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# Following-up the long-term efficacy of hepatitis B vaccine in immunization of risky occupational groups

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**Abstract**

Hepatitis B virus (HBV) infection is very common and contagious public health problem with serious pathological consequences (i.e. chronic liver failure, cirrhosis, hepatocellular carcinoma). Since HBV is frequently reported as an occupational disease factor, exposure risk is a concerning problem especially in health-care personnel. The aim of this study is to evaluate the time-dependent change of anti-HBs titer levels in various occupational groups. In the study, 2512 cases from 12 different occupational groups with HBV exposure risk who were applied to Ankara Occupational and Environmental Diseases Hospital Occupational Diseases Clinic for medical screening between October 2012 and November 2018 were examined and assessed. Protective titer levels of anti-HBs were determined in 64.8% people in the risky occupational group. HBV seropositivity rates were found as highest in dentists (94.5%) and lowest in kitchen workers (40.1%). The protective anti-HBs titer level in healthcare workers (i.e. dentist, x-ray technician, supporter healthcare personnel) was found to be 89.4%. Those with anti-HBs titer protective level (≥ 10 mIU / ml) were defined as Group-1 (n=1631), and those with Ab level (<10 mIU / ml) who were vaccination recommended and called for re-control defined as Group-2 (n=832). After the followe-up period, it was determined that the anti HBs titer fell below the protective level in 3% of Group-1, while 44.8% (n: 175) in Group-2 were vaccinated and all were immunized. This data shows that despite occupational exposure risk, vaccination following-up is not sufficient in workplace health units. Consequently, anti-HBs levels of workers who will work in high HBV exposure risky occupations should be screened and a vaccination program should be designated for those without protective titer level. Anti-HBs levels should be monitored since decrease in protective titer level depending on time. Adult vaccination is as important as childhood vaccination especially in occupational health and safety.

**Keywords:** Hepatitis B virus (HBV), anti-HBs titer, vaccination, occupational exposure

## Introduction

Hepatitis B virus (HBV) can cause both acute and chronic infections by effecting the liver. In high endemic regions, HBV usually passes from mother to child through the perinatal or horizontal route. HBV can also spreads through infected blood or body fluids. The hepatitis B virus can live outside the body for at least 7 days, and during this time it can still infect other people. The World Health Organization (WHO) reports that an estimated 257 million people have been infected with HBV in 2015, while 887,000 died from cirrhosis and hepatocellular carcinoma due to chronic hepatitis. The protection rate of hepatitis B vaccine varies between 98-100% [1]. WHO predicts that viral hepatitis will cease to be a risk that threatens public health and the risk of new infections will decrease by 90% by 2030 [2]. HBV infection is the most frequently reported occupational disease among health-care personnel [3].

Centers for Disease Control and Prevention (CDC) recommends that health-care personnel should be evaluated by testing HBV antibodies and managed according to occupational risks, in order to protect them from HBV infection after recruitment period [4].

Health-care personnels and students, medical waste workers, hospital cleaning workers, security personnel such as police,

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gendarmerie, prison execution protection officers, detention center officers and private security officers, barbers, hairdressers, first aiders in accidents and other disasters, staff works in emergencies or disasters, and in extraordinary situations, are at risk for the HBV infection [5]. Anti-HBs titer ≥ 10 mIU / ml is considered protective titer according to WHO recommendations [6].

Antibody titer level against hepatitis B surface antigen decreases over time [7]. Smoking, obesity, chronic diseases, using of drug, diabetes, male gender, age, genetic factors and suppressed immune also cause decrease in the vaccine response [8]. Besides, it was also shown that antibody protection has continued for more than 22 years in individuals who has immunocompetent response to vaccine [9].

Advisory Committee on Immunization Practices (ACIP) and CDC recommends to test healthcare workers for anti-HBs level prior to occupational exposure; no additional treatment if the antibody titer level is ≥10mUI / mL, administer one or more additional HBV vaccines if the level is <10mUI / mL, and to reassess the antibody titer level again [10]. Similarly, The Occupational Health and Safety Administration (OSHA) requires employers to recommend HBV vaccination to all employees with occupational risk, thereby ensuring that post-exposure prophylaxis is already available [10]. By appropriate vaccination programs, from 1983 to 2010, HBV infection rate among healthcare personnel has decreased by 98%, from about 17,000 infections to 263 acute HBV infections [11].

Based on the Occupational Health and Safety Law No. 6331 in our country, employers are obliged to take protective measures including safe and effective vaccines for workers at risk, with the regulation on the prevention of exposure to biological agents [12].

The aim of this study is to determine the levels of anti-HBs in people of 12 different occupational groups, including healthcare workers, who are at risk of HBV infection, and to analyze the change of antibody levels of those with anti-HBs titer level ≥10 mIU/mL during follow-up time. HBV infections can be reduced to a minimum with general precautions, vaccination, preventive measures and post-contact management, therefore, this study aims to raise awareness in following-up of anti-HBs protective titer levels especially among workplace physicians who manage risky occupational groups and family physicians who carry out vaccination process of people as a first healtcare stage.

## Materials and Methods

This study was conducted on workers who applied to the Occupational Diseases Polyclinic of Ankara Occupational and Environmental Diseases Hospital between October 2012 and November 2018 for medical screening. Occupational groups with high risk of exposure to HBV virus (dentist, nurse, health officer, dental technician, x-ray technician, health worker cleaning staff, health worker office clerk, firefighters, waterpipe worker, hairdresser, navvy, security staff) were included in the study.

Ethical approval was obtained from the Clinical Research Ethics Committee of Keçiören Education and Research Hospital (2012-KAEK-15/2006); a descriptive cross-sectional study was carried out and then the study continued as a retrospective cohort.

Demographic information and laboratory results of totally 2512 people were accessed from the hospital information management system (HIMS) and from patient files. Anti-HBs level ≥10 mIU / mL were considered as protective titer levels.

From 2512 total cases, 49 cases, of which 48 were HBS Ag positive and 1 anti-HCV positive, were excluded from the study. The data of remaining 2463 cases from 12 different professions were analysed. Immunization table of all cases included in the study was created. Of the cases, those with anti-HBs titer protective level were defined as Group-1; below the protective titer, and those who were recommended for vaccination and called for re-control were defined as Group-2.

Group-1 was followed up for preventive titer levels. Six-year protective titer levels were compared and time-dependent variation rates were calculated statistically. The patients with positive Hepatitis B surface antigen (HBsAg), Hepatitis B core antigen antibody (Anti-HBc), Hepatitis C virus antibody (Anti-HCV), Human immunodeficiency virus antibody (Anti -HIV) and those who have been vaccinated during the following-up period were excluded from the study. Also the cases having chronic diseases (i.e., diabetes mellitus, hypertension, chronic liver disease, immune deficiency etc.) were excluded since the chronic diseases could have altered the immun response of the organism and affect the Ab levels.

Anti-HBs titer levels of Group-2 were assessed after vaccination, and immunization rates were statistically evaluated

Hepatitis and HIV biomarkers were analyzed using Enzyme-linked Immunosorbent Assay (ELISA) Kits (Organon Teknika, Amsterdam, The Netherlands). Data of all cases were evaluated statistically using “The Statistical Package for Social Science” for Windows (SPSS v21, SPSS Inc, Chicago, IL, USA). Student’s t test was used for parametric data and Mann – Whitney U test was used for nonparametric data.

## Results

The schematic diagram of the case groups is presented in figure 1 (Figure 1). The total number of cases included in the study from 12 different occupational groups was 2463. The number of anti-HBs titer levels <10 mIU / mL and ≥10 mIU / mL were 832 (33.8%) and 1631 (66.2%), respectively. No anti-HIV positive cases were determined. 531 people in Group-1 and 390 people in Group-2 came for control and could be followed-up.

The seronegativity rates of occupational groups in terms of hepatitis B immunization were as follows; 5.5% in dentists, %14.3 in healthcare personnel assistant, 17.6% in x-ray technicians, 37.8% in healthcare office staff, 43.4% in healthcare cleaning staff, 46.5% in firefighters employees, 46.6% in waterpipe workers, 46.7% in hairdressers, 48.4% in navvy, 54% in security staff, 56.7% in printing workers, 59.9% in kitchen personnel. Consequently, the highest seropositivity was found in dentists and the lowest seropositivity was found in kitchen personnels (Table 1).

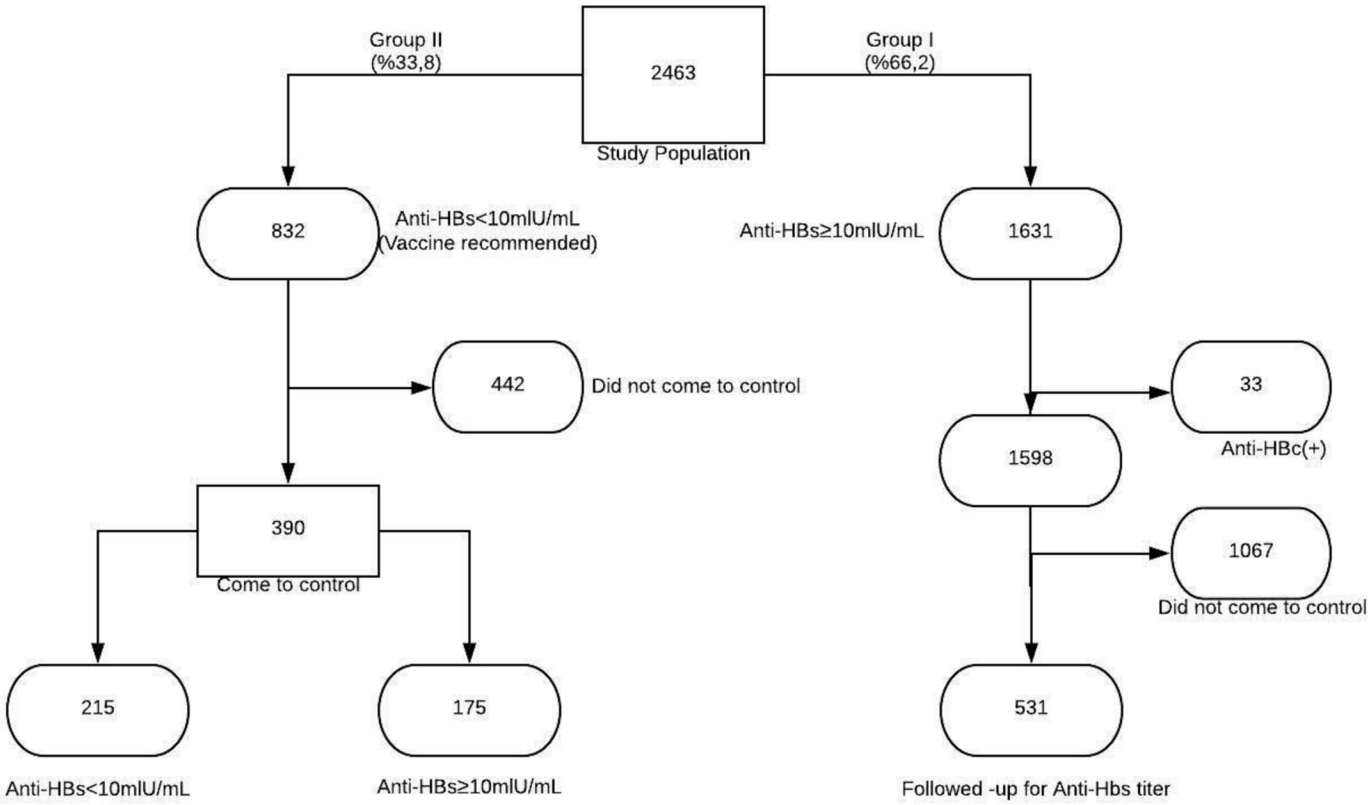


**Figure1.** Schematic diagram of case groups. As 1631 (Group-1) people with anti-HBs level above the protective titer (≥10 mIU / ml) and 832 people (Group-2) with anti-HBs level below the protective titer (<10 mIU / ml), totally 2463 people from 12 different profession groups were included in the study. Anti-HBs levels of 531 individuals from Group-1 cases could be monitored. It was determined that 175 (44.8%) of 390 people who came for control from Group-2 cases had been vaccinated and immunized

**Table 1.** Distribution of hepatitis immunization rates by occupation (n=2463)

| Occupational Groups (n) | Anti-HBs (-) (<10mIU/ml) | Anti-HBs (+) (0-99.9) mIU/ml | Anti-HBs (+) (≥100 mIU/ml) |
|---|---|---|---|
| **Kitchen personnel (172)** | 103 (59.90%) | 37 (21.5) | 32 (18.6) |
| **Printing workers (60)** | 34 (56.70%) | 11 (18.3) | 15 (25) |
| **Security staff (50)** | 27 (54%) | 14 (%28) | 9 (%18) |
| **Navvy (93)** | 45 (48.40%) | 14 (%15.1) | 34 (%36.6) |
| **Hairdressers (46)** | 7 (46.70%) | 4 (%26.7) | 4 (%26.7) |
| **Waterpipe workers (58)** | 27 (46.60%) | 13 (%22.4) | 18 (%31) |
| **Firefighters (804)** | 374 (46.50%) | 216 (%26.9) | 214 (%26.6) |
| **Healtcare cleaning staff (99)** | 43 (43.40%) | 17 (%17.2) | 39 (%39.4) |
| **Healtcare office staff (201)** | 76 (37.80%) | 69 (%34.3) | 56 (%27.9) |
| **X-ray technician (74)** | 13 (17.60%) | 21 (%28.4) | 40 (%54.1) |
| **Healthcare personnel assistant *(nurse, dental tecnician, laboratory workers, medical workers) (419)** | 60 (14.30%) | 128 (%30.5) | 231 (%55.1) |
| **Dentist (418)** | 23 (5.50%) | 105 (%25.1) | 290 (%69.4) |
| **Total (2463)** | 832 (33.8) | 649 (%26.3) | 982 (%39.9) |

Thirty-three healthcare personnel in Group 1 who were found to be anti HBc positive were excluded These cases were, HBs Ag negative and vaccination history. Of the remaining 1598 (64.8%) cases, 1067 did not come to the titer level control and 531 cases with a protective antibody level were followed up. Of these cases, 345 (65%) were male and 186 (35%) were female. The mean age of first control was 42.5 years ± 9.9 years, and the mean age of last control was 44.7 ± 9.6 years. The average follow-up period was 25.5 ± 18.2 months. The mean anti-HBs Ag titer level in first control and final control were 381.4 ± 364 mIU / mL and 212.8 ± 264.6 mIU / mL, respectively. The decrease rate in total titer level at the end of following-up was found to be 55.8%. During follow-up, no titer level decrease was observed in 27 (5.1%) of 531 cases, while 504 (94.9%) cases showed decrease in protective titer level (Table 2 and 3). The anti-HBsAg titer level of 16 (3%) cases was <10 mIU / mL, while 97% (515) cases remained at the protective titer level.

The first control and last control antibody titer levels of 16 cases in Group-1, whose anti HBs level decreased below 10 mIU/mL durind follow-up time are presented in Table 4. It was observed that the titer protection due to the vaccination varies among individuals.

**Table 2.** Group-1 Anti-HBsAg protective titer level follow-up results (n = 531)

| | First Control | Last Control |
|---|---|---|
| **Anti-HBs Ag mIU/mL (mean)** | 381.4 ±364 | 212.8±264.6 |
| **Anti-HBs Ag negative (0-9.9 mIU/ml) (n; %)** | -* | 16 (%3) |
| **Anti-HBs antibody positive titer level (10-99.9 mIU/ml) (n; %)** | 165 (%31.1) | 246 (%46.3) |
| **Anti-HBs antibody titer level ( ≥100 mIU/ml) (n;%)** | 366 (%68.9) | 269 (%50.7) |
| **Protective titer level percentage (%)** | %100 | %97 |

**Table 3.** Occupational information and first control and last control protective titer levels of Group-1 (n = 531)

| Occupational Groups | Anti-HBsAg (<10 mIU/ml) | | Anti-HBsAg (10-99.9 mIU/ml) | | Anti-HBsAg (≥100 mIU/ml) | | Anti-HBs ( mIU/ml) (Mean. ±SS) | |
|---|---|---|---|---|---|---|---|---|
| | First Control (n%) | Last Control (n%) | First Control (n%) | Last Control (n%) | First Control (n%) | Last Control (n%) | First Control | Last Control |
| **Kitchen personnel (n=16)** | 0 | 0 | 3 (18.8%) | 9 (56.3%) | 13(81.3%) | 7 (43.8%) | 317.9±239.9 | 96.5±83.3 |
| **Navvy (n=3)** | 0 | 1(33.3%) | 1 (33.3%) | 0 (0%) | 2 (66.7%) | 2 (66.7%) | 260.2±230.3 | 132.5±107.5 |
| **Hairdresser (n=1)** | 0 | 0 | 0 | 0 | 1 (100%) | 1 (100%) | 1000 | 995 |
| **Firefighters (n=223)** | 0 | 5 (2.2%) | 99 (44.4%) | 129 (57.8%) | 124 (55.6%) | 89 (39.9%) | 214±265 | 146.4±198.5 |
| **Healthcare cleaning staff (n=10)** | 0 | 0 | 1 (10%) | 4 (40%) | 9 (90%) | 6 (60%) | 644.9±400.5 | 241.5±302.3 |
| **Healthcare office staff (n=38)** | 0 | 3 (7.9%) | 14 (36.8%) | 23 (60.5%) | 24 (63.2%) | 12 (31.6%) | 447.4±384 | 124±144.2 |
| **X-ray technician (n=27)** | 0 | 0 | 8 (29.6%) | 14 (51.9%) | 19 (70.4%) | 13 (48.1%) | 418.6±368.3 | 234.6±263.4 |
| **Healthcare personnel assistant (n=75)** | 0 | 3 (4%) | 15 (20%) | 25 (33.3%) | 60 (80%) | 47 (62.7%) | 513.4±376.9 | 296±323.9 |
| **Dentist (n=138)** | 0 | 4 (2.9%) | 24 (17.4%) | 42 (30.4%) | 114 (82.6%) | 92 (66.7%) | 541±384.5 | 302.4±311.4 |
| **Total** | 0 | 16* | 165 | 246 | 366 | 269* | 381.4 ±364 | 212.8±264.6 |

**Table 4.** Titer level and time relation analysis of 16 cases whose antibody titer level decreased to non-protective level (<10 mIU/mL) (Group-1)

| | Occupation | Anti-HBsAg First Control | Anti-HBsAg Last Control | Followed-up period (month) |
|---|---|---|---|---|
| **1** | Healthcare personnel office staff | 1000 | 8.37 | 36 |
| **2** | Healthcare personnel office staff | 94.43 | 0 | 54 |
| **3** | Healthcare personnel office staff | 66.64 | 0 | 55 |
| **4** | Dentist | 15.29 | 7.76 | 36 |
| **5** | Dentist | 22.84 | 8 | 36 |
| **6** | Dentist | 45.24 | 8.48 | 55 |
| **7** | Dentist | 175.61 | 6.13 | 55 |
| **8** | Firefighters | 11.7 | 9.48 | 12 |
| **9** | Firefighters | 18 | 9.53 | 12 |
| **10** | Firefighters | 19.4 | 7.15 | 11 |
| **11** | Firefighters | 10.8 | 2.92 | 30 |
| **12** | Firefighters | 13.94 | 2.07 | 50 |
| **13** | Waterpipe workers | 15.33 | 8.75 | 65 |
| **14** | Healthcare personnel assistant | 12.16 | 9.41 | 39 |
| **15** | Healthcare personnel assistant | 460.23 | 8.77 | 54 |
| **16** | Healthcare personnel assistant | 208.01 | 0 | 55 |

When the correlation between the follow-up time and the first control / last-control anti-HBs titer level difference was evaluated, it was observed that the titer level difference increased as the following-up time increased, that is, there was a positive-low, moderately significant correlation between the follow-up time and the titer level difference. (R = 0.376; p <0.0001).

Only 390 people in Group-2 applied for re-control. Anti-HBs level was found to be ≥10 mIU / ml in all 44.8% (n: 175) of the cases who had either a single dose or more Hepatitis B vaccine. The antibody level was found to be <10 mIU / mL in 215 other cases (55.2%) who had no vaccination despite the recommendation.

When immunization rates of healthcare professionals (dentist, x-ray technician, healthcare personnel assistant (n=911)) are evaluated separately from other professions, 89.4% (n: 815) was found to be anti-Hbs ≥10.

**Discussion**

Hepatitis B vaccine was included into childhood vaccination schedule in 1998 in Turkey and it has been applied to every child after birth since 2003. As of this date, it is also applied to all adults free of charge who involved in certain risk groups. Vaccine coverage has increased steadily in recent years and the vaccination rate, which was 64% in 1999, increased to 98% by 2016 [2,5]. According to 2016-2021 global health sector strategy on viral hepatitis of WHO, it was predicted that, viral hepatitis will be no longer a risk that threatens public health by 2030. Also it is expected to observe 90% reduction of the risk of new infections, 80% reduction of hepatitis patients who may be treated, and a reduction in the mortality rate due to hepatitis to 65% [2].

According to the data obtained in our study; an average of 64.8% seropositivity was detected against HBV in risky occupational groups. This data indicates that vaccination awareness should be strengthened according to the occupational health and safety management system in our country. Workplace physicians should examine the personnel especially for HBV and perform required tests during recruitment. HBsAg positivity was found as 4% and antiHBc positivity was found as 30.6% in a study conducted on people over the age of 18 in 2009 in our country [13].

In our study, considering the seropositivity rates of risky occupational groups in terms of hepatitis B immunity, the highest rate was found in dentists and the lowest rate was found in kitchen workers. The rate of vaccination for hepatitis B in all healthcare personnel was determined as 89,4%. The WHO and the ACIP recommend that healthcare personnel should have the hepatitis B vaccination according to occupational health and safety management regulations. The rates of hepatitis B vaccination of health personnel varies in different countries as; 64.7% in the USA [14], 72.2% in Canada, 91.8% in France [15] and 70.1% in Italy [16]. The rate is 26 to 86% for Turkey [17,18].

In our study, the health personnel of "Oral and Dental Health Hospital" with anti HBc positive (1.5%), had anti-HBs level ≥10 mIU / mL, HBs Ag negative and had vaccination histories. It was concluded that some of these personnel were actively exposed to virus and the nucleus antigen antibody became positive.

According to the 2017-2019 National Vaccine Prevention Plan, sufficient immunization intervention is required to prevent and control transmission of HBV to ensure the protection of healthcare personnels who are already at maximum risk for exposure to HBV infection [19].

In our study, it was found that the anti-HBs protective titer level decreased over time. The Anti-HBs titer level of 531 cases was followed-up for an average of 25.5 ± 18.2 months; no changes were observed in 27 (%5) cases, the titer level of 504 (%94) cases decreased and in 16 (%3) cases eventually decreased below protective level (<10 mIU/ml) . After the followe-up period the protective antibody titer level of participants who were seropositive for Hepatitis B, decreased from 100% to 97%. There was a low-moderate but statistically significant correlation (r=0.376; p<0.0001). Between the follow-up time and of basal and last control anti-HBs titer level difference Studies show that anti-HBs titer levels tend to fall below the threshold of 10 mIU/mL depending on time in vaccinated cases. In a study by Alavian SM et al., it was found that protective antibody titer level decreased from 100% to 80.7% after 16 years period in participants who vaccinated against HBV [20]. Similarly, in a study of McMahon BJ et al. Protective antibody titer level was found to be decreased from 88% to 84% after 15 year period [21], Simo Minana et al. Concluded that the protective antibody titer level decreased by 50% after 7.5- 10.5 years [22]. In the study by Darvish Moghaddam et al., the level of protective antibody decreased to 98% after a year, to 94% over a 2- 5 year period, to 84% after a 5- 10 year period and similar to the result of Dienstag et al. Study, antibody re-detection is recommended after 5-10 years of first vaccination [23,24]. Coursaget et al. Recommends that individuals with titers of 10, 100 or 1000 mIU/mL should be vaccinated again after 2,5, 10 or 40 years, respectively, in order to keep anti-HBs titer levels above 10 mIU/mL in at least 90% of vaccinated individuals [25].

Genetic characteristic of host, age of vaccination, and the dose of vaccine are the factors that affect the duration of anti-HBs protective dose titer level [26,27]. One study concluded that the higher the antibody response after the primary vaccination cycle, the longer the anti-HBs concentration remains above the threshold of 10 mIU/mL [28]. Lastly in 2018, it was suggested by ACIP that healthcare personnel should be tested for anti-HBs levels prior to occupational exposure; one or more additional HBV vaccination should be done for those with levels below 10mIU/mL, anti-HBs concentration and subsequent re-testing also should be carried [10].

Despite the recommendation, the rate of vaccination was 44,8% (n: 175) in Group-2, suggesting that staff of workplace health units do not have sufficient awareness of vaccination against HBV in risky occupational groups.

A routinely antibody test is not recommended before or after vaccination by WHO. However, post-vaccination tests are recommended for personnel in risky occupational group (i.e. healtcare personnel) who are likely to be exposed to HBV infection. Antibody tests should be performed 1-2 months after the last dose of the vaccine series, using a method capable of quantitative measurement with a detection limit of <10 mIU / mL [29]

WHO [29], ACIP [10], CDC [30], the Occupational Health and

Safety Law [12] and HBV public health program recommend to primary care physicians and occupational physicians to develop vaccination strategies for all adults at risk for HBV infection.

## Conclusion

As a result; since anti-HBs protective titer level control time interval determination will vary individually, Anti-HBs level should be tested in occupational groups with high risk of HBV exposure before exposure. The vacination should be done to those without protective titer level and followed-up to keep the anti-HBs protective titer level. Especially workplace physicians whose primary aim is preventive medicine, family physicians and public health experts should follow up risky occupational groups for vaccination. "Which occupation you have?, What is your job?" questions have gained importance by Bernardino Ramazzini, who is considered the father of occupational diseases, these should be queried. The fact should be kept in mind that adult vaccination is as important as childhood vaccination to ensure the occupational health and safety.

**Conflict of interests**
*The authors declare that they have no conflict of interest.*

**Financial Disclosure**
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**Ethical approval**
*This study was approved by Research Ethics Committee of University of Health Sciences Kecioren Training and Research Hospital (Decision No: 2012-KAEK-15/2006). All participants signed their informed consent prior to this study.*

## References

1. Hepatitis B fact sheet. In: World Health Organization: media centre July 2016 update. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b accessed date 04.23.2020.
2. Global Hepatitis Report 2017, page 9.ISBN 978-92-4-156545-5, Geneva: World Health Organization;2017. https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf;jsessionid=BCDD1746BC15449CCA67A7DBAA1BA8A0?sequence=1 accessed date 04.22.2020.
3. Szeszenia-Dąbrowska N, & Wilczyńska U. Occupational diseases in Poland-An overview of current trends, Int J Occup Med Environ Health. 2013;26:457-70.
4. Hamborsky J, Kroger A, Wolfe S.13th edition. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Chapter 10: Hepatitis B, page:167, Washington D.C. Public Health Foundation, 2015. Available at: https://www.cdc.gov/vaccines/pubs/pinkbook/index.html
5. Turkey Viral Hepatitis Prevention and Control Program, page 6, ISBN: 978-975-590-688-1 Ministry of Health Publication No 1102, 2018, Ankara. Available at: https://hsgm.saglik.gov.trdepo/birimler/Bulasici-hastaliklar-db/duyurular/Turkiye_ Viral_Hepatit_Onleme_ve Kontrol_ Programi/ Turkiye_ Viral_Hepatit_ Onleme_ve_ Kontrol_Programi_TR.pdf
6. Weekly Epidemiological Record (WER), World Health Organization. October 2009; 84 (40): 405-20. Available at: https://www.who.int/wer/2009/wer8440.pdf?ua=1
7. Leuridan E, Van Damme P. Hepatitis B and the need for a booster dose. Clin Inf Dis. 2011;53:68-75.
8. Averhoff F, Mahoney F, Coleman P, et al. Immunogenicity of hepatitis B Vaccines. Implications for persons at occupational risk of hepatitis B virus infection. Am J Prev Med. 1998;15:1-8.
9. Coppeta L, Pompei A, Balbi O, et al. Persistence of immunity for hepatitis B virus among heathcare workers and italian medical students 20 years after vaccination. Int J Environ Res Public Health. 2019;16:1515.
10. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. Recommendations and Reports /January12, 2018; 67(1):1-31. https://www.cdc.gov/mmwr/volumes/67/rr/rr6701a1.htm?scid=rr6701a1_w.
11. Schillie S, Murphy TV, Sawyer M, et al. CDC guidance for evaluating health-care personnel for hepatitis B virus protection and for administering postexposure management. MMWR Recomm Rep 2013;62(No. RR-10):1–19. Available at:https://www.cdc.gov/ mmwr/ preview/mmwrhtml/rr6210a1.htm
12. Regulation on the Prevention of Exposure Risks to Biological Factors, health surveillance, article16. Official Journal Date:15.06.2013/28678, Availableat:https://https://www.mevzuat.gov.tr/MetinAspx?MevzuatKod=7.5.18485&MevzuatIliski=0&sourceXmlSearch=B%C4%B0YOLOJ%C4% B0K%20ETKENLERE accessed date 04.23.2020.
13. Tozun N, Ozdogan O, Cakaloglu Y, at al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect. 2015;21:1020-6.
14. Williams WW, Lu P, O'Halloran A, et al. Surveillance of Vaccination Coverage among Adult Populations-United States, 2015. MMWR Surveill Summ. 2017;66:1-28.
15. Haviari S, Benet T, Saadathan-Elahi M, et al. Vaccination of healthcareworkers: A review. Hum Vaccin Immunother. 2015;11:2522-37.
16. Fortunato F, Tafuri S, Cozza, et al. Low vaccination coverage among Italian healthcare workers in 2013: contributing to the voluntary vs. mandatory vaccination debate. Hum Vaccin Immunother. 2015;11:133-9.
17. Ineli B.U, Akdeniz M & Kavukcu E. The Assessment of the Knowledge About Adult Vaccine, And Vaccination Coverage in Adults Aged 18 and Older In Turkey. International Journal of Scientific and Technological Research.2019;5:17-25.
18. Özgüler M, Saltik-Güngör L, Kaygusuz T, et al Hepatitis A, hepatitis B, measles, and rubella seroprevalence of healthcare workers at Elâzığ training and research hospital. Klimik J. 2016;29:10.
19. Stefanati A, Bolognesi N, Sandri F, et al. Long-term persistency of hepatitis B immunity: an observational cross-sectional study on medical students and resident doctors. J Prev Med Hyg. 2019;60:184-90.
20. Alavian SM, Mansouri S, Abouzari M, et al. Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989-2005). Eur J Gastroenterol Hepatol. 2008;20:131-4.
21. McMahon BJ, Bruden DL, Petersen, et al. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up. Ann Intern Med 2005;142:333–41.
22. Simo Minana J, Gaztambide Ganuza M, Fernandez Millan P, et al. Hepatitis B vaccine immunoresponsiveness in adolescents: a revaccination proposal after primary vaccination. Vaccine. 1996;14:103–6.
23. Darvish Moghaddam S, Zahedi MJ, Yazdani R. Persistence of immune response after hepatitis B vaccination in medical students and residents. Arch Iranian Med. 2004;7:37–40.
24. Dienstag JL, Werner BG, Polk F, et al. Hepatitis B vaccine in health care personnel: safety, immunogenicity, and indicators of efficacy. Ann Intern Med. 1984;101:34–40.

25. Coursaget, P, Yvonnet B, Chiron J. P, et al Scheduling of revaccination against hepatitis B virus. Lancet. 1991;337:1180-3.

26. Zanetti AR, Mariano A, Romanò L, et al. Study Group. Long-term immunogenicity of hepatitis B vaccination and policy for booster: an Italian multicentre study. Lancet. 2005;366:1379-84.

27. Ryckman KK, Fielding K, Hill AV, et al. Host genetic factors and vaccine-induced immunity to HBV infection: haplotype analysis. PLoS One 2010;5:12273

28. Romanò L, Galli C, Tagliacarne C, et al. Study Group Persistence of immunity 18-19 years after vaccination against hepatitis B in 2 cohorts of vaccinees primed as infants or as adolescents in Italy. Hum Vaccin Immunother .2017;13:981-5.

29. World Health Organization .Hepatitis B vaccines: WHO position paper, July 2017- Recommendations. Vaccine. 2019;37:223-5.

30. Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2020 https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html accessed date 04.3.2020