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AGE – SPECIFIC SEROPREVALENCE OF HEPATITIS B VIRUS INFECTION*

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In this study, we have tried to determine the age-specific seroprevalence of hepatitis B virus (HBV) infection and to make some conclusions about the mode of transmission and vaccination strategy which should be chosen in Turkey.

Eight hundred and one patients between the ages of six months and 60 years of age were included in this study. According to the HBV serologic markers, (HBsAg, Anti-HBc and Anti-HBs), HBsAg positivity and HBV exposure rates were 6.5% and 32.8%, respectively. HBsAg positivity was 6.6% under one year of age. The highest rate of HBsAg positivity was in the 6-10 year age-group ($p < 0.05$). The prevalence of total hepatitis B virus seropositivity increased with age ($p < 0.05$). The HBV exposure rate was higher in males than in females ($p < 0.05$).

It was concluded that HBV infection is an important infection in Turkey and is acquired very early in life. A mass hepatitis B vaccination strategy should thus be chosen in Turkey.
Key words: seroepidemiology, hepatitis B virus, horizontal transmission, hepatitis B vaccination.

Hepatitis B virus (HBV) infection, with its chronic sequelae of cirrhosis of the liver and hepatocellular carcinoma (HCC), constitutes a major health problem in countries where HBV is hyperendemic[1]. Studies among Turkish adults have established the high prevalence of HBV infection in the general population and the significant contribution by HBV to acute viral hepatitis and chronic liver disease[2,3]. The positivity rates of hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs) are reported to differ by region in Turkey (1.7-13.9% and 26.2-68.8%, respectively)[2,3].

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The availability of safe and efficacious vaccines has led to the feasibility of effective control of HBV infection, especially in areas of high prevalence where most chronic HBV carriers acquire the infection very early in life[4-6]. The immunization strategy for preventing HBV infection may vary from country to country depending on: HBV endemicity; predominant modes of infection (i.e., sexual, vertical perinatal, early horizontal, needle sharing during drug abuse, etc.); age of infection; and health-care resources. An appropriate strategy for preventing HBV infection must be determined by large series seroepidemiologic studies.

Age-specific seroepidemiology of HBV infection gives some clues about the routes of transmission. Therefore, we can make some conclusions about the most cost-effective way of preventing this infection. Studies of this type have been few in Turkey. This study aimed to determine age-specific seroepidemiology of HBV infection and discuss which mode of prevention should be chosen in Turkey.

Material and Methods

Eight hundred and one patients were included in this study, which was carried out between October and December of 1993. The patients' ages ranged from six months to 60 years. The reason for choosing children older than six months was to minimize the possibility of passive immunization of infants from mothers who were previously exposed to HBV infection. Persons included in this study were matched according to the following age groups: six months to five years, 6-10 years, 11-15 years, 16-20 years, 21-25 years, 26-30 years, 31-35 years, 36-40 years and older than 40 years of age. Children who were less than ten years of age were also matched according to the following age groups: six months to one year, 2-3 years, 4-5 years, 6-7 years and 8-10 years of age. The distribution of the age groups and their characteristics are shown in Table I.

Table I: Characteristics of Studied Population

Age Groups (Years)	Number	%	Female (%)	Male (%)
1/2-1	30	3.7	16 (53.3)	14 (46.7)
2-3	32	4	14 (43.8)	18 (56.2)
4-5	29	3.6	13 (44.8)	18 (55.2)
6-7	57	7.1	29 (50.9)	28 (49.1)
8-10	61	7.6	36 (59)	25 (41)
11-15	52	6.5	29 (55.8)	23 (44.2)
16-20	64	8	29 (45.3)	35 (54.7)
21-25	130	16.2	26 (20)	104 (80)
26-30	140	17.5	28 (12.9)	112 (87.1)
31-35	74	9.3	9 (12.2)	65 (87.8)
36-40	49	6.1	5 (10.2)	44 (89.8)
≥ 41	83	10.4	27 (33.7)	56 (66.3)

Patients less than 20 and older than 40 years of age had applied to Bakırköy Maternity and Children's Hospital outpatient clinics for any reason except liver disease, and none had received transfusion of blood or blood products. Patients in the 21-40 years age-group were blood donors who came to the same hospital, and all of them were healthy and non-professional donors. There were more males than females (540 vs. 261) in our study because of a greater number of male blood donors.

Specimens of approximately five ml of blood were taken from all patients. Sera were separated by centrifugation and stored at -30 °C until tested within 15 days. Hepatitis B serologic markers (HBsAg, anti-HBc and anti-HBs) were investigated by ELISA. Using commercially available kits of Pasteur Diagnostics (Pasteur Institute, France).

Chi-square test was used to compare proportions. Statistical analysis was performed by StatView software. A p value of < 0.05 was considered significant.

Results

Among 801 persons studied, the prevalence of HBsAg was 6.5 percent (52/801). The HBV exposure rate was 32.8 percent (264/801) (Table II). As shown

Table II: Seroprevalence of Hepatitis B Virus in Studied Population

	HBsAg		Anti-HBc[a]		Anti-HBs[b]		Anti-HBc/ Anti-HBs		Seropositive[‡]		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Sex											
Male	34	6.3	36	6.7	24	4.4	98	18.1	192	35.6	540
Female	18	6.9	14	5.4	8	3.1	32	12.3	72	27.6	261
Age (Years)											
≤ 1	2	6.6	2	6.6	0		0		4	13.3	30
2-3	1	3.1	2	6.3	0		1	3.1	4	12.5	32
4-5	0		2	6.9	0		1	3.4	3	10.3	29
6-7	5	8.8	3	5.3	0		2	3.5	10	17.5	57
8-10	9	14.8	1	1.6	0		3	4.9	13	21.3	61
11-15	5	9.6	1	1.9	2	3.8	7	13.4	15	28.8	52
16-20	7	10.9	2	3.1	1	1.6	5	7.8	15	23.4	64
21-25	6	4.6	9	6.9	6	4.6	23	17.7	44	33.8	130
26-30	12	8.6	3	2.1	9	6.4	36	25.7	60	42.9	140
31-35	2	2.7	3	4.1	5	6.8	20	27	30	40.5	74
36-40	1	2	3	6.1	5	10.2	12	24.4	21	42.9	44
≥ 41	2	2.4	19	22.9	4	4.8	20	24.1	45	54.2	83
All ages	52	6.5	50	6.2	32	4	130	16.2	264	32.9	801

[a] Anti-HBc positive only.
[b] Anti-HBs positive only.
[‡] Total seropositive includes first four columns.

in Figure 1, the highest rate of HBsAg positivity belonged to the 6-10 years age-group (11.9%). After the 10-year age group, there were approximately steady rates of HBsAg positivity until age 21. Thereafter, there was a decline in the HBsAg positivity rate, except in the 26-30 year age-group. The high HBsAg positivity rate in the 6-10 year age-group was statistically significant when compared to the other age-groups ($p < 0.05$).

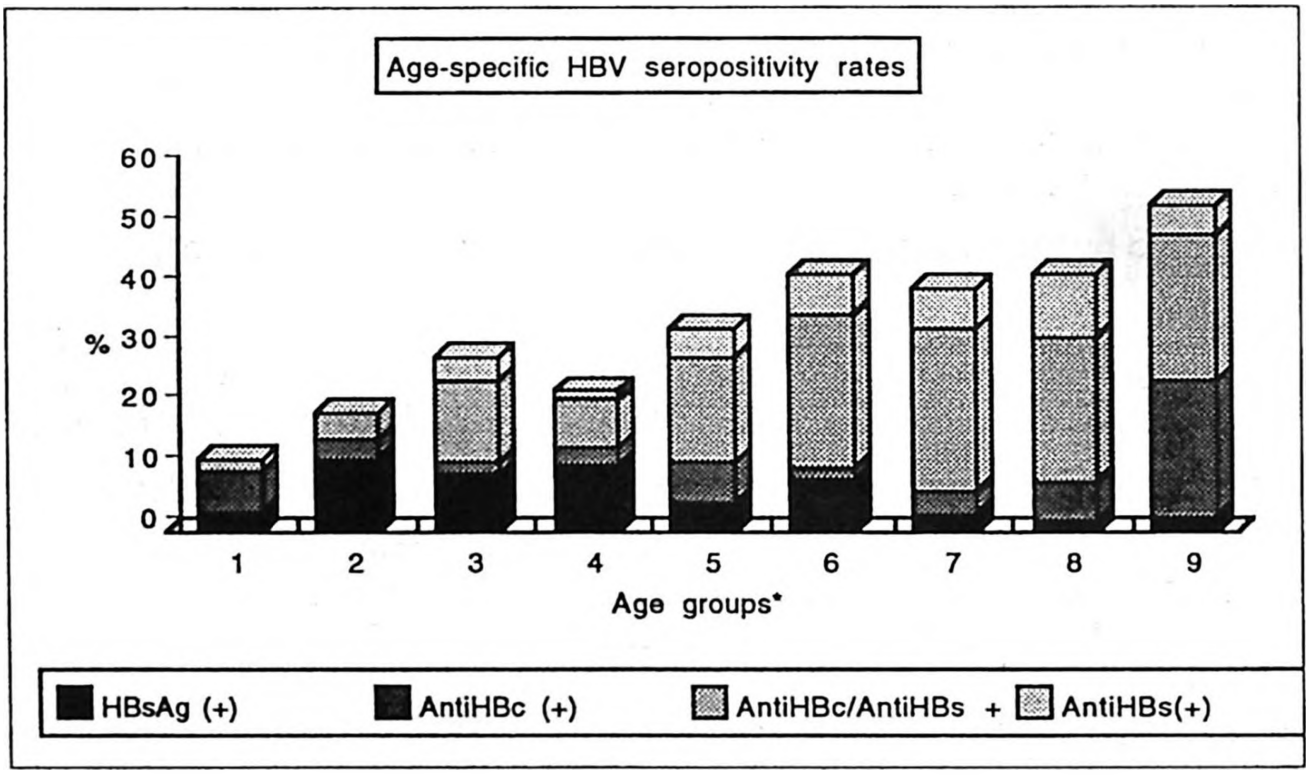

Fig. 1: Age-specific seroprevalence of the studied population.

* 1 = ≤ 5 years of age, 2 = 6-10 years, 3 = 11-15 years, 4 = 16-20 years, 5 = 21-25 years, 6 = 26-30 years, 7 = 31-35 years, 8 = 36-40 years, 9 = > 41 years.

Of 234 patients, 26 HBsAg-positive persons were found in the 6-20 year age-group (11.1%). Of 567, 26 HBsAg-positive persons were determined in the other age groups combined (4.59%) the difference was significant ($p < 0.05$). We concluded that HBV infection was generally acquired very early in the studied population.

The second peak age of HBsAg prevalence was in the 26-30 year age-group, but was not statistically significant when compared to other age groups. Excluding the 6-20 year age-group, the prevalence of HBsAg positivity was 3.29 percent (14/427). When we compare this rate with the prevalence of HBsAg in the 26-30 year age-group (8.57%), then the difference was significant ($p < 0.05$).

We found gradually increasing rates of HBV exposure with increasing age ($p < 0.05$).

When we examined the children between six months and 10 years of age with closer age intervals, we found the results as shown in Figure 2. The

HBsAg-positivity rate was 6.6 percent (2/30) under one year of age. Thereafter there was a decline among children 2-5 years in age. The highest HBsAg positivity rate was in the 8-10 year age group (14.8%). HBsAg positivity was 3.29% under five years of age and 11.8% over five years of age ($p < 0.05$). The difference in HBV exposure rates in children under and over five years of age was not statistically significant (12.1% vs. 19.4%).

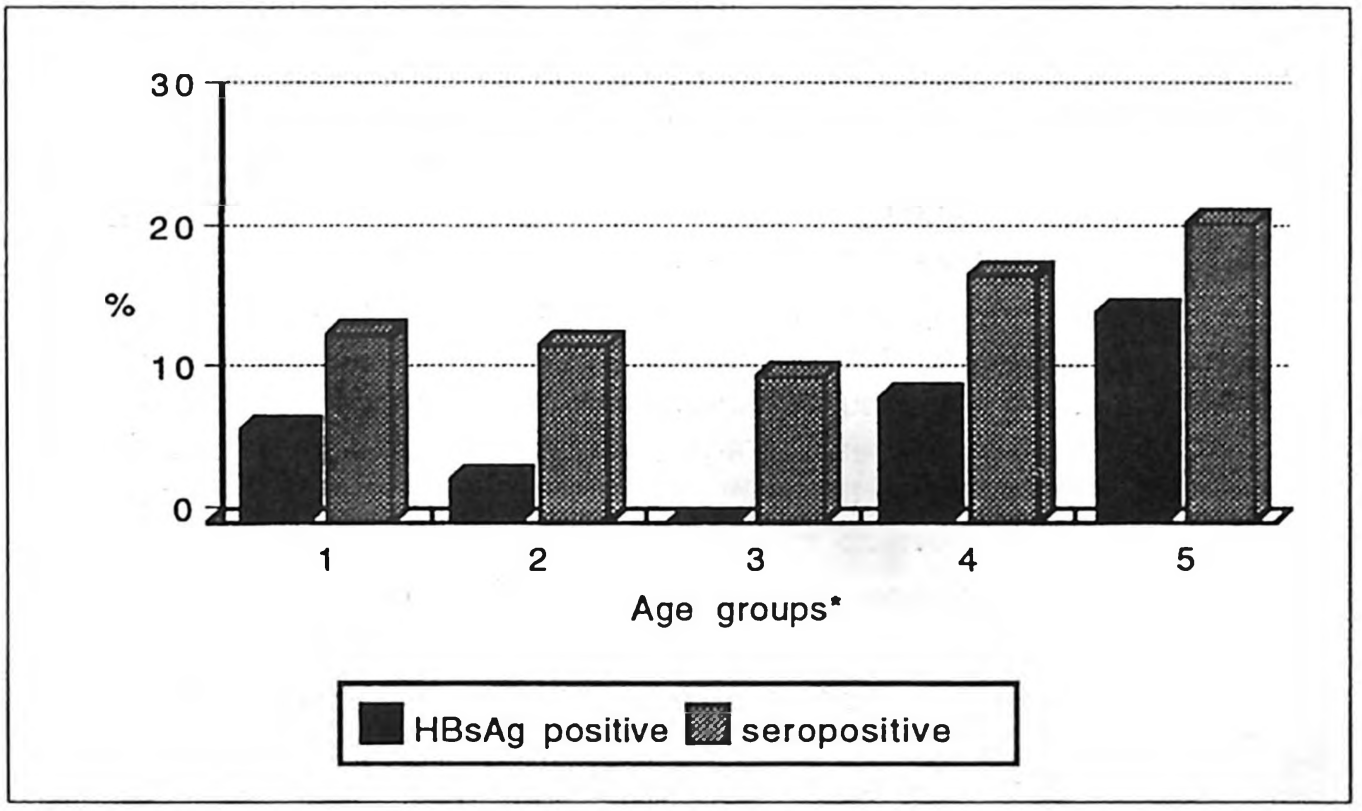

Fig. 2: Detailed age-specific seroprevalence of the children under ten years of age.

* 1 = ≤ 1 year of age, 2 = 2-3 years, 3 = 4-5 years, 4 = 6-7 years, 5 = 8-10 years.

The overall prevalence rate of HBsAg was 6.29% in males and 6.89% in females ($p > 0.05$). The seropositivity rate was higher in males than in females (35.6% vs. 27.6%) ($p < 0.05$).

Discussion

The serious consequences of HBV infection are a result of development of the persistent viral carrier state, which occurs in 70 to 90 percent of acute infections in infancy and declines to six to ten percent of infections which occur after the sixth year of life[7-9]. An estimated 25-30 percent of individuals who become persistent HBV carriers and who have an estimated life expectancy of at least 30 years at the time of infection will die of HBV-induced cirrhosis or hepatocellular carcinoma[7].

Studies have shown that HBV infection is the cause of most cirrhosis and HCC cases in Turkey[10-13], and that the HBeAg-positivity rate in Turkish chronic carriers

of HBsAg is not very high[14]. Therefore vertical transmission is probably not the major mode of transmission in Turkey, and few carriers originate from carrier mothers, most arising from horizontally transmitted infections. This is due to the much lower infectivity and lower HBeAg prevalence of Turkish HBsAg-carrier mothers.

The current study showed that 6.5 percent of people living in İstanbul are HBsAg-positive, and 33 percent have been exposed to HBV infection. The HBsAg prevalence was 6.6 percent in the first year of life, the same as the overall prevalence of HBV infection in the studied population. Both vertical and horizontal transmission must be responsible for the rate of HBsAg positivity in this period of life. The decrease in HBsAg prevalence after the first year and increase in the 6-10 year age-group show the importance of horizontal transmission in our study population. This finding in the pediatric age group has also emerged in other studies from Turkey and other endemic areas of the world[15-19].

The prevalence of HBsAg carriers did not consistently increase after the 6-10 year age-group, unlike the HBV-seropositivity rate. Exposure to the HBV infection increased across the age groups, showing that it continues throughout life; also, persons infected after 6-10 years of age seem to be much less likely to become persistent virus carriers than those infected as neonates or young children, but instead most of them develop immunity to HBV.

In some studies the prevalence of HBsAg has been higher in males than females[19, 20], but in our study it was not. However, the HBV exposure rate was higher in males.

We can make some conclusions about the major mode of transmission of the HBV infection in Turkey, although the numbers in this study are insufficient; moreover, multicenter age-specific seroprevalence studies and cost-benefit analyses including all regions of Turkey must be done. All of the seroepidemiologic studies from Turkey have shown that horizontal transmission was the major mode of transmission and HBV exposure occurred very early in our country[15-18].

Turkey has an intermediate endemicity for HBV infection. In areas of intermediate endemicity, infection occurs in both adults and children, but vertical perinatal transmission is relatively uncommon because most carrier mothers are HBeAg-negative. In intermediate as well as high endemic areas, immunization of all infants may be considered the proper approach for long-term control of hepatitis B[7]. Ideally, a combined program of infant and adolescent immunization together with other individuals at high risk should be applied where economically feasible and where appropriate infrastructure for delivery exists. In Italy, where approximately the same HBV infection prevalence and mode of transmission exists as in Turkey, vaccination of all newborns and 12-year-old adolescents has become compulsory under Italian Law[21]. Although the United States of America has a low endemicity for HBV infection, it is now recommended that all infants receive hepatitis B vaccine as part of their routine immunization schedule[22].

With the high HBsAg prevalence and HBV exposure rates and with horizontal transmission as a major mode of transmission, a mass HBV vaccination which is integrated into the expanded program of immunization (EPI) strategy should be chosen in Turkey. Universal immunization of all infants in Turkey can prevent horizontally transmitted HBV infections. Ideally, extension of HBV vaccination to all pre-school children for the next few years would, reduce the reservoir of HBV infection in these children. Screening and immunization of babies born to carrier mothers would not be an effective strategy, because it would not prevent horizontally transmitted HBV infection later in life to susceptible children who were not vaccinated in infancy due to having seronegative mothers.

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