TÜBİTAK

ORIGINAL ARTICLE

Turk J Med Sci
2009; 39 (2): 289-293
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E-mail: medsci@tubitak.gov.tr

Prevalence of Hepatitis B Infection among Schoolchildren in Southeast Turkey

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Aim: Hepatitis B virus (HBV) infection is a worldwide health problem. The objectives of this study were to determine the impact of the Expanded Programme on Immunization (EPI) on the prevalence of HBsAg carrier rate and immunity developed against HBV infection among schoolchildren in southeast Turkey.

Materials and Methods: The study population consisted of 147,200 healthy schoolchildren between 6 to 17 years of age living in the Mardin area. A total of 802 children were randomly selected by systematic sampling method. Hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc) were analyzed in blood samples by enzyme-linked immunosorbent assay (ELISA General Biological Corp., Taiwan).

Results: This study involved 420 (52.4%) male and 382 female (47.6%) schoolchildren with a mean age of 10.4 ± 2.3 years. The overall anti-HBs, anti-HBc, and HBsAg were positive in 724 (90.2%), 56 (7%), and 22 (2.7%) children, respectively. The overall HBV seroprevalence rate was 2.7% .

Conclusions: The introduction of the national EPI has successfully decreased the HBV seropositivity possibly by preventing perinatal and horizontal HBV transmission among schoolchildren in southeast Turkey.

Key Words: Hepatitis B, prevalence, vaccine

Türkiye'nin Güneydoğu Bölgesi Okul Çocuklarında Hepatit B Enfeksiyon Prevalansı

Amaç: Hepatit B enfeksiyonu (HBV) dünya genelinde bir sağlık problemidir. Bu çalışmanın amacı Türkiye'nin güneydoğu bölgesinde, okul çocuklarında HBV taşıyıcı sıklığı ve HBV enfeksiyona karşı bağışıklık yanıtın gelişmesinde genişletilmiş aşı programının etkisini saptamaktır.

Yöntem ve Gereç: Çalışma popülasyonu Mardin bölgesinde yaşayan 6-17 yaş arası sağlıklı 147.200 okul çocuğunu içerir. Toplam 802 çocuk, rabdomize olarak sistematik örnekleme yöntemi ile seçildi. Alınan kan örneklerinde Hepatit B yüzey antijeni (HBsAg), HBsAg antikoru (Anti-HBs), hepatit B kor antijen antikoru (Anti-HBc), ELISA (General Biological Corp., Taiwan) yöntemi ile çalışıldı.

Bulgular: Bu çalışma, yaş ortalamaları 10,4 ± 2,3 yıl olan 420'si erkek (% 52,4) ve 382'si kız (% 47,6) çocuğundan oluşmaktadır. Çocukların toplamda anti-HBs, anti-HBc ve HBsAg pozitifliği sırasıyla, 724 (% 90,2), 56 (% 7) ve 22 (% 2,7) idi. HBV seroprevalansı toplamda % 2,7 bulundu.

Sonuç: Genişletilmiş ulusal aşı programının başlamasıyla, Türkiye'nin güneydoğusunda okul çocuklarında perinatal ve horizontal geçişli HBV seropozitifliği başarılı bir şekilde azalmıştır.

Anahtar Sözcükler: Hepatit B, prevalans, aşı

Received: February 27, 2008
Accepted: November 13, 2008

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Introduction

The prevalence of hepatitis B virus (HBV) infection is high and constitutes a serious public health problem. There are approximately 350 million carriers of HBV in the world (1). The prevalence of HBV infection and the predominant mode of transmission vary greatly depending on the geographical region and epidemiologic factors (1-3).

Infections acquired in childhood are responsible for the majority of chronic HBV cases, with its related complications including cirrhosis and hepatocellular carcinoma (HCC). Prevention of childhood HBV infection has a large impact on the prevalence of chronic HBV infection and its sequelae (2,4). Immunization remains the most effective way to control HBV infection (5,6).

The World Health Organization (WHO), declared HBV immunization as an urgent requirement and recommended that every country should adopt this preventive strategy by the year 1997 (7). In accordance with recommendations made by the WHO, 152 countries had introduced the HBV vaccine into their Expanded Programme on Immunization (EPI) by November 2005 (8). Turkey has added HBV vaccine to its routine childhood immunization program and has provided it to all children since 1997.

Until 10 years ago, it was thought that most people are infected early in life, and the prevalence of hepatitis B surface antigen (HBsAg) carriage was 8%-10% in southeast Turkey (9). There are no data on the changing seroepidemiology of HBV infection in healthy schoolchildren living in urban areas of southeast Turkey from the initiation of routine HBV vaccination. Therefore, we aimed in this study to show possible changes in the prevalence of childhood HBV infection between the pre- and postvaccination periods. This is a prospective, community based, cross-sectional seroprevalence study. The objectives were to determine the impact of EPI on the HBsAg carrier rate and immunity developed against HBV infection among schoolchildren in southeast Turkey. We also aimed to investigate the correlations between epidemiological data and variables affecting serology results.

Materials and Methods

This was a cross-sectional type epidemiological study carried out in the central district of Mardin in southeast Turkey, with a population of 108,300; the population is 835,000 when the surrounding areas are added. According to the latest statistics, there are 605 schools and a total of 147,200 students. The numbers of primary schools and students who were between 6 and 17 years old were acquired from Mardin City National Education Directorship. The schools and students to be included in the study were designated. Age and gender of students were taken into account for the selection of students. A total of 802 subjects belonging to different socioeconomic classes were randomly included in the study based on the systematic sampling method.

Informed consent was obtained from the children's parents. A questionnaire regarding gender, age, the number of siblings, and parental occupation, education, and income was filled in by the children's parents. A history of some risk factors for HBV infection such as blood transfusion, injection, circumcision, dental therapy procedures, surgical operation, hospitalization, and vaccination against HBV infection was also recorded.

Venous blood samples were obtained from children, serum was separated, and serum specimens were stored at -80 °C before performing the laboratory procedures. Samples were tested for HBsAg, antibody to HBsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc) using a commercially available enzyme-linked immunosorbent assay (ELISA; General Biological Corp., Taiwan), which is highly sensitive and specific. A positive test result of at least 1 of these 3 parameters was considered seropositive.

A person was considered infected with HBV (including past and current infection) if HBsAg was positive (an initially HBsAg reactive sample was retested using the same ELISA and only the repeatedly reactive sample was considered positive for HBsAg) and anti-HBs negative, or HBsAg negative and anti-HBs positive (>10 mIU/ml) with no past history of vaccination. A person was considered as having immunity to HBV if anti-HBs >10 mIU/ml; a natural acquired immunity to HBV was defined as having anti-HBs titers >10 mIU/ml with no past history of HBV vaccination.

Statistical analysis

Chi-square test was used for the analyses of categorical variables, independent t test was used for analyses of numeric variables, and one-way ANOVA was used for analyzing multiple groups. Statistical analyses were carried out using SPSS 10.0 for Windows. A P value of <0.05 was considered significant.

Results

This study included 420 (52.4%) male and 382 female (47.6%) (a total of 802) students. Their mean age was 10.4 ± 2.3 years. The overall anti-HBs, anti-HBc, and HBsAg were positive in 724 (90.2%), 56 (7%), and 22 (2.7%) children, respectively (Table 1). When hepatitis B seropositivity was analyzed according to age and sex, it was found that they did not affect the seropositivity (Tables 1 and 2). The overall HBV seroprevalence rate was 2.7%.

Table 1. Distribution of HBV seropositivity according to age.

Age (Year)	Anti-HBs Ab n (%)	Anti-HBc Ab n (%)	HBsAg n (%)
6	5 (0.6)	-	-
7	73(9.2)	9(1.1)	3 (0.3)
8	108(13.4)	5(0.7)	-
9	84(10.5)	4(0.5)	2 (0.2)
10	94(11.7)	5(0.7)	1(0.1)
11	98(12.2)	10(1.1)	4(0.5)
12	90(11.2)	8(1)	5(0.7)
13	104(13)	7(0.9)	5(0.7)
14	55(6.8)	7(0.9)	2(0.2)
15	11(1.4)	1(0.1)	-
16	1(0.1)	-	-
17	1(0.1)	-	-
Total	724 (90.2)	56(7)	22(2.7)
P	>0.05	>0.05	>0.05

Table 2. Distribution of HBV seropositivity according to sex.

HBV Seropositivity	Male	Female	P
Anti-HBs Ab n (%)	377(47)	347(43.2)	>0.05
Anti-HBc Ab n (%)	33 (4.1)	23(2.9)	>0.05
HBsAg n (%)	11(1.4)	11(1.4)	>0.05

Girls and boys were equally affected. HBV seroprevalence was higher in children with a low socio-economic status although this difference was not statistically significant. Of the 802 children, 721 (90%) had one or more risk factors. No statistical difference was found between subjects with risk factors and those without.

When the educational status of parents was taken into account most of the mothers were non-educated (n = 315, 39.2%) (P < 0.0001) in contrast to the fathers, most of whom were highly educated (n = 264, 32.9%) (P < 0.0001), respectively. The mean number of persons and rooms in the house were 6.5 ± 2.1 and 3.1 ± 1.1, respectively. Most of the mothers were housewives (n = 777, 96.8%) (P < 0.0001), and the most common job of the fathers was government official (n=300, 37.4%) (P < 0.0001). The unemployment rate was extremely high (n = 111, 13.8%). The educational status of the parents and the number of siblings did not affect the rate of total seroprevalence or HBsAg seroprevalence.

Discussion

The majority of chronic HBV carriers are in hyperendemic areas and generally acquired their infections from HBsAg carrier mothers perinatally or in early childhood. HBV is especially dangerous for infants, since 90% of infants become chronic hepatitis B carriers (10,11).

Immunization remains the most effective way to control hepatitis B disease. HBV vaccine has been available since 1982 and is given simultaneously with other universally administrated vaccines at birth and after that and remains highly immunogenic. Globally, the prevalence of the HBsAg carrier state has changed rapidly since the availability of HBV vaccine and implementation of mass immunization in infants (12,13).

Turkey represents a bridge between Europe and Asia and as it is a country with special demographic and socioeconomic features, not only geographically but also in terms of epidemiology, disease behavior, and ethnical differences, it deserves special attention. Of the neighboring or nearby countries in the Middle East, Iran, Kuwait, and the Kingdom of Saudi Arabia have reached over 80% of the population with the hepatitis B vaccination. Thus they have shifted to low endemicity regions with HBsAg carrier rates of below 2% (14-16). Cyprus, Iraq, Georgia, and the United Arab Emirates are in the intermediate endemicity area with 2-5% rates (14,17,18). These countries with their EPI reached 68-90% of the population. In previous studies, the prevalence of HBV infection was found to be changing from region to region in Turkey and decreased from east to west from 10% to 4% with an average rate of 6% of the total population (9,19-22). A nationwide EPI for neonates has been implemented in Turkey since 1997. One of the most important results of HBV vaccination is the dramatic reduction in the HBsAg carrier rate among Turkish schoolchildren born after the introduction of the national EPI. However, in the present study we found a clear decline in the HBV seroprevalence rate in eastern Turkey compared with previous research performed in the same region.

It is known that similar successful examples occurred in the other parts of the world following mass

vaccinations. A study conducted by Tsen et al. (13,23) in Taiwan showed that the prevalence of HBsAg in children under 5 years of age decreased from 9.3% in 1984 to about 2% in 1989 after implementation of a nationwide HBV immunization program of newborns in 1984. A significant decrease in hepatitis B core antibody (anti-HBc) among children vaccinated with HBV vaccine indicates that immunization of newborns not only protects vaccinated children but also decreases horizontal transmission. Chen et al. (24) reviewed the seroepidemiology of HBV infection in children 10 years after the mass vaccination of newborns in Taiwan and reported a reduction in overall HBsAg carrier rate from 9.8% in 1984 to 1.3% in 1999 and an overall decline in anti-HBc rate from 24% in 1984 to 4.0% in 1994.

Previous studies in our region showed 10% of HBSAg positivity and after 10 years of mass HBV vaccination now we found 2.7% seropositivity in the same area. The southeast region of Turkey now can be labeled a low endemicity area according to the results of the present study (9,25).

Although the overall HBsAg seroprevalence rate decreased in our study, our observation of a gradual increase in seroprevalence with age is in fact an indication of horizontal transmission of HBV, usually seen in countries with intermediate endemicity (2). Most of the seroepidemiological studies from Turkey have shown that horizontal transmission was one of the major modes of transmission (9,19,21,22,26,27). Although the exact mechanism is not clear, horizontal transmission is thought to be due to the transfer of HBV by close contact. It is known that most infections are prevalent in rural regions due to poor, crowded conditions, in which large families live in small houses with many children sleeping together and sharing utensils and belongings. The other probable reason for the decrease in seroprevalence is an improvement in sanitary conditions over the last 10 years. HBsAg positive children in our region also were from large families living in unsuitable conditions.

HBV vaccine is very safe, with a low frequency of adverse effects; it has no cross-interference with BCG, poliovirus, or DTP vaccines. Globally, the prevalence of the HBsAg carrier state has been changing rapidly since the availability of HBV vaccine and implementation of the mass immunization of infants (13,28). Furthermore, in Turkey, the first dose of HBV vaccine is currently given in the hospital soon after birth with the aim of preventing mother-to-infant HBV transmission. The second dose is given during postnatal follow-up care in the second month, and the third dose is given either in the hospital or at a rural health center at 9 months of age. In Turkey the first children that received HBV vaccine under the EPI are now 10 years old. A 6-year primary school education is compulsory for all children aged from 7 to 15 years in this country, and the collection of data from primary schools is, therefore, fairly representative of Turkish schoolchildren's status to HBV infection after the implementation of EPI.

In conclusion, the introduction of the national EPI has successfully decreased the HBV seropositivity possibly by preventing perinatal and horizontal HBV transmission among schoolchildren in southeast Turkey. The HBsAg carrier rate has been reduced from 8%-10% to 2.7% by the implementation of the national EPI in the last decade.

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