Research Article

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Seroepidemiology of Hepatitis B Virus Infection in İstanbul: A 20-year Survey

İstanbul'da Hepatit B Virüsünün Seroepidemiyolojisi: 20 Yıllık Bir Çalışma

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ABSTRACT

Objective: Turkey is an intermediate endemic country for hepatitis B virus (HBV) infection, with the prevalence rates showing regional differences. The aim of this study was to determine the recent prevalence of HBV infection among adults in İstanbul and to evaluate the impact of national vaccination program that started in 1998.

Materials and Methods: Data of three healthcare centers from 3 different districts in İstanbul between 1995 and 2015 were obtained. HBV status of the participants was evaluated according to their hepatitis B surface antigen (HBsAg) and anti-HBs results. The change in HBV prevalence was evaluated by dividing the time included in the study into three periods: 1995-2002, 2003-2009 and 2010-2015. Statistical comparison between groups studied in each period was performed. To evaluate the impact of vaccination, the patients of 15-17 years of age were compared with the rest of the last study group.

Results: Totally, 26001 adult patients were included in the study. HBsAg and anti-HBs tested positive in 4.24% and 16.81% of patients, respectively. When the 20 years included in the study were divided into three periods and each studied separately, the positive results for HBsAg decreased from 5.34% to 4.8% and 3.08%, and positive anti-HBs results increased from 14.24% to 15.45% and 19.57%, the difference between the groups being statistically significant (p<0.001). In vaccinated group (n=287), no one tested positive for HBsAg and 30.3% of patients tested positive for anti-HBs, being statistically different from the rest of the group (p<0.001).

Conclusion: Despite the positive effects of vaccination, chronic HB remains a serious health problem.

Keywords: Hepatitis B virus, seroprevalence, vaccination, İstanbul

ÖZ

Amaç: Hepatit B virüsü (HBV) enfeksiyonu Türkiye'de orta düzeyde endemik bir enfeksiyondur ve prevalansı bölgesel olarak farklılıklar gösterir. Bu çalışmanın amacı İstanbul'daki yetişkinlerde HBV enfeksiyonunun son prevalansını belirlemek ve 1998'de başlatılan ulusal aşılama programının etkisini değerlendirmektir.

Gereç ve Yöntemler: İstanbul'da üç farklı ilçenin aile sağlık merkezlerinden elde edilen veriler 1995'ten 2015'e kadar retrospektif olarak tarandı. Katılımcıların HBV açısından durumu hepatit B yüzey antijeni (HBsAg) ve anti-HBs sonuçlarına bakılarak değerlendirildi. HBV prevalansındaki değişim ise çalışmaya dahil edilen süre üç döneme, 1995-2002, 2003-2009 ve 2010-2015 yılları kapsayan dönemler olarak, bölünerek değerlendirildi. Her bir dönemde incelenen gruplar arasındaki farklar istatistiksel olarak karşılaştırıldı. Aşılamanın etkisini değerlendirmek için, 2010-2015 zaman aralığındaki grupta 15-17 yaşındaki hastalar, grubun geri kalanıyla karşılaştırıldı.

Bulgular: Toplamda 26001 yetişkin hasta çalışmaya dahil edildi. HBsAg ve anti-HBs, sırasıyla hastaların %4,24 ve %16,81'inde pozitif tespit edildi. Çalışmaya alınan 20 yıllık süre, üç ayrı döneme ayrılıp her bir dönem ayrı ayrı incelendiğinde, HBsAg'de pozitiflik oranının %5,34'ten %4,8 ve %3,08'e düştüğü; anti-HBs'de pozitiflik oranının %14,24'ten %15,45'e ve %19,57'ye yükseldiği gözlemlendi. Gruplar arasındaki farklar istatistiksel olarak anlamlı bulundu (p<0,001). Aşılanmış grupta (n=287), HBsAg pozitif hasta yoktu, anti-HBs pozitiflik oranı %30,3 ve istatiksel olarak grubun geri kalanından farklı bulundu (p<0,001).

Sonuç: Her ne kadar aşılamanın olumlu bir etkisi olduğu tespit edilmişse de, kronik HBV enfeksiyonu önemli bir sağlık sorunu olmaya devam etmektedir.

Anahtar Kelimeler: Hepatit B virüsü, seroprevalans, aşılama, İstanbul

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Introduction

Hepatitis B (HB) is one of the most common infectious diseases in the world with approximately 2 billion infected people (1,2). HB virus (HBV) is a major pathogen in the etiology of chronic hepatitis and approximately 40% of all chronic HB cases develop cirrhosis, liver failure, or liver cancer (3,4). HB prevalence is highest in sub-Saharan Africa and East Asia; high rates are also found in the Amazon and southern parts of eastern and central Europe. Western Europe and North America have lower prevalence of HBV infection (1). Turkey is one of the countries with intermediate (28%) endemicity for HB. It is determined that the overall rate of HB surface antigen (HBsAg)-positive population in Turkey is 4.6%. Wide range of seropositivity, from 3% to 12%, has been reported in different studies. These studies were performed in specific populations and in certain cities, and HBV prevalence changes according to the region of the country and the occupation of the population studied (2,5,6,7,8,9,10). An effective and safe vaccine against HBV has been available since 1982. In Turkey, a national vaccination program for HBV was launched in 1998. All infants are vaccinated at birth, at 1 month and at 6 months of age; adults are vaccinated on request.

The aim of our study was to determine the HBV prevalence in İstanbul by studying a large population that do not belong to specific occupational group such that can better represent the general population; also, we aimed to evaluate the periodical change in seroprevalence of HBV markers over 20 years, and to determine the effect of HBV vaccination.

Materials and Methods

After obtaining the local Ethics Committee Approval, HBsAg and anti-HBs results of patients having applied to the healthcare centers in the Fatih, Üsküdar and Kadıköy districts of İstanbul were obtained from the patients' file records. Although being called differently throughout the time period of the study, "family health centers" in 2015, are the centers where primary care health service is given. Because of the characteristics of the patient population (regular check-up, chronic disease follow-up), the parameters, such as anti-HBc, HB envelope antigen (HBeAg) and anti-HBe, were not evaluated. The patient's serum samples were studied using an automatic analyzer (Abbott C8000).

Three periods, namely 1995-2002, 2003-2009 and 2010-2015, were determined and studied separately. Adult patients between the ages of 15 and 90 years were included and children, accepted as individuals younger than 15 years of age, were excluded from the study. All patients whose HBV records were available were included in the study.

Statistical Analysis

The sex ratios and mean age of each group were determined. HBsAg and anti-HBs prevalence was determined for each group and compared statistically calculating chi-square value on Microsoft Excel (2011). After forming the contingency tables by determining expected frequencies, the deviances of each cell of the table were calculated and the general sum representing the chi-square value was converted to p value using quick p value calculator on web (11). The comparison was done for female patients, male patients and total numbers separately for both HBsAg and anti-HBs prevalence. Patients being 15-17 years old in the last group represented the patients having been vaccinated as a part of national vaccination program for HBV that started in 1998. This group of patients was also evaluated separately. Those patients were compared with the rest of the group by one-sample t-test. A p value of less than 0.05 was considered statistically significant.

Results

Totally, 26001 patient's HBsAg and anti-HBs results were evaluated (8791 females and 17210 males). The prevalence of HBsAg and anti-HBs in all of the patients included and according to the sex is presented in Table 1 and Table 2.

The first time interval was the 8-year-period from 1995 to 2002. The average age of patients included was 27±5.2 years. Totally, 5098 patients were evaluated (2951 females and 2147 males), 27 (0.91%) females and 245 (11.41%) males, totally 272 (5.34%) patients tested positive for HBsAg; 343 (11.62%) females and 383 (17.84%) males, totally 726 (14.24%) patients tested positive for anti-HBs.

The second time interval was the 7-year-period beginning from 2003 and ending at 2009. The average age of the patients was 29±6.3 years. Totally, 10843 patients were included (1198 females and 9645 males); HBsAg and anti-HBs tested positive in 4.8% and 15.45%, respectively. Of the females, 46 (3.84%) and 699 (58.35%) tested positive for HBsAg and anti-HBs, respectively. In male patients, those rates were found to be 4.92% and 10.12%, respectively.

The last time interval studied was the 5-year period covering the years from 2010 to 2015. The average age of the patients in this group was 30±5.7 years. Sixty-eight (1.46%) female patients and 242 (4.47%) male patients, totally 310 (3.08%) patients tested positive for HBsAg and 957 (20.62%) female, 1012 (18.68%) male, totally 1969 (19.57%) patients were found to be positive for anti-HBs. In this group, the patients between 15 and 17 years of age were evaluated separately as vaccinated group and in this group, there were 115 females and 172 males, totally 287 patients. Among those patients, there was no HBsAg-positive patient and anti-HBs positivity rate was determined as 30.3%. Vaccinated group showed a statistically significant difference with the rest of the group for HBsAg and anti-HBs prevalence ($p<0.001$).

For the total of 20-year period, 1103 out of 26001 patients (4.24%) were HBsAg-positive and 4370 (16.81%) were anti-HBs-positive. The positive results for HBsAg decreased from 5.34% to 4.8% and 3.08%, and positive anti-HBs results increased from 14.24% to 15.45% and 19.57% when the whole 20 years included were divided into three different periods, namely 1995-2002, 2003-2009 and 2010-2015. There was a statistically significant difference in the prevalence rates between the periods ($p<0.001$).

Discussion

HBV is still a risk for developing countries and the mode of transmission shows differences in these countries when compared with the developed ones. In developing countries, horizontal and vertical transmissions, in developed countries, parenteral drug use, sexual transmission, hemodialysis and surgical interventions

are responsible for HBV transmission (12,13). HBV prevalence in Europe and USA was reported to be about 0.1-0.5%, and in Far East, China and tropical countries the HBV prevalence increases to 5-20% (14,15,16). As HBV prevalence shows differences in different geographic areas and countries, it can also be reported different in various areas inside a country. This is the case for Turkey. The large regional differences in HBV prevalence in Turkey are mainly due to differences in socioeconomic status, lifestyles, infrastructure, and access to health services. In a meta-analysis of 399 studies, the estimated overall population prevalence in Turkey was calculated as 4.57%, and the outcomes of the age-specific groups varied from 2.84%, for the 0-14-year olds to 6.36% in the 25-34-year-old group (5).

With the aim to determine the HBV prevalence in İstanbul, the city of Turkey with the highest socioeconomic status, we conducted this study. Also, we wanted to find out the changes in of HBV prevalence in the last 20 years and the effects of national HBV vaccination program (17).

Several studies aiming to determine HB seroprevalence in İstanbul have been conducted. Koçak et al. (18) analyzed HBV seropositivity in blood donation centers in İstanbul from 1987 to 2003 and showed a decrease from 5.98% in 1987 to 2.07% in 2003. Özsoy et al. (19) determined HBV seroprevalence in healthcare workers in a training hospital in İstanbul from 1998 to 2000 as 3%. That rate was 2.1% in blood donors in that hospital for the same period of time. Erden et al. (20) studied HBsAg and anti-HBs frequencies in randomly selected patients attending a university hospital in İstanbul. The prevalence for HBsAg was determined as 6.6% and for anti-HBs as 28.1%. These data belong to the period of the years 1998 to 2001. In a survey from a hospital in İstanbul, the seroprevalence of HBV positivity was determined as 2.39% in blood donors from 1998 to 2004 (21). Another survey performed in İstanbul found HBV seroprevalence as 5% in emergency patients (22). Tigen et al. (23) investigated the HBsAg positivity rate in blood donors in a university hospital in İstanbul from 2004 to 2011. HBsAg positivity rate was found to be 1.54%, decreasing each year. Doğan et al. (24) retrospectively screened the seropositivity rate of HB in pregnant women in İstanbul from 2008 to 2013. The seropositivity was found to be 1.2% for HBsAg and 26.3% for anti-HBs. From the same cohort of that study, we analyzed pregnant women in a separate study and found it to be 1.5% for HBsAg and 11.5% for anti-HBs. Totally, 7605 pregnant women were evaluated for the period of 20 years, from 1995 to 2015 (25). It can be seen that the HBV prevalence is lower in blood donors, probably because those who are aware of their HBV status do not apply for blood donation. The rates are higher in patients and healthcare workers as expected. It also can be seen that the HBV prevalence decreases by time.

The results of our study are important in aspect that they show the change in HBV prevalence in the last 20 years in İstanbul. In the first period studied, 1995-2002, HBsAg was found positive in 5.3% and anti-HBs in 14.2% of patients. Routine newborn HBV vaccination started at that period, in 1998. Since our study group included adults only, the effect of vaccination was not seen and anti-HBs levels were found to be quite low. In the second period, 2003-2009, the effect of the routine vaccination could not be seen, because the study group began with 15-year-old patients. However, the fall in HBsAg prevalence to 4.8% and the increase of anti-HBs prevalence to 15.4% can be explained by the increased awareness of the illness and adult vaccination. In the third period, between 2010 and 2015, the effect of vaccination can be partly observed. In this period, the decrease in the rate of HBsAg-positive patients to 3.08% and the increase in anti-HBs positives to 19.5% were found to be statistically significant ($p<0.001$).

After vaccination started, good results have been reported from Turkey and all over the world. Since the implementation of national vaccination program for HBV for all children and risk groups, a decline in the prevalence of HBV has been observed (26). A study from the United States shows patterns in the success of vaccination in healthcare workers (27). In our study, we evaluated the vaccinated population in our third group. The patients of 15-17

Table 1. The seroprevalence of hepatitis B surface antigen in three different periods

Time period	Female			Male			Total		
	Positive	Total	%	Positive	Total	%	Positive	Total	%
1995-2002	27	2951	0.91	245	2147	11.41	272	5098	5.34
2003-2009	46	1198	3.84	475	9645	4.92	521	10843	4.80
2010-2015	68	4642	1.46	242	5418	4.47	310	10060	3.08
1995-2015	141	8791	1.60	962	17210	5.59	1103	26001	4.24

Table 2. The seroprevalence of anti-hepatitis B in three different periods

Time period	Female			Male			Total		
	Positive	Total	%	Positive	Total	%	Positive	Total	%
1995-2002	343	2951	11.62	383	2147	17.84	726	5098	14.24
2003-2009	699	1198	58.35	976	9645	10.12	1675	10843	15.45
2010-2015	957	4642	20.62	1012	5418	18.68	1969	10060	19.57
1995-2015	1999	8791	22.74	2371	17210	13.78	4370	26001	16.81

years of age were totally 287 patients with no HBsAg positivity and 30.3% anti-HBs positivity that are significantly higher than the rest of the group that is 19.2% ($p<0.001$). The study sample was quite small, when the number of vaccinated patients reaches that of non-vaccinated ones, more clear results can be obtained. Among the people born before the vaccination started, the prevalence of HBV is still relatively high. Although the awareness against the disease has increased, the routes of transmission of the virus and the need for vaccination are not known enough, thus, the prevalence rates of HBV in Turkey are much higher than those in the developed countries.

Despite the availability of safe and effective vaccine for more than 17 years, because of its asymptomatic nature, chronic HB remains a serious health problem.

Ethics

Ethics Committee Approval: Medical Park Local Ethics Committee, Informed Consent: None (a retrospective study).

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Yavuz Furuncuoğlu, Recep Öztürk, Design: Yavuz Furuncuoğlu, Füsun Bölükbaş, Data Collection or Processing: Yavuz Furuncuoğlu, Filiz Sağlam, Cengiz Bölükbaş, Analysis or Interpretation: Yavuz Furuncuoğlu, Filiz Sağlam, Literature Search: Yavuz Furuncuoğlu, Filiz Sağlam, Writing: Yavuz Furuncuoğlu, Filiz Sağlam.

Conflict of Interest: No conflict of interest was declared by the authors.

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