

ORIGINAL ARTICLE

Medicine Science 2020;9(4):967-9

Research into Hepatitis B seroprevalence among children aged 1-18 years in Usak province and comparison with seroprevalence in other provinces and Turkey Selcuk Gurel,  Mehmet Ucar¹*Department of Pediatrics, Faculty of Medicine, Bahcesehir University, Istanbul, Turkey*

Received 09 July 2020; Accepted 17 August 2020

Available online 30.10.2020 with doi: 10.5455/medscience.2020.07.131

Abstract

Hepatitis B (HBV) infection is a significant health problem around the world. Turkey is a country with moderate endemicity. This study aims to investigate the seroprevalence of HBV and anti-Hbs seropositivity among children and young adults aged 1 to 18 years living in Usak province of Turkey. This is a retrospective review of 720 children, 394 boys and 326 girls, aged 1 to 18 years who were admitted to Usak Private Medical Park Hospital for any reason between January 2017 and December 2018. Anti-Hbs seropositivity was identified in 471 children including 63% of the boys (249/394) and 68% of the girls (222/326) in the study cohort. Only one case of HbsAg positivity (0.001%) was specified among 720 children. Anti-Hbs seropositivity was 83% in Group 1 (82/99), 61% in Group 2 (62/101), 55% in Group 3 (51/92), 56% in Group 4 (43/77) and 66% in Group 5 (233/350). To the best of our knowledge, this hospital-based cross-sectional study is the first clinical research of the 1-18-year age group for HbsAg seroprevalence and anti-Hbs seropositivity in Usak province. When compared with other provinces and Turkey in general, HbsAg seropositivity rate is relatively low in this study.

Keywords: HBV, seroprevalence, childhood, vaccination**Introduction**

Hepatitis B (HBV) is a virus that may cause both acute and chronic disease. The World Health Organization (WHO) estimated that 257 million people were living with chronic HBV infection in 2015. In 2015, 887000 deaths were reported due to cirrhosis and hepatocellular carcinoma, mostly derived from HBV infection [1].

Turkey is located in a region with moderate endemicity, with 6500 new cases reported each year in spite of vaccination. In highly endemic regions, HBV is transmitted mainly through perinatal or horizontal routes or by exposure to infected body fluids. Vaccination is the cheapest and most effective method for protection against HBV infection.

In Turkey, the HBV vaccination was included in the national vaccination program in 1998. Beginning during the neonatal period, it is administered in three doses at 0, 1 and 6 months [2].

After full dose vaccination, immunity is induced in 95% of children and adolescents and 90% of adults [3]. In healthy individuals, serum anti-HBs level being 10 mIU/mL and above is accepted as protective against HBV infection [4].

The clinical progression of HBV infection is associated with the age at the time of infection. It is symptomatic in only 10% of affected children and 20-30% of affected adults. In adults, 1% of acute HBV infections has fulminant progression and may require liver transplantation. HBV may become chronic in 90% of the cases if transmitted during the perinatal period, in 20-30% of the cases if transmitted up to the age of five and 2-5% of the cases if transmitted in adults [5]. In Turkey, one out of every three people under the age of 18 years has encountered HBV and more than two million adults have HBV antigen (HbsAg) positivity. Of these people, only about 12% were identified to be aware of this situation [6]. This is significant in terms of showing that awareness about this situation is very low in our country.

This study aims to investigate the seroprevalence of HBV among children and young adults aged 1 to 18 years living in Usak province of Turkey.

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Material and Methods

This is a retrospective review of 720 children, 394 boys and 326 girls, aged 1 to 18 years who were admitted Usak Private Medical Park Hospital for any reason between January 2017 and December 2018. Ethical approval was obtained from Usak University Education and Research Hospital (grant no: 212-06, date: 11.07.2019)

Children were allocated in 5 groups according to age: 1-3 years (Group 1), 4-6 years (Group 2), 7-10 years (Group 3), 11-14 years (Group 4) and 15-18 years (Group 5). As the vaccination program encompasses the first six months of life, the children and young adults aged 1 to 18 years were included in this clinical search. The children and young adults who had no data related with HbsAg positivity and anti-HBs levels were excluded from this study.

HbsAg positivity and anti-HBs levels were assessed by Micro Enzyme Linked Immunosorbent Assay (ELISA) method on an Abbott Architect (USA) device in accordance with the recommendations of the manufacturer. HbsAg level >0.9 COI and anti-HBs level >10 IU/L were accepted as positive. HbsAg positivity and anti-HBs levels were examined according to sex and age group in this study.

Collected data were analyzed by Statistical Package for Social Sciences version 22 (SPSS IBM, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to test the data distribution. Mann-Whitney U, ANOVA and post-hoc tests were used for the comparisons. Two-tailed p values less than 0.05 were accepted to be statistically significant.

Results

The study included 720 children, with 394 boys and 326 girls. Of the 720 children, only one was identified to have HbsAg positivity (0.001%).

Anti-Hbs positivity was specified in 471 children including 63% of the boys (249/394) and 68% of the girls (222/326) in the study cohort. There was no statistically significant difference between the boys and girls in terms of anti-HBs positivity ($p=0.169$) (Table 1).

Table 1. Anti-HBs Seropositivity by Sex

Sex	Anti-HBs negative	Anti-HBs positive
Male	145 (37%)	249 (63%)
Female	104 (32%)	222 (68%)
Total	249 (35%)	471 (65%)

Mann-Whitney U test, $p=0.169$

Table 2 shows anti-Hbs seropositivity in age group. Anti-HBs seropositivity was 83% in Group 1 (82/99), 61% in Group 2 (62/101), 55% in Group 3 (51/92), 56% in Group 4 (43/77) and 66% in Group 5 (233/350). There were significant differences among the age groups in terms of anti-HBs seropositivity ($p=0.001$). Post hoc analysis was performed to designate Group

1 (1-3 years) as the age group which resulted in statistical significance among the age groups. The first group was identified to be significantly higher in comparison with Group 2 ($p=0.009$), Group 3 ($p=0.001$), Group 4 ($p=0.002$) and Group 5 ($p=0.025$). Comparisons between the other age groups did not display any statistical significance.

Table 2. Anti-HBs Seropositivity by Age groups

Groups	n	Anti-HBs positive	Anti-HBs negative
1-3 years	99	82 (83%)	17 (17%)
4-6 years	102	62 (61%)	40 (39%)
7-10 years	92	51 (55%)	41 (45%)
11-14 years	77	43 (56%)	34 (44%)
15-18 years	350	233 (66%)	117 (34%)
Total	720	471 (65%)	249 (35%)

Anova test, $p = 0.001$

Post-hoc analysis, Group 1 vs 2, $p = 0.009$; Group 1 vs 3, $p = 0.001$;

Group 1 vs 4, $p = 0.002$; Group 1 vs 5, $p = 0.025$

Discussion

This hospital-based and cross-sectional study indicated anti-HBs positivity as 65% in children and young adults aged 1 to 18 years who are living in Usak province. Complying with literature, no significant correlation was identified between sex and anti-HBs positivity [7].

Since HBV vaccination was added to the national vaccination program in 1998, there has been a prominent increase in HbsAg seroprevalence and decrease in anti-HBs seropositivity. The best example of this is a study of children living in Sanliurfa by Kösecik et al. in 1997 when HbsAg seroprevalence was 12.5% [8]. In 2002, the study by Zeyrek et al. identified HbsAg seroprevalence as 2% and anti-HBs seropositivity as 31% in Sanliurfa [9].

Turkey is located in a region with moderate endemicity for HBV infection. HbsAg seroprevalence was found to be 0.001 in this study. This low value indicates that routine HBV vaccination program has been performed successfully and efficiently. Before being included in the national vaccination program, HbsAg seroprevalence was reported to differ between 0.7% and 8.3% with anti-HBs seropositivity of 6.6% to 13.3% in the pediatric age group [10]. In the United States of America, HBV vaccination was included in the national vaccination program in 1991 and a study of children over the age of six reported that HBV seroprevalence was reduced by 68% between 1996 and 2004 [7].

Studies performed in various provinces of Turkey yielded different seroprevalence rates. HbsAg seroprevalence was 2.4% and anti-HBs seropositivity was 79% in a study of 0 to 18-year-old individuals living in Rize [11]. On the other hand, HbsAg seroprevalence was 0.2% and anti-HBs seropositivity was 72.5% in a cohort of 0 to 18-year-old individuals living in Van [12]. A study by Altan et al. identified the HbsAg seroprevalence as 0.8%, and anti-HBs seropositivity as 75.3% in Turkish children

and young adults [13]. A study in Karabük province found HbsAg seroprevalence as 0.2% and anti-HBs seropositivity as 61.1% in the pediatric age group [14]. Another study in Sivas identified HbsAg seroprevalence as 0.001% and anti-HBs seropositivity as 68.3% in a cohort of children and young adults [15]. A study in İstanbul clarified anti-HBs seropositivity as 88.5% for children aged nine months to three years and 89.5% for children aged three to five years [10]. A similar study conducted in İstanbul found anti-HBs seropositivity as 96.2% in one to five-year-old children [16]. A study held in Manisa identified anti-HBs seropositivity as 86.8% [17]. Another study in Antalya reported anti-HBs seropositivity as 99% in a cohort of 200 infants with an age of ten months and complete vaccination [18].

As for the present study, seroprevalence rates were similar to those in Karabük, Sivas and Van, and lower than the rates evaluated in other provinces. The main reasons for this finding are the reduction of seroprevalence by increasing age and the inclusion of younger children who received three-dose vaccination. In the present study, anti-HBs seropositivity is significantly higher in Group 1 (1-3 years) than the other age groups. According to literature, lower seropositivity is expected with increasing age [15, 10]. The statistically insignificant elevation in Group 5, [13-18 years) might be attributed to the increase in environmental and social exposure to HBV and activation of the immunity during adolescence. This elevation in Group 5 may be also related to the vaccination programs between 1998 and 2002 which were being performed at 3, 4 and 9 months. Similarly, the study by Altan et al. found significantly higher anti-HBs positivity in the nine-month to two-year and 12 to 16 year age groups [13]. In 15-45% of the individuals vaccinated in the first years of life and developing immunity, anti-HBs levels cannot be measured or are measured at very low levels after a period of 5 to 22 years [19]. However, studies have shown that individuals with developing immunity still have sufficient protection against HBV even if anti-HBs levels are very low [19].

To the best of our knowledge, this is the first clinical research of the 1-18-year age group for HbsAg seroprevalence and anti-HBs seropositivity in Usak province. When compared with other provinces and Turkey in general, HbsAg seropositivity is relatively low in this study. Despite the fact that three-dose vaccination rate is 97% in Turkey and 98% in Usak [5], the seropositivity in the 1-18-year age group is lower than expected. This study has been preformed to specify HbsAg seroprevalence and efficacy of HBV vaccination. The findings of the present study would help to take precautions for decreasing HbsAg seroprevalence and appoint extra measures for increasing the success rates of vaccination schedules in children and young adults.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

There are no financial supports.

Ethical approval

This study was approved by Ethical Committee of Usak University (grant no: 212-06, date: 11.07.2019).

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