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Anti-HBs Levels 18–26 Years After the Initial Hepatitis B Vaccination Series in a Low-to-Medium Prevalence Region: Is a Booster Dose or a Second Vaccine Series Necessary?

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Abstract

This cross-sectional study aimed to evaluate the persistence of immunity provided by hepatitis B (Hep B) vaccine 18–26 years after primary vaccination among 628 participants. Blood samples were collected for Hep B surface antigen (HBsAg), anti-HBs antibody (anti-HBs), and core antibody (anti-HBc) analyses. For participants with anti-HBs levels of < 10 mIU/mL, booster dose was administered and anti-HBs titers were monitored 4–6 weeks after vaccination was completed. If the response to Hep B vaccine was inadequate, two additional Hep B vaccine doses were administered. Of the 628 participants, 269 were excluded based on the exclusion criteria, and 359 were included in the final analysis. Three participants were found to be HBsAg-positive, resulting in an HBsAg carrier rate of 0.83%. Moreover, 55.4% participants had anti-HBs levels of ≥ 10 mIU/mL, with a geometric mean concentration (GMC) of 82.59 mIU/mL (95% confidence interval [CI]). Among 125 participants with anti-HBs levels of < 10 mIU/mL, 93.1% reached anti-HBs levels of ≥ 10 mIU/mL after booster dose, with a GMC of 493.47 mIU/mL. A prebooster anti-HBs cutoff level of 1.28 mIU/mL was predictive for an immune response, with a sensitivity and specificity of 71.2% and 71.4%, respectively (p = 0.001, 95% CI, likelihood ratio: 2.49). Among 14 participants unresponsive to the booster dose, 78.5% responded to the second vaccine series with a GMC of 670.82 mIU/mL. Approximately 44.6% of participants required a booster dose 18–26 years after primary vaccination. Prebooster anti-HBs titration may predict the response to booster doses. Further studies with larger groups are needed to confirm these findings.

Introduction

Hepatitis B virus (HBV) is transmitted through birth, contact with infected blood or bodily fluids, sexual contact, and intravenous drug use. According to the World Health Organization (WHO), hepatitis B (Hep B) accounted for 1.1 million deaths globally in 2022, primarily due to cirrhosis and hepatocellular carcinoma [1]. Although comprehensive HBV vaccination programs in Europe have led to a reduction in Hep B cases, approximately 11 million people remain infected [1]. Individuals residing in regions with a prevalence of Hep B surface antigen (HBsAg) ≥ 2% (e.g., Turkey, Eastern Europe, Asia, and Africa), those with high exposure to HBV, and patients undergoing immunosuppressive

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therapy are recommended to be tested before vaccination [2]. In the early 1980s, plasma-derived Hep B vaccines were introduced. In the following years, yeast-derived recombinant Hep B vaccines were developed by cloning the HBV S gene into yeast cells. Currently, recombinant DNA technology–based vaccines are used in universal immunization programs [3]. Since 1992, WHO has recommended the inclusion of the HBV vaccine in newborn vaccination schedules [4]. HBV vaccine was introduced in Turkey in 1998 [5]. Despite this, in 2015, Turkey reported approximately 4 million people infected with HBV, with an HBsAg positivity rate of 4% and an anti-HBs positivity rate of 32% [6]. Studies suggest that vaccine-induced protection diminishes over time, with protective rates of 40–60% after 15–20 years and only 25% after 22–28 years [7, 8]. In addition, some studies have shown that immune response still continues for more than half of the participants 30–35 years after HBV vaccination [9, 10]. In fact, it is also declared that immune response could be life-long protective with strong immune memory [11]. The Centers for Disease Control and Prevention recommends that individuals aged 18 years and older in regions with moderate-to-high HBV prevalence should undergo a three-panel test for HBsAg, anti-Hep B surface antigen (anti-HBs), and Hep B core antibody (anti-HBc) at least once in their lifetime [2]. Monitoring long-term persistence of immunity after the initial vaccine series is essential for controlling Hep B infection. Total anti-HBc detects immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies and these antibodies do not form in vaccinated individuals. However, isolated anti-HBc positivity can represent chronic infection in which HBsAg is not detectable by serology, passive transfer of anti-HBc to an infant born to an HBsAg-positive mother, occult Hep B infection, a false positive or mutant HBsAg strain. Currently, no commercial standalone test is available for detecting anti-HBc IgG [3, 12]. WHO organizes annual World Hep B Day campaigns to increase awareness regarding viral Hep B. For World Hep B Day 2023, the WHO emphasized on the theme "One life, one liver," highlighting the importance of the liver for a healthy life and the need to enhance viral Hep B prevention, testing, and liver disease prevention to achieve the goal of eliminating Hep B by 2030 [1]. The aim of this cross-sectional study was to determine whether immunity against HBV persisted 18–26 years after Hep B vaccination, administer a booster dose or a second Hep B vaccine series to those without immunity, assess the response level, evaluate whether the response was associated with previous anti-HBs titration levels, and detect Hep B carrier status if present [13]. In Turkey, HBV vaccination started in the first months of 1998; therefore, the oldest individuals vaccinated with the first HBV series were 26 years old in 2024. The youngest participant group consisted of 18-year-old junior students from the faculties of medicine and dentistry.

Materials and Methods

Students from the Kafkas University Faculties of Medicine and Dentistry, Kars, northeastern Turkey were included in this study. These students were from various regions across Turkey, including Eastern and Southeastern Anatolia, Central Anatolia, the Black Sea, the Aegean, the Mediterranean, and the Marmara regions. All students of the Faculty of Medicine and Dentistry of Kafkas University who were at risk of HBV infection were invited to this study. Therefore, sample size was not calculated.

The inclusion criteria were as follows: those who had not previously received a booster dose, those who had completed the three-dose HBV vaccine series, those born in Turkey, and those who could document their vaccination dates. Participants for whom documentation was unavailable, information was obtained from parents. The exclusion criteria were as follows: people who had received a booster dose of HBV vaccination, those who had gone out of town for reasons such as internship within the study period, those who rejected the study, and those who had a history of nutritional deficiency in their lives' first year or at present. The study was conducted from January 20 to October 12, 2024, among 628 participants. All participants were born after 1998 and vaccinated with recombinant Engerix®-B (GlaxoSmithKline) and Genhevac® B (10 mcg/0.5-ml) according to the Ministry of Health recommendations. Of these, 359 people were investigated after excluding 269 who did not participate in the study. The reasons for not participating were history of taking additional doses, accounting for 50.1% (n = 135), being in other cities of the country for internship purposes (n = 72), and rejection (n = 62).

In Turkey, HBV vaccinations were administered according to the following schedule by birth year [5]: For those born between 1998 and 2002, vaccinations were given at 3, 4, and 9 months of age (n = 244). For those born between January 2003 and September 2006, vaccinations were given at 0, 2, and 9 months of age (n = 115). Since November 2006, vaccinations have been given at 0, 1, and 6 months of age (n = 0).

After obtaining written and informed consent, each subject completed a questionnaire that included his/her name, sex, date of birth, hometown, height, weight, mother's HBV status, any existing diseases, and history of receiving additional Hep B vaccines.

Laboratory Technique

A 5-ml blood sample was isolated aseptically and stored at − 20 °C until testing. The samples were analyzed at the

central laboratory of Kafkas University Health Research and Application Hospital in Kars. HBV serum markers (HBsAg, anti-HBs, and anti-HBc) were measured using commercial immunoenzymatic assays (Abbott-Architech plus i2000, Germany). The system used in our laboratory was the chemiluminescent micro particle immunoassay (CMIA). This device can detect anti-HCV in serum, plasma, whole blood, or urine, but in this study, we used serum samples of the patients. We used yellow top tubes known as "clot activator tubes." A clot activator tube is a type of blood collection tube used in medical laboratories for obtaining serum samples. Samples were centrifuged as soon as possible at 1500 rpm for 15 min. After serum separation, the tube caps were removed, and the samples were placed in this device, which provided results within 1 h. In this system, anti-HBs titration values of ≥ 10 mIU/mL were considered reactive. This system does not provide values higher than 1000 mIU/mL; thus, for statistical purposes, values above 1000 mIU/mL were processed as equal to 1000 mIU/mL.

Anti-HBs titer < 10 mIU/mL was considered unresponsive.

Anti-HBs titer ≥ 10 mIU/mL was considered protective.

A patient positive for HBsAg was considered to have HBV infection, and a natural immunity was defined as anti-HBc positive while HBsAg was negative [14].

HBV DNA quantification was performed through real-time polymerase chain reaction (PCR) using the Artus HBV RG PCR Kit (Artus™ GmbH, Germany) in conjunction with the Rotor-Gene Q real-time PCR instrument. The detection limit of HBV DNA was 10 IU/ mL (10–20 000 000 IU/mL). For participants with anti-HBs levels < 10 mIU/mL, a booster dose was recommended, with re-testing after 4–6 weeks. If the levels remained < 10 mIU/mL, an additional dose was administered immediately, followed by another dose at 6 months. The specificity of the tests used was 99.67%, and sensitivity was 97.54%. The anti-HBc test used in this study is referred to as the total anti-HBc test, with a cutoff level of relative light units (RLU) of < 1.0 mIU/mL for nonreactive results and ≥ 1.0 mIU/mL for reactive results. The American Association for the Study of Liver Diseases defines chronic infection as the presence of HBsAg for at least 6 months. Therefore, those who were HBsAg-positive were re-analyzed after 6 months [15].

Statistical Analysis

For statistical evaluation, SPSS v.21.0 (IBM Corporation, New York, USA) was used. Anti-HBs positive rate, geometric mean concentration (GMC), and their 95% confidence intervals (CI) were calculated for participants with anti-HBs levels of 10–1000 mIU/mL. Because antibody titers generally do not fit a linear scale, GMC was used. When data are skewed and do not exhibit normal distribution, calculating geometric mean as a representation of results is more robust than calculating arithmetic mean [16]. The differences in the positive rates of HBV markers across years after vaccination as well as by sex, comorbidity, vaccination timing, and body mass index (BMI) (using weight in kilograms divided by the square of height in meters) were examined using chi-squared test or Fisher's exact test. In addition, for participants with insufficient immunity, prebooster anti-HBs levels and postbooster response levels were categorized, and a receiver operating characteristic curve analysis was performed. Results were evaluated according to $p < 0.05$ and 95% CI.

Results

Among the 628 participants born between 1998 and 2006 who had completed primary HBV vaccination, the number of eligible participants was 359. Of these, 203 participants were female, and 160 participants had anti-HBs levels < 10 mIU/mL, 3 of whom were HBsAg-positive. After 32 participants refused the booster dose, the remaining 125 participants were given a booster dose. The overall anti-HBs positivity rate among the 359 participants was 55.4% (Table 1). After 18–26 years of HBV vaccination, the GMC of anti-HBs–positive participants was 82.5 mIU/mL (95% CI: ± 304.7 SD). The GMCs of anti-HBs titers of participants after a booster dose and the second series of the HBV vaccine are shown in Table 2(95% CI: 493.47, SD ± 396.7 and 670.8, SD ± 355,1 IU/ mL, respectively). There was no statistically significant difference in the response rates to the vaccine after the first HBV vaccination (18–26 years later), booster dose, and second series based on sex ($p = 0.162$, $p = 0.380$, and $p = 0.515$, respectively). Similarly, comorbidity and BMI did not show a statistically significant difference. Of the 14 participants who received a second series of the HBV vaccine, 11 achieved a protective response. Their average age was 22.6 ± 1.5 years, whereas the mean age of nonresponders was 23.3 ± 1.1 years ($p = 0.435$). In addition, there was no statistically significant difference in anti-HBs levels after 18–26 years or after the booster dose between those who were initially vaccinated at 3, 4, and 9 months and those vaccinated at 0, 2, and 9 months ($p = 0.125$ and $p = 0.346$, respectively) (Table 3). Three HBsAg-positive participants were found in this study, all of whom were men (Table 4). One of the three participants who did not respond to the second series had systemic lupus erythematosus (Table 5). A prebooster anti-HBs cutoff of 1.28 mIU/mL was predictive of an immune response with 71.2% sensitivity and 71.4% specificity ($p = 0.001$, 95% CI, likelihood ratio: 2.49) (Table 6, Fig. 1).

Table 1 Anti-HBs, HBsAg and anti-HBc titers of participants after 18–26 years of first HBV vaccination

Time after vaccination (Age)	Gender ratio (female/male) (n)	Does immunity persist? yes/no (n)	GMC of anti-HBs titers ≥ 10 mIU/ mL	GSD	HBsAg positive (n)	Number of HBsAg positive /Total n(%)	anti-HBc total* positive n(%)
18	10/11	3/18	120.7	538.9	–	0/21	–
19	31/13	18/26	45.8	311.9	–	0/44	–
20	36/16	30/22	64.7	234.4	–	0/52	–
21	17/16	12/19	47.4	281.6	2	2/33(6.0)	2/33(6.0)
22	34/29	32/30	66.8	246.7	1	1/63(1.5)	1/63(1.5)
23	41/23	37/27	58.7	182.3	–	0/64	–
24	21/19	30/10	134.6	322.8	–	0/40	
25	8/18	21/5	247.4	394.6	–	0/26	–
26	5/11	16/0	113.6	367.3	–	0/16	–
Total	203/156	199/157	82.5	304.7	3	3/359(0.8)	3/359(0.8)

Anti-HBs anti- Hepatitis B surface antigen; *HBsAg* Hepatitis B surface antigen; *anti-HBc total* Hepatitis B core antibody; *GMC* Geometric mean concentration; *GSD* geometric standard deviation

* = Anti-HBc level > 1 mIU/mL are taken as positive

Table 2 GMC of anti-HBs levels after the booster dose of HBV vaccine and the second series according to participants' age

Participants' age	After a booster dose: Number of responders(anti-HBs titers ≥ 10 mIU/ mL):111 Number of non-responders:14			After the second series: Number of responders(anti-HBs titers ≥ 10 mIU/ mL):11 Number of non-responders:3		
	n	GMC of anti-HBs titers ≥ 10 IU/ mL	GSD	n	GMC of anti-HBs titers ≥ 10 IU/ mL	GSD
18	10	300.1	314.4	2	582.50	590.4
19	15	336.3	349.2	2	992.06	11.2
20	15	434.5	413.0	–	–	–
21	16	677.7	405.2	–	–	–
22	25	516.0	385.7	2	500.00	197.9
23	20	722.1	375.0	4	626.25	440.4
24	7	213.8	205.9	–	–	–
25	3	175.2	216.4	1	725.00	–
Total	111	493.4	396.7	11	670.82	355.1

HBV Hepatitis B virüs; *GMC* Geometric mean concentration; *GSD* Geometric standard deviation

Discussion

In a previous study conducted in China, the protection rate 17–20 years after HBV vaccination in newborns was 74.5%, with 5–10% showing an insufficient response. In addition, a decrease in antibody titers over time was observed, emphasizing the need for testing antibody levels over the long-term [17]. Another study provided strong evidence that protection against Hep B via HBV vaccination lasts at least 35 years, supporting the current Advisory Committee on Immunization Practices recommendations that booster doses are unnecessary [10]. However, in the previously mentioned study, the positive anti-HBs rate was as low as 24.9% after 22–28 years [9]. Another study found that 85%–90% of those vaccinated during adolescence were still immune to HBV 10 years after vaccination [7]. In a study conducted in Palestine, anti-HBs levels of ≥ 10 mIU/mL were detected in 75% of those who received the first series vaccine in the age group of 18–22 years after HBV vaccination [18]. In a 2020 study, 52.4% of participants exhibited protection 20–31 years after HBV vaccination, although 0.6% of the participants (6/949) were found to be HBsAg-positive [19].

This variation could have various causes. Factors such as deficiencies in vaccine administration, including improper freezing of the vaccine, may lead to vaccination failure. These varying results were also shown in a 2009 study conducted at five surveillance centers. In China, particularly in underdeveloped areas, mother-to-child transmission

Table 3 Binary comparison of anti-HBs level with age, gender, comorbidity, BMI and time of first vaccination series using Student-t test, Fisher's exact test and Chi-square test

Independent variables		Dependent variable(Anti-HBs-mIU/mL)								
		18–26 years after first vaccination(n = 359)			Afters a booster dose(n = 125)[a]			After second series of vaccinations(n = 14)		
		Anti-HBs < 10 n(%)	Anti-HBs ≥ 10 n(%)	p	Anti-HBs < 10 n(%)	Anti-HBs ≥ 10 n(%)	p	Anti-HBs < 10 n(%)	Anti-HBs ≥ 10 n(%)	p
Age	Mean(SD)	21.0(1,9)	22..4(2.1)	0.190	20.6(2.5)	212(1.8)	0.434	23.3(1.1)	22.6(1.5)	0.431[b]
Gender n(%)	Female	97(47.8)	106(52.2)	0.162	7(9.2)	69(90.8)	0.385	1(14.3)	6(85.7)	0.515
	Male	63(40.4)	93(59.6)		7(14.3)	42(85.7)		2(28.6)	5(71.4)	
Comorbidity	No	146(43.8)	187(56.2)	0.711	12(10,3)	104(89.7)	0.271	2(16.7)	10(83.3)	0,283
	Yes	11(47.8)	12(52.2)		2(22.2)	7(77.8)		1(50.0)	1(50.0)	
BMI	< 25	125(46,5)	144(53.5)	0.212	13(12.5)	91(87.5)	0.308	–	–	[d]
	≥ 25	35(38.9)	55(61.1)		1(4.8)	20(95.2)		–	–	
Vaccination time	3, 4 and 9.months of life	102(41.8)	142(58.2)	0.125	12(13.3)	78(86.7)	0.344[c]	3(25.0)	9(75.0)	[d]
	0, 2 and 9.months of life	58(50.4)	57(49.6)		2(5.7)	33(94.3)		0(0.0)	2(100.0)	
Total		160(44.6)	199(55.4)		14(11.2)	111(88.8)		3(21.4)	11(78.6)	

[a]32 out of 160 participants whose anti-HBs < 10 mIU/mL declined the booster vaccination and since 3 participants were HbsAg positive and booster vaccination was applied to remaining 125 participants; [b] = with Student-t test; comorbidity: Asthma (n:2); Chronic urticarial (n:4); Hashimoto disease (n:4); Hypothyroidism (n:1); PCOS or Polymenorrhea(n:4); Systemic Lupus Erythematosus (n:1); Ulcerative colitis (n:1); Multiple sclerosis (n:1); Mitral regurgitation (n:1); Operated Graves disease (n:1); Epilepsy (n:2); Gilbert (n:1); BMI = Body Mass Index(weight [kg]/height^2 [meters]); [c]with Fisher's exact test; [d] = Statistics were not performed because one group was 0

Table 4 Characteristics of three HBsAg positive cases

Characteristics of three HBsAg positive cases			
Identity	1	2	3
Gender	Male	Male	Male
Date of birth	19.04.2003	27.05.2002	31.01.2002
Time of primary immunization	0, 2 and 9. months of life	3, 4 and 9. months of life	3, 4 and 9. months of life
When was HBsAg positivity first detected?	5 years old	they learned with this study (22 years old)	they learned with this study (22 years old)
Mother's carrying status	positive	positive	negative
History of HBIG administered at birth	unknown	unknown	–
Time of mother's carrying status	2008	unknown	–
Mother's anti-HBs	negative	negative	positive
Region of residence in Turkey	Mediterrenian	Eastern Anatolia	Eastern Anatolia
Anti-HBs (mIU/mL)	1.98	0.10	0.29
HBsAg[a] (< 1 mIU/mL)	3357	5103	4345
Anti-HBc-IgG (0–1 mIU/mL)	9	10	10
HBeAg(Range:0–1 mIU/mL)	477	0.107	0.119
Anti-HBe (Range:0–1 mIU/mL)	2.37	0.002	0.002
HBV-DNA (linear range: 10–20 000 000 IU/mL)	95,000	30	462
ALT (Range:0–35 IU/mL)	89	22	24
AST (Range:0–35 IU/mL)	39	20	19
Transfusion of blood or blood products	no	no	no

HBIG hepatitis B immunoglobulin; *ALT* Alanine aminotransferase; *AST* Aspartate aminotransferase

[a] = Studied twice with 6 months interval

Table 5 Characteristics of three participants who do not respond to hepatitis B vaccine second series

Identity	1	2	3
Time of primary immunization	3, 4 and 9. months of life	3, 4 and 9. months of life	3, 4 and 9 months. of life
Age(Year)	22	24	24
Gender	male	male	female
Anti-HBs(mIU/ mL) levels:			
18–26 years after first vaccination	0.25	0.17	0.20
After a booster dose	0.67	2.08	0.24
After second series of vaccinations	0.10	0.95	3.16
HBsAg(mIU/ mL)	0.25	0.27	0.33
Anti-HBcIgG(Range:0–1 mIU/mL)	0.05	0.18	0.20
Comorbidity	no	no	SLE

SLE Systemic lupus erythematosus

Table 6 Anti-HBs' predictive cut-off level with 71,2% sensitivity and 71, 4% specificity for immune response before hepatitis B vaccine booster dose

Risc factor: Anti-HBs (mIU/mL	AUC(95%CI)	Cut-off (mIU/mL)	p	Sensitivity (%)	Specificity (%)	LR
	0.780 (0.651 to 0.909)	1.28	0.001	71.2	71.4	2.49

AUC Area under the curve; *LR* Likelihood ratio

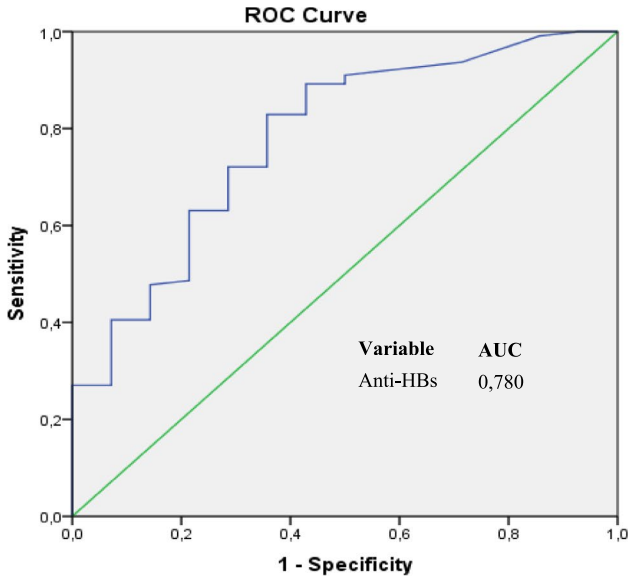


Fig. 1 Receiver operating characteristic curve, which shows anti-HBs levels of participants before one booster Hep B vaccination and the immunity response after the booster vaccine

accounts for most HBV transmission. In Long'an, the HBsAg prevalence rate was 16.9%, which was higher than that in Zhengding in 1985 (8.1%) [20].

Therefore, given the high rates of HBsAg seroprevalence, lower anti-HBs rates in some areas seem reasonable. In the present study, participants from various regions of Turkey, including a low-to-medium prevalence area and born in various cities, were enrolled. The anti-HBs positivity rate was 55.4% (199/359) and the GMC was 82.59 mIU/mL (SD: 304.70) 18–26 years after HBV vaccination. After a booster dose of the HBV vaccine, the GMC of anti-HBs–positive participants reached 493.47 mIU/mL (SD: 396.75). For anti-HBs levels prior to the booster dose, a cutoff of 1.28 mIU/mL yielded an immune response with 71.2% sensitivity and 71.4% specificity ($p = 0.001$, 95% CI, likelihood ratio: 2.49, Table 6 and Fig. 1). Zhao et al. found that participants with anti-HBs levels of 2.5–10 mIU/mL before the booster dose had a higher response rate to the booster than those with levels below 2.5 mIU/mL [17]. Even if anti-HBs titers are below 10 mIU/mL, lifelong protection may still be provided due to memory immunity and a booster dose may not be necessary. Healthcare workers and medical students remain at high risk of HBV exposure and are four times more likely to contract the infection than the general population [21]. Therefore, for those who are not immune, Hep B immunoglobulin (HBIG) assessment may be considered for any type of exposure on an individual basis [22]. Several factors have been suggested to influence vaccine response. These include improper storage conditions, age, BMI, alcohol, smoking, chronic kidney disease, organ transplantation, hemodialysis, and type 1 diabetes, which have all been associated with lower response rates [23]. In the present study, no statistically significant difference was found in anti-HBs levels 18–26 years after primary vaccination or after the booster dose with respect to BMI. However, a previous study suggested that obesity negatively impacts vaccine response [24]. In addition, a genome-wide association study systematically investigated the associations between polymorphisms and polygenic disorders and concluded that genetic variants in human leucocyte antigen (HLA)-DR, HLA-DQ, and HLA-DP may influence vaccine response [25, 26]. When conducting pairwise comparisons, no difference was found between sex and HBV vaccine response. However, it has been suggested that sex hormones exert different effects on the immune system; for instance, estrogens play a crucial role in adaptive immunity by enhancing B-cell differentiation and immunoglobulin production through humoral responses [27]. Conversely, testosterone inhibits the production of IgM and IgG from B lymphocytes and reduces the production of IL-6 from monocytes [28]. In addition, difference in the timing of primary vaccination may affect the production of antibodies and maintenance of immunity against Hep B [29]. However, in the present study, no statistically significant difference in protection levels against HBV was found between participants vaccinated at 3, 4, and 9 months and those vaccinated at 0, 2, and 9 months, either 18–26 years after primary vaccination or after the booster dose (Table 3).

In the present study, HBsAg positivity was confirmed in three male participants with repeated tests 6 months apart. When the history of the first participant, a 21-year-old, was investigated further, it was found that they had been positive since the age of 5 years and their mother was also HBsAg-positive in the same year. However, the onset of the mother's positive status was unknown. It is possible that the mother was HBsAg-positive during pregnancy, and because the HBV serology of the participant was not tested at birth, the possibility of an intrauterine infection cannot be ruled out. Possible scenarios regarding this participant could be as follows: First, since the vaccination response level was not tested after the initial vaccination series, it is possible that this participant did not respond to the HBV vaccination from the beginning. Second scenario is the possibility of a decline in immune response over time.

The second participant, who knew that their mother was previously HBsAg-positive, expressed that they never felt the need to check their HBV serology because they were vaccinated against HBV as an infant. This participant became aware of their HBsAg-positive status during this study. The possible causes of HBsAg positivity for the first case can be interpreted in a similar way for this participant. No official documentation or information from the parents could be obtained regarding whether either of these students received HBIG at birth.

The mother of the third participant was HBsAg-negative and anti-HBs–positive. Several scenarios can explain this participant's possible HBV exposure: the mother may have had acute Hep B around the time of birth with mild clinical symptoms or the participant may have initially failed to respond to the HBV vaccine, leading to potential HBV exposure later in life. Screening pregnant women for HBsAg is crucial for identifying newborns who require active and passive immunoprophylaxis [30]. When administered alone, the HBV vaccine and HBIG are 75% and 71% effective in preventing perinatal HBV transmission, respectively; however, their combined effectiveness is 94% [3].

Our study had few limitations. First, serological surveys were not conducted every year. Second, the HBV status of the mothers of the two participants who were found to be HBsAg-positive during pregnancy could not be determined. Third, the anti-HBs levels of the participants 4–6 weeks after the first HBV vaccine series were not known. Perhaps some participants' antibody levels may have been insufficient from the beginning.

Conclusions

In the present study, the anti-HBs positivity rate 18–26 years after primary vaccination was 55.4%, suggesting that a booster dose is necessary for adolescents and young adults. Further studies are needed to compare antibody titration levels before and after booster vaccination.

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Data Availability Data will be available upon request.

Declarations

Competing Interests No potential conflict of interest was reported by the author(s).

Ethical Approval The study was approved by the Kafkas University Faculty of Medicine Health Research and Application Hospital, Kars, Turkey (Date and Number: 09.11.2023/6 and 80576354-050-99/333). Each subject voluntarily signed an informed consent form before the questionnaire survey and blood sample collection. The study was performed in accordance with the Helsinki Declaration of 1975 and its later amendments.

Consent for Publication All authors consent for publication.

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