Barriers Against Hepatitis B Vaccination in High-Risk Adults: A Cross-Sectional Study

Abdullah Tarık Aslan $m{m{D}}$ ı, Başak Şaşmazer $m{m{D}}$ ı, Yasin Ayar $m{m{D}}$ ı, Zeynep Cansu Duran $m{m{D}}$ 2, Murat Akova $m{m{D}}$ 2

¹Department of Internal Medicine, Hacettepe University Faculty of Medicine, Sıhhiye Campus, Sıhhiye, Ankara, Turkey ²Department of Infectious Diseases and Clinical Microbiology, Hacettepe University Faculty of Medicine, Sıhhiye Campus, Sıhhiye, Ankara, Turkey

Cite this article as: Aslan AT, Şaşmazer B, Ayar Y, Duran ZC, Akova M. Barriers against hepatitis B vaccination in high-risk adults: A cross-sectional study. *Turk J Gastroenterol.* 2022;33(5):427-433.

ABSTRACT

Background: The hepatitis B vaccination has been strongly recommended by regulatory bodies. However, there are great discrepancies between routine practices and the recommendations of regulatory agencies in many countries. We aimed to identify the barriers against Hepatitis B Vaccination (HBV) for high-risk patients by comparing the awareness, attitude, and knowledge among vaccinated and unvaccinated patients.

Methods: A 34-item questionnaire was applied to 156 patients, consisting of renal transplant recipients, allogeneic hematopoietic stem cell transplant recipients, and patients with chronic hepatitis C. Multiple logistic regression analysis was employed to identify independent predictors for patients receiving the hepatitis B virus vaccination.

Results: The multiple logistic regression analysis revealed that the independent risk factors against the HBV vaccination were a requirement of a separate appointment for hepatitis B virus vaccination (aOR: 3.35, 95% Cl, 1.18-9.47), and fear of severe side effects that can be related with hepatitis B virus vaccination (aOR: 3.67, 95% Cl, 1.18-9.47). However, taking a recommendation for hepatitis B virus vaccination at least once from a health care provider (aOR: 0.04, 95% Cl, 0.01-0.11), and having a health insurance (aOR: 0.09, 95% Cl, 0.01-0.55) were independent protective factors for being vaccinated. In further analysis among patients with at least a single dose of vaccine, the lack of recommendation from a health care provider for hepatitis B virus vaccination and the absence of a healthcare provider who is responsible for monitoring the completion of the 3-dose vaccination were identified as independent risk factors for failure to complete the 3-dose hepatitis B virus vaccination.

Conclusion: In high-risk adults, the barriers against hepatitis B virus vaccination should be handled by a comprehensive action plan to achieve the WHO 2030 hepatitis elimination target.

Keywords: Hepatitis B virus, immunity, risk groups, vaccination

INTRODUCTION

The hepatitis B virus (HBV) infection is a significant global public health problem. The World Health Organization (WHO) estimated that 257 million people worldwide had chronic hepatitis B infection in 2015.¹ The infection can lead to compensated and decompensated cirrhosis, hepatocellular carcinoma, and acute fulminant hepatitis that can result in liver failure or death.²⁻⁴ Furthermore, HBV infections are associated with a considerable economic burden in many countries.⁵⁻⁷

The Advisory Committee on Immunization Practices (ACIP) and the WHO strongly recommend HBV vaccination as the most efficient tool for prevention of HBV infection. Although adults who are at high risk for HBV infection, including healthcare workers, persons with hepatitis C virus (HCV) infection, patients with diabetes, dialysis-dependent patients, renal transplant (RT) recipients, allogeneic hematopoietic stem-cell transplant (AHSCT) recipients, and people who constantly require blood or blood products are at the forefront of these recommendations^{1,4,8} but the advice is also extended for all adults seeking protection against hepatitis B infection.⁴ Despite the recommendations of the WHO and ACIP, HBV vaccination rates of high-risk adults are far from the optimal level, even in developed countries.9 Given the low HBV vaccination rates among highrisk patients in the literature, it is imperative to investigate the barriers against HBV vaccination in high-risk adults. Previous studies identified significant gaps in the knowledge and a wide variation in screening and immunization practices among physicians regarding HBV immunization for patients with chronic HCV infection,¹⁰ and the barriers against HBV vaccination among homosexual men.¹¹

Corresponding author: Abdullah Tarık Aslan, e-mail: aslanabdullahtarik@gmail.com Received: March 18, 2021 Accepted: July 13, 2021 Available Online Date: April 10, 2022 © Copyright 2022 by The Turkish Society of Gastroenterology · Available online at turkjgastroenterol.org DOI: 10.5152/tjg.2022.21257 To the best of our knowledge, there is no study reporting the hurdles against HBV vaccination in RT recipients, AHSCT recipients, and patients with chronic hepatitis C (CHC) in the literature. In this cross-sectional study, we aimed to identify the barriers against HBV vaccination among high-risk patients by comparing awareness, attitude, and knowledge of vaccinated and unvaccinated patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in 1000-bed tertiary-care academic hospital (Hacettepe University Faculty of Medicine Hospital). The HBV serology data of patients recruited for another study were examined after a waiver of informed consent was obtained. Patients aged \geq 18 years with a history of RT (159 recipients), AHSCT (47 recipients), and CHC (83 patients), were evaluated. The data for HBV serology and HBV DNA from January 1, 2014 to June 30, 2019 were reviewed. The patients who had chronic HBV infection, occult hepatitis B, and HBV immunity gained by previous exposure were excluded. No compensation was given to the patients for participating in the study. All data were anonymously collected on a secured dataset by the primary investigators. No identifying data were collected. The 34-item questionnaire (see supplementary data) was applied to 156 patients by telephone call. The responses to these guestions were mostly set as "Yes" and "No." This guestionnaire was constructed based on factors hypothesized to be linked to HBV vaccination in the literature, and the final 10 questions of the questionnaire were reserved for

Main Points

- Despite the recommendations of the WHO and ACIP, the hepatitis B virus (HBV) vaccination rates of high-risk adults are far from the optimal level, even in developed countries.
- The requirement for a separate appointment for HBV vaccination, and the fear of severe side effects that could occur with HBV vaccination were identified as independent risk factors against HBV vaccination.
- Taking a recommendation for HBV vaccination at least once from a health care provider and having a health insurance had a significant positive effect on vaccination.
- The lack of recommendation from a health care provider for HBV vaccination and the absence of a healthcare provider who is responsible for monitoring the completion of the 3-dose vaccination were main determinants of failure to complete the 3-dose HBV vaccination.
- In order to vaccinate the entire population of high-risk patients, possible barriers against HBV vaccination should be identified and multifaceted action plans should be constructed.

evaluation of the patients' level of knowledge about HBV. If the sum of correct answers to the 10 knowledge-based questions exceeded 5, these participants were accepted as adequately knowledgeable. The remaining questions were constructed to identify the awareness and attitude of patients against HBV vaccination. The questionnaire was piloted among 10 patients who were not included in this study, to assess its clarity and acceptability before its use in the actual study. The ethics approval for this study was obtained from Hacettepe University Local Ethics Committee (study approval identification code: GO 19/1091). Informed consent was obtained from all participants.

Statistical Analysis

Descriptive statistics were reported to demonstrate the baseline characteristics of the vaccinated and unvaccinated groups. Mean ± standard deviation or median (minimum-maximum) values were computed for continuous variables. Frequency (%) was stated for categorical variables. The normality and variance homogeneity assumptions were assessed by applying the Shapiro-Wilk test and Levene's test, respectively. The independent t-test was used for comparing 2 groups when these assumptions were satisfied. Otherwise, the Mann-Whitney U-test was applied. While comparing the 2 distinct groups in terms of categorical variables, the Pearson chi-square test or the Fisher's exact test was used. Odds ratios were utilized for comparing the vaccinated and unvaccinated groups with respect to investigated outcomes. In order to eliminate confounding factors that could affect outcomes, adjusted odds ratios (aOR) were obtained by constructing multiple logistic regression analysis (MLRA) models. Variables with a P-value <.1 in univariate analysis were studied as potential confounders. To assess the goodness of fit of the model, the Hoshmer-Lemeshow test was used. Multicollinearity analysis and correlation analysis were used to clear possible collinearity and correlation issues among variables incorporated into multiple logistic regression models. A 2-sided P-value ≤.05 was considered significant. All statistical analyses were run using Statistical Package for Social Sciences (IBM Corp.; Armonk, NY, USA) version 23.0 for Windows.

RESULTS

A total of 200 high-risk patients who had an indication for HBV vaccination were identified. Among these patients, 44 patients could not be included in this study due to the following reasons: death (10 patients), unwillingness to participate in this study (9 patients), and the inability to reach patients on their phone (25 patients). Among the 156 patients included, there were 97 RT recipients, 25 AHSCT recipients, and 34 CHC patients. The rates of lifetime self-reported HBV vaccination of at least 1 dose were 59.8% (58 patients) among RT recipients, 45.8% (11 patients) among AHSCT recipients, and 38.2% (13 patients) among CHC patients. Even in patients having type 2 diabetes mellitus as a concomitant comorbidity, the lifetime vaccination rate was 57.9%. Baseline characteristics of vaccinated and unvaccinated patients are shown in Table 1. There was no significant difference in any variable between the comparison groups. However, a trend toward significance in variables involving age (unvaccinated patients tended to be older) and having a health insurance (more patients in the vaccinated group had insurance) was detected. The adequacy of knowledge about HBV among the vaccinated and unvaccinated patients was evaluated by the final 10 questions of the questionnaire (see supplementary data). There was no significant difference between the vaccinated and unvaccinated patients in terms of rates of correct answers for any question. However, knowledge was insufficient for questions querying the most frequently affected organ in HBV infection (the rate of correct answers 58.1% among all patients), whether the incidence of chronic hepatitis B is more than 20% in Turkey (rate of correct answers was 41.3% among all patients), and 2 different transmission routes of HBV infection (rate of correct answers was 32.9% among all patients). In the remaining 7 questions, the correct answer rates were \geq 65.2% and patients were

evaluated as adequately knowledgeable. The responses of vaccinated and unvaccinated patients regarding their awareness and attitude against HBV vaccination are demonstrated in Table 2. In the unadjusted analysis, 4 different variables, including taking a recommendation for HBV vaccination at least once from a health care provider (82.5% vs 18.9%, P < .001), a requirement of getting a separate appointment for HBV vaccination (18.3% vs 39.2%, P = .007), fear of severe side effects that can be related with HBV vaccination (11.0% vs 29.7%, P = .006), and presence of any healthcare staff who are responsible for monitoring patients' completion of 3-dose HBV vaccination (59.8% vs 29.7%, P < .001) were significantly different between the 2 comparison groups. To understand the independent parameters affecting HBV vaccination among these high-risk patients, a multiple logistic regression model was constructed with 7 different variables (Table 3). In this model, 2 variables were detected as independent risk factors for lower rate of HBV vaccination as follows: a requirement of getting a separate appointment for HBV vaccination (aOR: 3.35, 95% CI, 1.18-9.47), and fear of severe side effects that could be related with HBV vaccination (aOR: 3.67, 95% CI, 1.18-9.47). In contrast, the other 2 variables including taking a recommendation for HBV vaccination at least once from a health care provider (aOR: 0.04, 95% CI, 0.01-0.11), and having a health insurance (aOR: 0.09, 95% CI, 0.01-0.55) were found as independent protective factors for HBV vaccination. In addition, the patients being vaccinated with at least 1 dose of the HBV vaccine were analyzed to understand

Table 1. Baseline Characteristics of Vaccinated and Unvaccinated I	Patients
--	----------

Characteristics	Vaccinated (n = 82)	Unvaccinated (n = 74)	Р
Age	41.5 (20-68)	45 (20-84)	.07°
Male sex	39 (47.6%)	39 (52.7%)	.52ª
Low income*	40 (48.8%)	33 (44.6%)	.30ª
High-risk occupation	3 (3.7%)	1 (1.4%)	.62 ^b
Low level of education**	47 (57.3%)	40 (54.1%)	.68ª
Having health insurance	79 (96.3%)	65 (87.8%)	.06ª
Living close to Ankara***	54 (65.9%)	47 (63.5%)	.76ª
Being married	53 (64.6%)	51 (68.9%)	.69ª
Average number of routine visits in a year (>10 in a year)	32 (39.0%)	25 (33.8%)	.49ª
Presence of diabetes	11 (13.4%)	8 (10.8%)	.80ª
Adequate knowledge about HBV	71 (86.6%)	61 (82.4%)	.62ª

HBV, hepatitis B virus; n, sample size.

*Low income indicates that a monthly income is <2000 Turkish Lira. **Low level of education indicates the level of education up to high school. ***Living close to Ankara indicates that patients are living in Ankara or other neighboring cities.

^aP value was obtained by Pearson chi-square test, ^bP value was obtained by Fisher's exact test, ^cP value was obtained by the Mann–Whitney U-test.

Turk J Gastroenterol 2022; 33(5): 427-433

Aslan et al. Barriers to HBV Vaccination in High-Risk Adults

Table 2.	Awareness	and Attitudes	of Patients	Against HBV	Vaccination
----------	-----------	---------------	-------------	-------------	-------------

Variables	Vaccinated (n = 82)	Unvaccinated (n = 74)	Р
I think that economic problems have unfavorable impact on getting vaccinated against HBV.	13 (15.9%)	14 (18.9%)	.76ª
At least once, a health care provider recommended HBV vaccination to me.	66 (82.5%)	14 (18.9%)	<.001ª
I know that there is a requirement of taking a separate appointment to be vaccinated for HBV.	15 (18.3%)	29 (39.2%)	.007ª
I think that the 3-dose schedule of HBV vaccine makes HBV vaccination more difficult.	17 (20.7%)	20 (27.0%)	.46ª
I think that HBV vaccination is not sufficient to prevent HBV-associated diseases.	8 (9.8%)	9 (12.2%)	.82ª
I think that HBV vaccination carries the risk of severe (life threatening) side effects.	9 (11.0%)	22 (29.7%)	.006ª
I support the recent publications and posts that contain anti-vaccination content and are propagated through social media.	7 (8.5%)	13 (17.6%)	.14ª
I think that psychological or emotional pressure (stigma) may be an obstacle to receiving an HBV vaccine.	13 (15.9%)	18 (24.3%)	.26ª
In my opinion, I have enough information about hepatitis B (transmission routes, related health problems, frequency in our country, etc.).	28 (34.1%)	20 (27.0%)	.43ª
I know that HBV vaccination can be received in the same department in which I have been followed (e.g., nephrology, hematology, or gastroenterology) without the need to apply to another department.	17 (20.7%)	7 (9.5%)	.08ª
I know that the HBV vaccine can be administered on the same day as my routine visit to the department where I have been followed for my primary disease.	13 (15.9%)	18 (24.3%)	.26ª
I know that there is a healthcare provider (nurse, doctor, other healthcare professional) who monitors whether I have completed 3 doses of HBV vaccine in particular.	49 (59.8%)	22 (29.7%)	<.001ª
I think that fear of injections is an obstacle for HBV vaccination.	13 (15.9%)	12 (16.2%)	1.0ª
HBV, hepatitis B virus; n, sample size.			

the possible hurdles against completion of the 3-dose vaccination. Among 82 patients who were vaccinated for HBV with at least 1 dose, 56 patients completed the 3-dose HBV vaccination. Baseline characteristics and

the variables exploring the awareness and attitude of patients vaccinated with at least 1 dose (1 or 2 doses) and those who completed the 3-dose vaccination can be seen in Supplementary Table 1 and Supplementary

Table 3. Logistic Regression Analysis Identifying Predictors for Receiving At Least One Dose of Hepatitis B Vaccine Among theHigh-Risk Adults

Variables	aOR	95% CI
Age	0.97	0.93-1.0
At least once, a health care provider recommended HBV vaccination to me.	0.04	0.01-0.11
I know that there is a requirement of taking a separate appointment to be vaccinated for HBV.	3.35	1.18-9.47
I think that HBV vaccination carries the risk of severe (life threatening) side effects.	3.67	1.09-12.32
I have health insurance.	0.09	0.01-0.55
I know that HBV vaccination can be received in the same department in which I have been followed (e.g., nephrology, hematology, or gastroenterology) without the need to apply to another department.	0.64	0.13-3.03
I know that there is a healthcare provider (nurse, doctor, other healthcare professional) who monitors whether I have completed 3 doses of HBV vaccine in particular.	0.70	0.26-1.90
HBV, hepatitis B virus; aOR, adjusted odds ratio.		

Table 2, respectively. After further analysis was performed in patients vaccinated with at least 1 dose the lack of recommendation from a health care provider for HBV vaccination and the absence of a healthcare provider monitoring the completion of the 3-dose vaccination of these patients were identified as independent risk factors for failure to complete the 3 doses of HBV vaccination (Table 4).

DISCUSSION

The rates of HBV vaccination among high-risk adults are varied, and far from the recommended level in many countries. A study from Turkey showed that only 24.6% (16 out of 65 patients) of AHSCT recipients were vaccinated against HBV before transplantation. Consequently, 2 recipients never developed a protective level of anti-HBs antibody and 8 of the remaining 14 vaccinated individuals (57.1%) lost HBV immunity during follow-up after transplantation.¹² In another study investigating the HBV immunization status of liver and kidney transplant recipients in Germany, the immunization rates in all patients and the seroprotection rate of anti-HBc-negative individuals were 66.5% and 42.5% among RT recipients, respectively.¹³ In a study involving 88 456 patients with chronic HCV infection, the vaccination rate for HBV was found as 21.9%.¹⁴ Despite these unfortunate vaccination rates among high-risk adults, very few studies investigated possible barriers for HBV vaccination in these patients. In this study, we found that a requirement of getting a separate appointment for HBV vaccination and fear of severe side effects that can be related with HBV vaccination were significant barriers against HBV vaccination. In reality, every adult patient who wants to be vaccinated against HBV can be vaccinated free of cost and does not need a separate appointment in our hospital. Injecting the HBV vaccine may cause swelling, pain, hyperemia at the injection site and muscle pain relatively frequently, but life-threatening complications are extremely rare.4 The HBV vaccine is able to provide sustainable HBV immunization in vaccinated individuals even 30 years later, suggesting high vaccine efficacy.¹⁵ The variable fear of severe side effects that can be related with HBV vaccination can be a hurdle against HBV vaccination for 2 possible reasons. The first is that the heuristic approach of lay people leads to a misbelief that the disease is not a serious threat for them. These people often have low perceptions pertaining to the risk of contracting HBV infection. However, HBV is highly contagious and HBV transmission may occur in the absence of visible blood or any other body fluid exposure. HBV may remain viable for 7 days or more on inanimate surfaces.^{16,17} In addition, some people underestimate the risk of chronic hepatitis and cirrhosis caused by HBV based on the fact that between 1% and 12% of acute HBV infections progress to chronic hepatitis and cirrhosis in adults.^{18,19} Therefore, they prioritize the uncommonly seen severe side effects rather than the potential benefits of HBV vaccination. Furthermore, some anti-vaccinationists consider vaccines as unnatural products and some of them also overstate their claims by supporting gaining immunity from the disease itself as more natural and healthier way of immunization.²⁰ Additionally, some patients are not aware of scientific truths regarding the efficacy and safety of HBV vaccination. Thus, they have not realized the true impact of HBV vaccination for themselves and for the rest of the population yet. In addition to these risk factors, taking a recommendation for HBV vaccination at least once from a health care provider and having a health insurance were identified as 2 independent protective variables for receiving the HBV vaccination. It is evident that a strong recommendation from a health care provider is one of the best predictors of vaccination behavior in both parents (deciding for their children) and adults (deciding for themselves).²¹ In a randomized controlled trial, Kasting et al²² showed that patients taking a recommendation from a healthcare provider received significantly more vaccine doses than those in the vaccine-offered condition (mean = 0.95 vs 0.82, RR = 1.16, 95% CI = 1.05-1.28). Confirming the findings of this study, Dehnen et al²³ showed that providing

 Table 4.
 Logistic Regression Analysis Identifying Predictors for Completing the 3-Dose Hepatitis B Vaccine Among the At Least-1-Dose-Vaccinated Group

Variables	aOR	95% CI
Age	1.04	0.98-1.09
At least once, a health care provider recommended HBV vaccination to me.	0.23	0.06-0.83
I know that there is a healthcare provider (nurse, doctor, other healthcare professional) who monitors that I have completed 3 doses of HBV vaccine in particular.	0.29	0.10-0.87
HBV, hepatitis B virus; aOR, adjusted odds ratio.		

2 interventions (including written recommendations addressing immunization needs) to the primary care physicians and asking the patients to bring their immunization documents on their next visit, to extract immunization history, improved the rates of at least 1-dose HBV vaccination and the need of HBV booster vaccination significantly. These results should encourage health care providers to make a strong recommendation for HBV vaccination rather than just offering it to the patients. Similarly, Alshammari et al²⁴ investigated the knowledge, awareness, attitude, and practice of health care providers in Saudi Arabia and reported that female gender (OR = 2.03, 95% CI = 1.02-4.04), the presence of standard procedures and protocols to vaccinate new staff members in health centers (OR = 3.30, 95% CI = 1.21-9.00), the presence of standing orders regarding hepatitis B vaccine in health centers (OR = 4.83, 95% CI = 2.00-12.39), and the awareness of the ACIP guidelines for hepatitis B vaccination among health care providers (OR = 2.80, 95% CI = 1.13-6.94) were independent predictors for health care providers' acceptance for HBV vaccination.

The other variable that was an independent predictor for patients getting at least a single dose of vaccine was having a health insurance. In line with this finding, Launay et al²⁵ conducted a pre-post cluster randomized study to investigate the effects of training of healthcare staff, free on-site vaccine availability, and the combination of these 2 interventions. Interestingly, training of healthcare staff was not associated with any beneficial effect on either vaccination acceptance or coverage. However, the group receiving the combination of 2 interventions had significantly higher vaccination acceptance than the free on-site vaccination group. Therefore, training of healthcare staff and free on-site vaccine availability are important issues that need to be addressed to increase HBV vaccination coverage. Although the Turkish Ministry of Health has provided HBV vaccine for all high-risk adults free of charge irrespective of whether they have a health insurance since 1998, unvaccinated patients noted lack of health insurance more frequently as a barrier for HBV vaccination as compared with those who were vaccinated. This misperception and attitude should be corrected via training programs prepared for high-risk adults.

Completing the hepatitis B vaccine dose-series is critical for optimal immune response.^{8,16} However, a pilot study conducted in the United States demonstrated that among persons who received dose 1, 40.4% received dose 2, and 22.3% received dose 3.²⁶ This study underlined the challenges in completing the 3-dose HBV

vaccination and inconsistencies in the use of electronic tracking systems across hospitals. In a study from Germany, a detailed recommendation for vaccination in the discharge letter was evaluated as an intervention to improve completion of the dose-series of HBV vaccination among patients with chronic liver diseases assessing for liver transplantation. Despite only 34 patients being included and a significant drop-out in the number of participants for various reasons in month 2 (only 26 patients were tested) and month 8 (only 10 patients were tested) in this study, the authors concluded that this is an easily applicable intervention to improve previously inadequate vaccination rates in the outpatient settings.²⁷ In our study, out of 82 patients who were vaccinated with at least 1 dose, 56 patients completed the HBV vaccination schedule. In MLRA, the lack of recommendation from a health care provider for HBV vaccination and the absence of a healthcare provider monitoring the completion of 3-dose vaccination were identified as independent predictors for failure to complete the 3-dose HBV vaccination. This study clearly demonstrated that health care providers do not recommend HBV vaccination to their patients sufficiently and this situation has substantial negative effects on both receiving at least 1 dose of HBV vaccine and completing the 3-dose vaccination schedule. Therefore, a team constituted by dedicated healthcare staff who continuously assess the HBV vaccination status of patients, and the checklists, obligatory orders, or online reminders for HBV vaccination need to be established in our hospital. In addition to these measures, electronic tracking systems can make it easier to monitor the 3-dose vaccination schedule.

There are many limitations in this study. It was conducted at a single center. Therefore, the results cannot be generalized over larger populations. The data were collected via a questionnaire which might have had a risk of recall bias. The questionnaire was administered by telephone call rather than a face-to-face interview. Additional confounding factors may have been present that were not included. Finally, the questionnaire used was not validated by independent studies and was prepared based on the parameters hypothesized to be associated with HBV vaccination in the literature.

In conclusion, in order to vaccinate the entire population of AHSCT recipients, RT recipients, and CHC patients against hepatitis B, the possible barriers against the HBV vaccination should be identified and multifaceted action plans should be constructed. **Ethics Committee Approval:** The ethics approval for this study was obtained from Hacettepe University Local Ethics Committee (study approval identification code: GO 2019/1091).

Informed Consent: Informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.T.A., M.A.; Design - A.T.A., M.A.; Supervision - A.T.A., B.Ş., Z.C.D., Y.A., M.A.; Resources - A.T.A., M.A.; Materials - A.T.A., Data collection and/or Processing - A.T.A., B.Ş., Z.C.D., Y.A.; Analysis and/or interpretation - A.T.A., B.Ş., Z.C.D., Y.A., M.A.; Literature search - A.T.A., B.Ş.; Writing Manuscript - A.T.A., B.Ş., M.A.; Critical Review - A.T.A., B.Ş., Z.C.D., Y.A.,

Acknowledgment: All authors sincerely acknowledge and thank Dr. Şefika Nur Ayar for her assistance and cooperation during the patient enrollment process.

Declaration of Interest: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. World Health Organization. Hepatitis B Fact Sheet. 2016. Available at: http://www.who.int/mediacentre/factsheets/fs204/en/.

2. Pungpapong S, Kim WR, Poterucha JJ. Natural history of hepatitis B virus infection: an update for clinicians. Mayo Clin Proc. 2007;82(8):967-975. [CrossRef]

3. McMahon BJ. The natural history of chronic hepatitis B virus infection. Hepatology. 2009;49(suppl 5):S45-S55. [CrossRef]

4. 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. MMWR Recomm Rep. 2018;67(1):1-31. [CrossRef]

5. Zhang S, Ma Q, Liang S, et al. Annual economic burden of hepatitis B virus-related diseases among hospitalized patients in twelve cities in China. J Viral Hepat. 2016;23(3):202-210. [CrossRef]

6. Lee TA, Veenstra DL, Iloeje UH, Sullivan SD. Cost of chronic hepatitis B infection in the United States. J Clin Gastroenterol. 2004;38(10) (suppl 3):S144-S147. [CrossRef]

7. Yang BM, Kim CH, Kim JY. Cost of chronic hepatitis B infection in South Korea. J Clin Gastroenterol. 2004;38(10)(suppl 3):S153-S157. [CrossRef]

8. Schillie S, Harris A, Link-Gelles R, Romero J, Ward J, Nelson N. Recommendations of the Advisory Committee on Immunization Practices. Recommendations of the Advisory Committee on immunization practices for use of a hepatitis B vaccine with a novel adjuvant. MMWR Morb Mortal Wkly Rep. 2018;67(15):455-458. [CrossRef]

9. Williams WW, Lu PJ, O'Halloran A, et al. Surveillance of vaccination coverage among adult populations—United States, 2015. MMWR Surveill Summ. 2017;66(11):1-28. [CrossRef]

10. Tenner CT, Herzog K, Chaudhari S, Bini EJ, Weinshel EH. Knowledge, attitudes and barriers regarding vaccination against hepatitis A and B in patients with chronic hepatitis C virus infection: a survey of family medicine and internal medicine physicians in the United States. Int J Clin Pract. 2012;66(10):1009-1013. [CrossRef]

11. Rhodes SD, Hergenrather KC. Exploring hepatitis B vaccination acceptance among young men who have sex with men: facilitators and barriers. Prev Med. 2002;35(2):128-134. [CrossRef]

12. Idilman R, Ustün C, Karayalçin S, et al. Hepatitis B virus vaccination of recipients and donors of allogeneic peripheral blood stem cell transplantation. Clin Transplant. 2003;17(5):438-443. [CrossRef]

13. Chesi C, Günther M, Huzly D, et al. Immunization of liver and renal transplant recipients: a seroepidemiological and sociodemographic survey. Transpl Infect Dis. 2009;11(6):507-512. [CrossRef]

14. Kramer JR, Hachem CY, Kanwal F, Mei M, El-Serag HB. Meeting vaccination quality measures for hepatitis A and B virus in patients with chronic hepatitis C infection. Hepatology. 2011;53(1):42-52. [CrossRef] 15. Bruce MG, Bruden D, Hurlburt D, et al. Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose. J Infect Dis. 2016;214(1):16-22. [CrossRef]

16. Krugman S, Overby LR, Mushahwar IK, Ling CM, Frösner GG, Deinhardt F. Viral hepatitis, type B: studies on natural history and prevention re-examined. N Engl J Med. 1979;300(3):101-106. [CrossRef]

17. Hoofnagle JH, Di Bisceglie AM. Serologic diagnosis of acute and chronic viral hepatitis. Semin Liver Dis. 1991;11(2):73-83. [CrossRef] 18. Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. Clin Infect Dis. 1995;20(4):992-1000. [CrossRef] 19. Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. Proc Biol Sci. 1993;253(1337):197-201. [CrossRef]

20. Jacobson RM, St Sauver JL, Finney Rutten LJ. Vaccine hesitancy. Mayo Clin Proc. 2015;90(11):1562-1568. [CrossRef]

21. Johnson DR, Nichol KL, Lipczynski K. Barriers to adult immunization. Am J Med. 2008;121(7)(suppl 2):S28-S35. [CrossRef]

22. Kasting ML, Head KJ, Cox D, Cox AD, Zimet GD. The effects of message framing and healthcare provider recommendation on adult hepatitis B vaccination: a randomized controlled trial. Prev Med. 2019;127:105798. [CrossRef]

23. Dehnen D, Herwig A, Herzer K, Weltermann B. Improving the vaccination status of liver transplant patients: effectiveness of personally addressing patients and written recommendations to family physicians after 3 years. Transpl Infect Dis. 2019;21(5):e13140. [CrossRef] 24. Alshammari TM, Aljofan M, Subaie G, Hussain T. Knowledge, awareness, attitude and practice of healthcare professionals towards hepatitis B disease and vaccination in Saudi Arabia. Hum Vaccin Immunother. 2019;15(12):2816-2823. [CrossRef].

25. Launay O, Le Strat Y, Tosini W, et al. Impact of free on-site vaccine and/or healthcare workers training on hepatitis B vaccination acceptability in high-risk subjects: a pre-post cluster randomized study. Clin Microbiol Infect. 2014;20(10):1033-1039. [CrossRef]

26. Bridges CB, Watson TL, Nelson NP, et al. Challenges with hepatitis B vaccination of high risk adults: a pilot program. Vaccine. 2019;37(35):5111-5120. [CrossRef]

27. Herta T, Petroff D, Engelmann C, et al. Hepatitis B vaccination in patients with liver cirrhosis evaluated for liver transplantation: a simple intervention ensures high adherence. Ann Transplant. 2019;24:527-531. [CrossRef]

Supplementary Table 1. Baseline Characteristics of Patients Vaccinated With 1 or 2 Doses and Those Who Completed the 3-Dose Vaccination Schedule

Characteristics	At least 1-dose vaccinated (n = 26)	3-dose vaccinated (n = 56)	P-value
Age	38.5 ± 12.9	43.0 ± 10.9	.11°
Male sex	13 (50.0%)	25 (44.6%)	.54ª
Lower income*	14 (53.8%)	27 (48.2%)	.68ª
Low level of education**	9 (34.6%)	27 (48.2%)	.26ª
Having a health insurance	26 (100.0%)	53 (94.6%)	.54ª
Living close to Ankara***	14 (53.8%)	39 (69.6%)	.34ª
Being married	14 (53.8%)	38 (67.9%)	.43ª
Average number of routine visits in a year (>10 in a year)	12 (46.1%)	19 (33.9%)	.33ª
Presence of diabetes	3 (11.5%)	9 (16.1%)	.48 ^b
Adequate knowledge about HBV	22 (84.6%)	49 (87.5%)	.73ª

HBV, hepatitis B Virus; n, sample size.

*Low income indicates that monthly income is <2000 Turkish Lira. ** Low level of education indicates the level of education up to high school. *** Living close to Ankara indicates that patients are living in Ankara or other neighboring cities. ^aP Value was obtained by the Pearson chi-square test, ^bP Value was obtained by Fisher's exact test, ^cP Value was obtained by the independent sample *t*-test.

Supplementary Table 2. Awareness and Attitudes of Patients Vaccinated With 1 or 2 Doses and Those Who Completed the 3-Dose Vaccination Schedule

Variables	At least 1-dose vaccinated (n = 26)	3-dose vaccinated (n = 56)	P-value
I think that economic problems have an unfavorable impact on getting vaccinated against HBV.	3 (11.5%)	11 (19.6%)	.32 ^b
At least once, a health care provider recommended HBV vaccination to me.	16 (61.5%)	50 (89.3%)	.01ª
l know that there is a requirement of taking a separate appointment to be vaccinated against HBV.	5 (19.2%)	10 (17.9%)	1.0 ^b
I think that the 3-dose schedule of HBV vaccine makes HBV vaccination more difficult.	5 (19.2%)	12 (21.4%)	1.0 ^b
I think that HBV vaccination is not sufficient to prevent HBV-associated diseases.	2 (7.6%)	6 (10.7%)	.92 [⊾]
I think that HBV vaccination carries the risk of severe (life threatening) side effects.	3 (11.5%)	6 (10.7%)	1.0 ^b
I support recent publications and posts that contain anti-vaccination content and propagate through social media.	2 (7.6%)	6 (10.7%)	1.0 ^b
l think that psychological or emotional pressure (stigma) may be an obstacle to getting an HBV vaccine.	0 (0.0%)	13 (23.2%)	.007 ^b
In my opinion, I have enough information about hepatitis B (transmission routes, related health problems, frequency in our country, etc.).	6 (23.0%)	21 (37.5%)	.35ª
I know that HBV vaccination can be received in the same department in which I have been followed (e.g., nephrology, hematology, or gastroenterology) without the need to apply to another department.	5 (19.2%)	11 (19.6%)	1.0 ^b
I know that the HBV vaccine can be administered on the same day as my routine visit to the department where I have been followed for my primary disease.	6 (23.0%)	21 (37.5%)	.35ª
I know that there is a healthcare provider (nurse, doctor, other healthcare professionals) who monitors whether I have completed 3 doses of HBV vaccine in particular.	10 (38.4%)	38 (67.9%)	.03ª
I think that fear of shots is an obstacle for HBV vaccination.	4 (15.3%)	9 (16.1%)	1.0 ^b
HBV, hepatitis B virus; n, sample size. *P Value was obtained by the Pearson chi-square test. *P Value was obtained by Fisher's exact test.			

SUPPLEMENTARY DATA **Questionnaire Form** A- Social and Demographic Data

4- If your answer to the previous question is yes, how many doses have you received?

.....

C- Awareness and Attitude

1- Do you think that economic problems prevent getting 2- Having a high-risk occupation (e.g., health care vaccinated against HBV? provider) A-Yes B-No A-Yes B-No 2- Have you ever taken a recommendation for being vac-3- Mean income in a month is lower than 2000 Turkish cinated against HBV from a health care provider? Lira A-Yes B-No A-Yes B-No 3- Is there a requirement to make a separate appoint-4- Completed high-school education ment to be vaccinated against HBV? B-No A-Yes B-No A-Yes 5- Having a health insurance 4- Do you think that the 3-dose vaccination schedule makes HBV vaccination more difficult? A-Yes B-No A-Yes B-No 6- Living in Ankara or a city that is close to Ankara 5- Do you think that HBV vaccines are effective in prevention of HBV-related diseases? A-Yes B-No 7- Being married A-Yes B-No A-Yes B-No 6- Do you think that HBV vaccines cause life-threatening complications? **B- Medical History** A-Yes B-No 1- Number of hospital visits within the last year (>10 visits/year) 7- Do you agree with the publications and posts that have been propagated through social media containing anti-A-Yes B-No vaccination content in recent years? 2- Having chronic comorbid diseases such as diabetes A-Yes B-No mellitus 8- Do you think that psychological or emotional pressure A-Yes B-No (stigma) is an obstacle to vaccinate against HBV?

A-Yes

B-No

A-Yes B-No

1-Age

.....

3- Being vaccinated against HBV

9- Do you think that hepatitis B disease?	you have enough knowledge about	4- What is the most infection?	effective way to prevent HBV	
A- Yes	B-No	A- Correct answer C- Have no idea	B-Wrong answer	
10- Could you get vaccinated against HBV in the depart- ment that you have been followed (e.g., nephrology, hematology, or gastroenterology) without any need to		5- In which organ doe most damage?	s hepatitis B infection cause the	
A- Yes	B-No	A- Correct answer C- Have no idea	B-Wrong answer	
11- Could you get va day of your routine vis	ccinated against HBV on the same it?	6- Is the incidence of chronic HBV infection more than 20% in Turkey?		
A- Yes	B-No	A- Correct answer C- Have no idea	B-Wrong answer	
12- Do you know that there is a healthcare staff (nurse, doctor, intern doctor, other healthcare professionals) who especially monitors you for completion of 3-dose HBV		7- Can you give 2 exam mission to humans?	nples for the routes of HBV trans-	
A- Yes	B-No	A- Correct answer C- Have no idea	B-Wrong answer	
13- Do you think that fear of injections prevents an indi- vidual from getting vaccinated against HBV?		8- Which patients should not be vaccinated against HBV?		
A- Yes	B-No	A) Pregnant patients		
D- HBV Knowledge L	evel Measurement Test	B) Immunocompromised patients		
1- Do you think that H population) in Turkey'	HBV is very rare (<1% of the general ?	C) Newborn patients		
A- Correct answer	B-Wrong answer	D) Patients who are alle	ergic to HBV vaccine	
C- Have no idea		9- Can HBV transmit from a patient having asympto atic chronic HBV infection?		
2- Do you think that I HBV transmission?	HBV vaccines can sometimes cause	A- Correct answer C- Have no idea	B-Wrong answer	
A- Correct answer C- Have no idea	B-Wrong answer	10- Can HBV infect a pe	erson more than once?	
3- Can HBV infection	become chronic?	A- Correct answer C- Have no idea	B-Wrong answer	
A- Correct answer C- Have no idea	B-Wrong answer			