral transmission of HBV among siblings plays a major role in infecting the household of HBsAg carriers in an area of intermediate endemicity [16].

The introduction of an immunization program to most western countries and to some third world countries, along with checking blood derivates for the virus, caused a decline in the incidence of new cases of HBV infection. However, such a



Figure 1. Age distribution of HbsAg-positive blood donors

decline was not detected in heterosexual transmission, including among spouses [17].

Although the present study demonstrated that family physicians routinely evaluated the seropositivity of spouses and offspring, none of the 47 community doctors accurately estimated the significance of diagnosing the serological status of the siblings and parents of these HBV carriers. In the light of these findings we recommend that a full epidemiological screening include not only spouses and siblings, but also parents and siblings, and that family physicians be trained to screen all family members of HBV carriers.

References

- 1. Alter MJ, Mast EE. The epidemiology of viral hepatitis in the United States. *Gastroenterol Clin North Am* 1994;23(3):437–56.
- Kane M. Global programme for control of Hepatitis B infection. *Vaccine* 1995;13(Suppl):s47–9.
- Bar-Shany S, Green MS, Slepon R, Gilon E. Ethnic differences in the prevalence of hepatitis B surface antigen among Israeli blood donors: changes between 1972 and 1988. *Int J Epidemiol* 1991;20(1):271–5.
- Bogomolski-Yahalom V, Granot E, Linder N, Adler R, Korman S, Manny N, Tur-Kaspa R, Shouval D. Prevalence of HBsAg carriers in a native and immigrant pregnant population in Israel and passive/active vaccination against HBV of newborns at risk. *J Med Virol* 1991;34:217–22.
- Nashef L, Thalji A. Hepatitis B serology among the Palestinian population. Ann Trop Paediatr 1992;12(3):321–5.
- Issacsohn M, Halevy J, Eidelman AI, Rudensky B, Tadmor OP. Prevalence of HBsAg carriers in pregnant women in Jerusalem: risk for horizontal transmission to family members. *Isr J Med Sci* 1994;30:368–70.
- Zamir D, Zamir C, Weiner P. Vaccination for HAV infection an update. *Harefuah* 1998;135:114–18 (Hebrew).
- 8. Lachaux A, Lapillone A, Bouvier R, Martin MH, Blanc JF, Descos B,

Raudrant D, Trepo C, Hermier M. Transplacental transmission of hepatitis B virus: a familial case. *Pediatr Infect Dis J* 1995; 4:60–3.

- Zamir C, Dagan R, Zamir D, Rishpon S, Fraser D, Rimon N. Evaluation of screening for hepatitis B surface antigen during pregnancy necessary in a population with a high prevalence of HBsAg positive/HbeAg-negative carriers. *Pediatr Infect Dis J* 1999;18:262–6.
- 10. Mosley JW. Epidemiology of viral hepatitis: an overview. *Am J Med Sci* 1975;270:253–70.
- Perrillo RP, Gelb L, Campbell C, Wellinghoff FR, Overby L, Aach BD. Hepatitis B e antigen, DNA polymerase activity, and infection of household contacts with hepatitis B virus. *Gastroenterology* 1979;76:1319–25.
- Koff RS, Slavin MM, Connelly JD, Rosen DR. Contagiousness of acute hepatitis B: secondary attack rates in household contacts. *Gastroenterology* 1977;72:297–300.
- 13. Redeker AG, Mosley JW, Gocke DJ, McKee AP, Pollack W. Hepatitis B immune globulin as a prophylactic measure for spouses exposed to acute type B hepatitis. *N Engl J Med* 1975;293:1055–9.
- 14. Cruz M, Dieguez A, Fos E, Hierro F. Epidemiologic survey on hepatitis B in Gypsy women. *Eur J Epidemiol* 1988£4:314–17.
- Goh KT, Kong KH, Heng BH, Oon CJ. Seroepidemiology of hepatitis B virus infection in a Gurkha community in Singapore. J Med Virol 1993£41:146–9.
- 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 risk. *Am J Epidemiol* 1991;134:641–50.
- Ferraz ML, Yoradjian A, Barbieri A, Figueirredo V, Lopes N, Cruz CN, Silva AE. Epidemiology of acute hepatitis B in a university hospital in Sao Paulo, Brazil: retrospective study of two five-year periods. *Rev Paul Med* 1998;116:1695–9.

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