



Evaluation of Hepatitis B Serology and the Effectiveness of Vaccination Program in Individuals Under the Age of Twenty-Four

Yirmi Dört Yaş Altı Bireylerde Hepatit B Serolojisinin ve Aşı Programının Etkinliğinin Değerlendirilmesi

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ABSTRACT

Objectives: The hepatitis B vaccine have been included in the routine vaccination program in our country since 1998 as part of the fight against hepatitis B virus (HBV). This study aimed to determine the HBV serology and to determine the effectiveness of the hepatitis B vaccination program in individuals born after the start of the hepatitis B vaccination program.

Materials and Methods: Data from 302 patients born after the hepatitis B routine vaccination program and 172 persons born before the vaccination program were evaluated. Those with hepatitis B surface antibody (anti-HBs) <10 mIU/mL were defined as non-immune, those with anti-HBs ≥10 mIU/mL were defined as immune, and those with isolated anti-HBs positivity were defined as the vaccinated group.

Results: Of the patients included in the study, 49.4% were female and 50.6% were male, with a mean age of 29.7±15.6 years. Anti-HBs, hepatitis B surface antigen (HBsAg), and anti-hepatitis B core antigen (anti-HBc) total positivity in patients were 41.4%, 3.2%, and 12.2%, respectively. 53% of the patients were unvaccinated, 36.5% were vaccinated, 4.4% were naturally immune, 3.2% were chronic hepatitis B, and 3% were isolated anti-HBc total positivity. A statistically significant difference was found in terms of HBsAg seropositivity anti-HBs seropositivity and naturally immune in individuals born before and after the routine hepatitis B vaccination program (p<0.05).

Conclusion: With the data obtained at the end of our study, it was determined that there was a significant decrease in HBsAg seropositivity and innate immunity numbers following the implementation of the routine vaccination program. This highlights the importance of the vaccination program and the usefulness of vaccination in preventing HBV infections.

Keywords: Anti-HBs, Turkey, vaccination

ÖZ

Amaç: Hepatit B aşısı, hepatit B virüsü (HBV) ile mücadele kapsamında ülkemizde 1998 yılından itibaren rutin aşılama programına alınmıştır. Bu çalışmada hepatit B aşılama programına başladıktan sonra doğan bireylerde HBV serolojisinin belirlenmesi ve hepatit B aşılama programının etkinliğinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Hepatit B rutin aşılama programından sonra doğan 302 hasta ve aşılama programından önce doğan 172 kişiden alınan veriler değerlendirildi. Hepatit B yüzey antikorunu (anti-HBs) <10 mIU/mL olanlar non-immün, anti-HBs ≥10 mIU/mL olanlar immün ve izole anti-HBs pozitifliği olanlar ise aşılanan grup olarak tanımlandı.

Bulgular: Çalışmaya alınan hastaların %49,4'ü kadın, %50,6'sı erkekti ve yaş ortalaması 29,7±15,6 idi. Hastalarda anti-HBs, hepatit B yüzey antijeni (HBsAg) ve anti-hepatit B çekirdek antijeni (anti-HBc) toplam pozitifliği sırasıyla; %41,4, %3,2 ve %12,2 idi. Hastaların %53'ü aşılanmamış, %36,5'i aşılanmış, %4,4'ü doğal bağışık, %3,2'si kronik hepatit B ve %3'ü izole anti-HBc total pozitifliği. Rutin hepatit B aşılama programı öncesi ve sonrası doğan bireylerde HBsAg seropozitivitesi, anti-HBs seropozitivitesi ve doğal bağışıklığı açısından istatistiksel olarak anlamlı fark bulundu (p<0,05).

Sonuç: Çalışmamız sonunda elde edilen verilerle rutin aşılama programının uygulanmasını takiben HBsAg seropozitivitesinde ve doğuştan gelen bağışıklık sayılarında anlamlı azalma olduğu belirlendi. Bu, aşılama programının önemini ve aşılanmanın HBV enfeksiyonlarını önlemedeki yararlılığını vurgulamaktadır.

Anahtar Kelimeler: Anti-HBs, Türkiye, aşılama



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Introduction

Hepatitis B virus (HBV) is a serious cause of mortality and morbidity worldwide. Nearly one-third of the global population has been exposed to HBV (1). HBV is an enveloped DNA virus belonging to the orthohepadnavirus subgenus of the Hepadnaviridae family. The main transmission of the virus, which primarily infects liver cells, is parenteral contact with infected blood or body secretions, sexual contact, and perinatal, vertical, and intrafamily close contact (horizontal) (2). In highly endemic areas, the transmission is mostly parenteral or horizontal during childhood (3). Turkey, where the HBV carrier rate is 4-10%, is considered to be a moderately endemic region in terms of HBV incidence and HBV transmission in our country is mostly horizontal in childhood and adulthood (4).

Acute HBV infection becomes chronic at highly variable rates depending on age and HBV transmission routes. The risk of developing a chronic infection after exposure to HBV is 1-5% in adults and reaches 90% in the neonatal period (5). More than 250 million people worldwide live with viral hepatitis and the virus causes approximately 900.000 deaths annually due to hepatocellular carcinoma (HCC) and cirrhosis.

In 2016, the World Health Organization set the goal of eliminating hepatitis B globally by 2030 (2). Within the scope of this goal, it was decided to include the hepatitis B vaccine in the routine vaccination schedule of all countries as of 1997 (3). The hepatitis B vaccine has been included in the routine vaccination program in Turkey since 1998. This program prevents HBV infection and its complications including cirrhosis and HCC.

This study aimed to determine HBV serology in individuals born after the start of the routine hepatitis B vaccination program and to compare them with individuals born before the start of routine hepatitis B vaccination.

Materials and Methods

Patient Population

In our study, 474 patients whose hepatitis B surface antibody (anti-HBs), anti-hepatitis B core antigen (anti-HBc) total, and hepatitis B surface antigen (HBsAg) tests were studied for various reasons in the infectious diseases clinic of our hospital between January and September 2022 were retrospectively evaluated. Demographic characteristics and examination results of the patients were obtained from the hospital information system

records. The patients were divided into two groups: those born before and after 1998 when the hepatitis B vaccination program started in our country. According to hepatitis B serology, patients with anti-HBs <10 mIU/mL were defined as non-immune, those with anti-HBs ≥10 mIU/mL were defined as immune, and those with isolated anti-HBs positivity were defined as vaccinated.

Statistical Analysis

The SPSS 21 program was used for the statistical analysis of the data. The chi-square test was used for comparison between groups born before and after 1998. P<0.05 was accepted as a statistical significance level.

Ethical Permission

Before starting the study, the approval of the Scientific Research Ethics Committee of the Ağrı İbrahim Çeçen University Faculty of Medicine was obtained (approval number: 244, date: 08.11.2022).

Results

Of the patients included in the study, 49.4% were female and 50.6% were male, with a mean age of 29.7±15.6 years. Anti-HBs, HBsAg, and anti-HBc total positivity rates were 41.4%, 3.2%, and 12.2%, respectively. 52.7% of the patients were unvaccinated, 36.5% vaccinated, 4.4% naturally immune, 3.4% chronic hepatitis B, and 3% isolated anti-HBc total positivity. Hepatitis B serologies according to gender are shown in Table 1.

Of the 302 patients born after 1998, when the routine hepatitis B vaccination program started in Turkey, 39.1% were female, 60.9% were male, and the mean age was 20.4±1.65 years. Of the 172 patients born before 1998 who were taken as the control group, 67.4% were female, 32.6% were male, and the mean age was 46.1±15.86 years.

HBsAg positivity was detected in 7 (2.3%) of 302 patients in the study group who were born from the year the routine hepatitis B vaccine program started. Anti-HBs were positive in 128 (43.3%) and anti-HBs negative in 167 (56.6%) of 295 patients found to be HBsAg negative. Isolated anti-HBs positivity was found in 124 (96.6%) of 128 patients with anti-HBs positive, anti-HBc total positivity in 4 patients (3.1%), and a serological profile indicating a previous infection was detected.

HBsAg positivity was detected in 8 (4.7%) of 172 patients in the control group born before hepatitis B vaccination was started. Anti-HBs were positive in 68 (41.4%) and anti-HBs negative in 96 (58.5%) of 164 HBsAg-negative patients. Isolated anti-HBs

Table 1. Hepatitis B serology by gender

Parameter	Females (%)	Males (%)	Total (%)	p-value
HBsAg positivity	2.1	4.2	3.2	0.2
Anti-HBs positivity	41	41.7	41.4	0.8
Anti-HBc total positivity	12.4	12.1	12.2	0.9

HBsAg: Hepatitis B surface antigen, Anti-HBs: Hepatitis B surface antibody, Anti-HBc total: The hepatitis B core total antibody

positivity in 49 (72%) of 68 patients with anti-HBs positive and anti-HBc total positivity in 20 patients (29.4%) and a serological profile indicating a previous infection were detected.

Considering the isolated anti-HBs positivity rates showing that the hepatitis B vaccine was applied; 28.5% of those born before the routine hepatitis B vaccination program and the rate determined as 41.1% in those born after the vaccination program. A statistically significant difference was found in terms of HBsAg seopositivity, anti-HBs seopositivity, and naturally immune in individuals born before and after the routine hepatitis B vaccination program ($p < 0.05$). Serological data of the patients in both groups are shown in Table 2, There was no statistical difference between males and females in terms of isolated anti-HBs positivity, anti-HBs negativity, and HBsAg positivity both in the pre-vaccination and post-vaccination period, while HBsAg positivity was approximately 2 times higher in males than females in both groups (Table 3).

Discussion

Our country is among the middle endemic regions in terms of HBV frequency, and it is estimated that approximately 3 million people are infected with HBV (4). In the 2010 Report of the European Center for Disease Prevention and Control, the prevalence of hepatitis B in the general population in Turkey was reported to be between 2% and 8%, although it varies according to region (5). In various studies conducted in our country, it has been reported that the prevalence of hepatitis B varies between 4 and 10%, increases from west to east, and the HBsAg positivity rate reaches 10% in Diyarbakır (6,7,8,9). This regional difference in HBV positivity reemphasizes the role of close contact and intrafamilial transmission in HBV seroprevalence in regions with large families and poor hygiene conditions.

The population-based investigation of the prevalence of hepatitis B in Turkey was carried out for the first time by the

Turkish Liver Research Association. In the study in which 5,471 people were screened, HBsAg, anti-HBs, and anti-HBc total positivity were found to be 4.0%, 32.0%, and 30.6%, respectively (10). In the study in which the TURHEP study group investigated the seroprevalence of HBV and HCV infections in the general population of Turkey in 2015, HBsAg seropositivity was found to be 4% and anti-HBs positivity was 30.9% (11). In our study, similar to the literature, HBsAg positivity was found to be 3.4% and anti-HBs positivity was 41.4%.

When isolated anti-HB positivity was evaluated according to age groups, the highest rate was seen in the 17-24 age group with 41.1%, while the lowest rate was observed in the group over 70 years of age (18.8%). Anti-HB positivity was increasing gradually, starting from the group over 70 years of age and progressing toward younger ages. This high rate observed in the younger age group is associated with the effective implementation of the vaccination program. It was determined that innate immunity and HBsAg positivity rate was high in middle-aged groups with a low isolated anti-HBs positivity rate. This situation shows once again the importance of the hepatitis B vaccine in the prevention of HBV exposure.

In various seroprevalence studies conducted in our country, HBsAg positivity rates were found to be higher in men and women (12,13,14). In our study, there was no significant difference between males and females in terms of anti-HBs and anti-HBc total positivity, whereas HBsAg positivity was found to be 2 times higher in males (4.2%) than females (2.1%). However, the difference was not statistically significant. HBsAg positivity was found to be 3.4% in females and 8.9% in males in the pre-vaccination group, this rate was 1.7% in females and 2.7% in males in the post-vaccination period. This situation can be associated with risky procedures such as shaving, tattooing, and circumcision in men where aseptic precautions are not adequately applied.

Table 2. Hepatitis B serology of individuals born before and after the hepatitis B vaccination program

	Those born after the HBV vaccination program (n=302)		Those born before the HBV vaccination program (n=172)		p-value
	n	%	n	%	
Isolated anti-HB positivity	124	41.1	49	28.5	0.03
Anti-HBs negativity	178	60	90	52.3	-
Anti-HBs positivity, anti-HBc total positivity	1	0.3	20	11.6	<0.01
HBsAg positivity	7	2.3	13	7.5	0.03
Isolated anti-HBc total positivity	1	0.3	14	8.1	<0.01

HBV: Hepatitis B virus, HBsAg: Hepatitis B surface antigen, Anti-HBs: Hepatitis B surface antibody, Anti-HBc total: The hepatitis B core total antibody

Table 3. Hepatitis B serologies by gender in pre- and post-vaccination groups

	Those born after the HBV vaccination program (n=302)		Those born before the HBV vaccination program (n=172)		p-value
	Females (%)	Males (%)	Females (%)	Males (%)	
Isolated anti-HB positivity	42.4	40.2	29.3	26.8	0.7
Anti-HBs negativity	55.9	56.3	50.9	37.5	0.7
HBsAg positivity	1.7	2.3	3.4	8.9	0.6

HBV: Hepatitis B virus, HBsAg: Hepatitis B surface antigen, Anti-HBs: Hepatitis B surface antibody, Anti-HBc total: The hepatitis B core total antibody

The primary goal of the hepatitis B vaccination program is to vaccinate all newborns to prevent the occurrence of HBV infection in early childhood. Since 1998, HBV vaccination has been given free of charge to all newborns. In various studies conducted in various regions of our country and evaluating the serology of hepatitis in babies born after the vaccination program, the anti-HBs level varies between 66-85% in the post-routine vaccination period (15,16). In our study, the average anti-HBs positivity rate was found to be 41.1% in those born in 1998 and later, and a lower rate was found compared to other studies. In this case, it is thought that regional differences in vaccination may be effective.

In various studies conducted in our country, the rates of previous infection and immunization vary between 0.4% and 44.5% (17,18,19). In our study, the rate of innate immunity was found to be 4.4%. These differences in the rates of previous infection and immunization show that hepatitis B seroprevalence results, which may vary from region to region, are observed, as the HBV seroprevalence in our country increases gradually from west to east (20,21,22). In our study, the rate of natural immunity was found to be 11.6% in those born before the routine vaccination program and 0.3% in those born after vaccination. This clearly shows the effect of the vaccine against HBV infection.

Detection of HBsAg positivity in 7 patients who were born after the vaccination program shows that this situation of HBsAg-positive mothers is still unknown during pregnancy and their babies cannot be vaccinated + hepatitis B immunoglobulin at birth. It is thought that this may be caused by deficiencies in pregnancy screenings or deliveries outside the hospital.

Study Limitations

The most important limitation of our study is that it was conducted in a single province and with a limited number of patients. If this study were based on a population in more than one city from different regions, the results would more accurately reflect the population. Another limitation of our study is that because all patients with anti-HBs <10 were included in the unvaccinated group and vaccinated anti-HBs >10, but the titer decreased over time, we accepted unvaccinated patients and could not accurately estimate the immune population.

Conclusion

As a result, HBV infection is still among the infectious diseases that do not lose their currency and importance in the world and our country. The most effective way to reduce the frequency of this disease, as in all infectious diseases that can be prevented by vaccination, is to mass vaccination. The national vaccination program has changed the epidemiology of HBV in Turkey, resulting in a significant reduction in HBsAg positivity and innate immunity rates. However, the same is not the case in the pre-vaccination period, and adult HBV vaccination should be expanded, especially in risk groups and those with HBsAg-positive cases in their families.

Ethics

Ethics Committee Approval: Before starting the study, the approval of the Scientific Research Ethics Committee of the

Ağrı İbrahim Çeçen University Faculty of Medicine was obtained (approval number: 244, date: 08.11.2022).

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: Y.C., Concept: Y.C.K., FT., Design: Y.C., K.F.T., Data Collection or Processing: K.F.T., Analysis or Interpretation: K.F.T., Literature Search: Y.C., Writing: Y.C.

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