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Age-Specific Anti-HBs Seropositivity Among Individuals Eligible for the Childhood Hepatitis B Vaccination Program: A Single-Center Study

Ulusal Çocukluk Çağı Hepatit B Aşılama Programı Kapsamına Giren Bireylerde Yaşa Göre Anti-HBs Seropozitifliği: Tek Merkezli Bir Çalışma

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Abstract

Introduction: Hepatitis B (HB) vaccination is the most effective strategy for preventing HB virus infection. This study evaluated age-specific HB antibody responses among individuals eligible for the national childhood HB vaccination program to optimize vaccination follow-up policies.

Materials and Methods: This single-center retrospective study included individuals aged 1–22 years who underwent HB serological testing between January 2022 and January 2023. Individuals with positive HBsAg results, missing data, or foreign nationality were excluded. Initial HB surface antibody (anti-HBs) results and age at the time of testing were analyzed. Participants were categorized into five age groups: 1–3, 4–6, 7–12, 13–18, and 19–22 years.

Results: A total of 3,082 individuals were included [47% female; median age, 18 years (interquartile range, 10–20)], of whom 1,766 (57.3%) tested positive for anti-HBs. Higher rates of antibody positivity were observed among children aged 1–3 years. The median age of anti-HBs-negative individuals was significantly higher than that of anti-HBs-positive individuals ($p < 0.001$). Females had a higher anti-HBs seropositivity rate than males (59.6% vs. 55.3%, $p = 0.016$). In the multivariable analysis, older age groups had significantly lower odds of anti-HBs seropositivity than the 1-3-year age group [odds ratio (OR) range = 0.12–0.31], whereas female sex was independently associated with higher odds of seroprotection (OR = 1.26).

Conclusion: The rate of protective antibody detection decreased with age among individuals targeted by the national childhood HB vaccination program. Particularly in settings with intermediate or high HB endemicity, early identification of individuals without detectable antibodies may help optimize immunization monitoring strategies, prevent unnecessary revaccination, and improve resource allocation.

Keywords: Child vaccination schedule, hepatitis B, post-vaccination monitoring, seroprotection

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Öz

Giriş: Hepatit B (HB) aşılaması, HB virüsü enfeksiyonunu önlemenin en etkili stratejisidir. Bu çalışmada, aşılama sonrası takip politikalarını optimize etmek amacıyla, ulusal çocukluk çağı HB aşılama programı kapsamında yer alan bireylerde yaşa özgü HB antikor yanıtları değerlendirilmiştir.

Gereç ve Yöntem: Bu tek merkezli, retrospektif çalışmaya Ocak 2022 ile Ocak 2023 tarihleri arasında HB serolojisi bakılan 1–22 yaş arası bireyler dahil edilmiştir. HBsAg pozitif olan, verileri eksik olan ve yabancı uyruklu bireyler çalışmadan çıkarılmıştır. İlk HB yüzey antikoru (anti-HBs) sonucu ve testin yapıldığı yaştaki değerler analiz edilmiş; yaş, beş kategoriye ayrılmıştır (1–3, 4–6, 7–12, 13–18 ve 19–22 yaş).

Bulgular: Çalışmaya dahil edilen 3082 bireyden (%47'si kadın, ortanca yaş 18 yıl, çeyrekler arası açıklık 10-20), 1766'sında (%57,3) anti-HBs testi pozitif saptandı. En yüksek antikor pozitiflik oranları 1–3 yaş arasındaki çocuklarda gözlendi. Anti-HBs negatif bireylerin ortanca yaşı, pozitif olan bireylere göre anlamlı derecede daha yüksekti ($p < 0,001$). Kadınlarda anti-HBs seropozitifliği erkeklere göre daha yüksekti (%59,6'ya karşı %55,3, $p = 0,016$). Çok değişkenli analizde, 1-3 yaş grubuna kıyasla daha ileri yaş gruplarında anti-HBs seropozitifliği olasılığının anlamlı derecede daha düşük olduğu görüldü [olasılık oranı (OR) aralığı ==0,12-0,31], kadın cinsiyeti ise daha yüksek seroproteksiyon olasılığı ile bağımsız olarak ilişkili bulundu (OR =1,26).

Sonuç: Ulusal aşılama programımızın hedeflediği yaş grubunda koruyucu antikor saptanma oranının yaşla birlikte azaldığı görüldü. Özellikle orta veya yüksek HB endemisitesine sahip bölgelerde, tespit edilebilir antikorları olmayan bireylerin erken dönemde belirlenmesi, aşılama sonrası izlem stratejilerinin optimize edilmesine, gereksiz yeniden aşılamaların önlenmesine ve kaynakların daha etkin kullanılmasına katkı sağlayabilir.

Anahtar Kelimeler: Çocuk aşılama programı, hepatit B, aşılama sonrası izleme, seroproteksiyon

Introduction

Hepatitis B virus (HBV) infection is a major public health problem worldwide and can cause chronic liver disease, cirrhosis, and hepatocellular carcinoma[1]. According to the World Health Organization, over 250 million people were living with chronic hepatitis B infection in 2022, and most infections occurred in individuals over 30 years of age, an age group for which universal hepatitis B vaccination has not been implemented[2]. Although antiviral treatments can suppress viral replication, they cannot eliminate the virus, and HBV remains a major global cause of morbidity and mortality. Consequently, hepatitis B vaccination has proven to be highly effective in preventing HBV infection and its complications[3].

Hepatitis B vaccination programs are an important public health strategy for establishing sustained immunity within the community and reducing the disease burden. The effectiveness of public health systems increases as long-term community immunity is achieved. Hepatitis B vaccination programs targeting infants and young children have been implemented in many countries worldwide[4]. However, routine post-vaccination monitoring of antibody responses is not universally practiced, and the optimal timing for assessing long-term vaccine-induced immunity remains unclear.

Türkiye is considered a country with intermediate hepatitis B endemicity, with an HBsAg prevalence of approximately 4% in the general population[5]. The hepatitis B vaccination program was incorporated into the national childhood immunization schedule in 1998, targeting infants at 0, 1, and 6 months of age[6]. We aimed to evaluate antibody responses across age groups comprising individuals eligible for the national childhood hepatitis B vaccination program. We hypothesized that anti-HBs seropositivity would decline with increasing age and sought to provide evidence to support immunization monitoring policies in countries with intermediate or higher hepatitis B endemicity.

Materials and Methods

Study Design and Population

This single-center, retrospective study was conducted at Recep Tayyip Erdoğan University Hospital. Individuals who underwent HBsAg and hepatitis B surface antibody (anti-HBs) testing at our hospital between January 1, 2022, and January 1, 2023, during either inpatient care or outpatient visits for clinical evaluation or routine screening, were assessed. Among these, individuals aged 1-22 years who were eligible for the national childhood hepatitis B vaccination program in our country were included. Foreign nationals (owing to uncertain vaccination history), patients with missing data, and those who tested positive for HBsAg were excluded. Sex was defined as a biological variable (male/female) as recorded at birth in the hospital electronic medical records.

Data Collection

For eligible individuals, all historical HBV serology results recorded in our system were retrieved. The analysis focused on the earliest available anti-HBs result for each individual, along with the individual's age at the time of testing. Anti-HBs levels were analyzed according to age at the time of testing. Individual vaccination records were not available in the hospital database; therefore, vaccination status was inferred based on eligibility for the national childhood hepatitis B vaccination program introduced in 1998.

Laboratory Methods

Anti-HBs levels were quantitatively measured using a chemiluminescent microparticle immunoassay in a single laboratory. An anti-HBs titer of ≥10 mIU/mL was considered positive.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.; 2013). The normality of age was assessed using the Kolmogorov-Smirnov test. Because age was not normally distributed, the data are presented as the median and interquartile range (IQR). The Mann-Whitney U test was used to compare the median age between individuals who were anti-HBs positive and those who were anti-HBs negative. Categorical variables were compared using the Pearson chi-square test. Age was categorized into five clinically relevant groups (1-3, 4-6, 7-12, 13-18, and 19-22 years) for binary logistic regression analysis, with anti-HBs serostatus as the outcome variable. Age category (with 1-3 years as the reference group) and sex were included as independent variables. A p-value of <0.05 was considered statistically significant.

Ethics

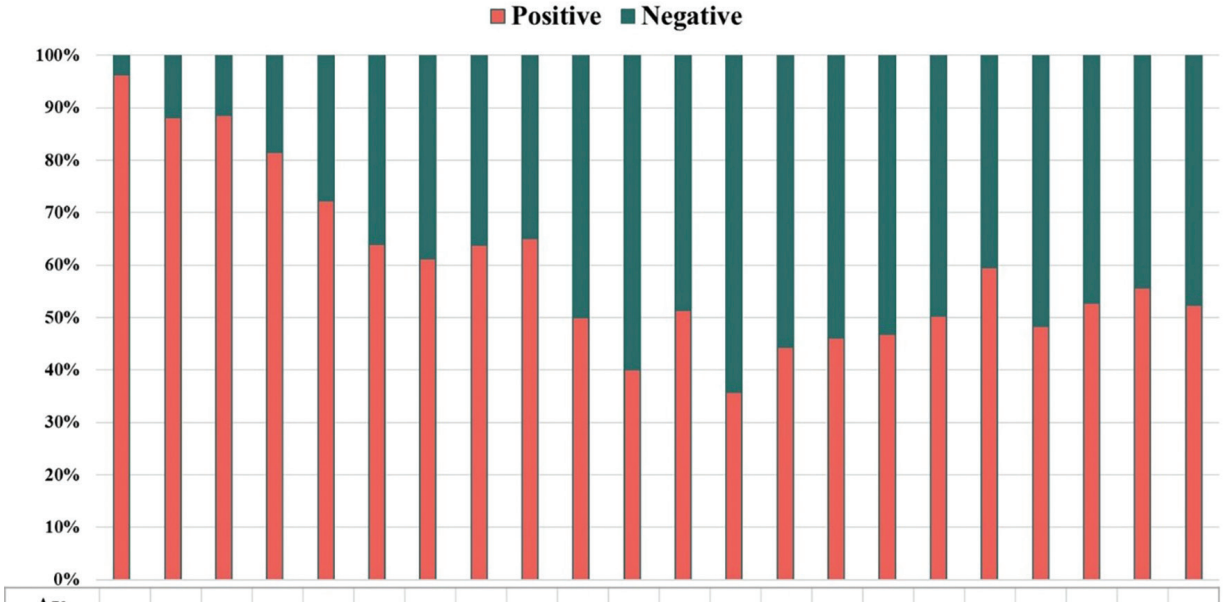
The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Recep Tayyip Erdoğan University (decision no: 2023/237, date: 12.10.2023). Informed consent was waived because of the retrospective nature of the study.

Results

The records of 3,191 individuals who underwent HBV serologic testing within the specified date and age range at our hospital were evaluated. Data from 45 individuals without an HBsAg test, 20 individuals who tested positive for HBsAg, and 44 foreign nationals were excluded, resulting in a final study population of 3,082 individuals. Of these, 1,447 (47.0%) were female, and the median age was 18 years (IQR, 10-20 years).

At the initial hospital visit, 1,766 (57.3%) individuals tested positive for anti-HBs, whereas 1,316 (42.7%) tested negative. Anti-HBs positivity ranged from 35.7% to 96.3%, depending on age, with the highest seropositivity rates observed among individuals aged 1, 3, and 2 years, respectively (Figures 1 and 2A). The median age of individuals with negative anti-HBs results was significantly higher than that of individuals with positive results ($p < 0.001$) (Table 1). The proportion of individuals with protective anti-HBs levels was significantly higher among females than among males (59.6% vs. 55.3%, $p = 0.016$) (Figure 2B).

A binary logistic regression model including age category and sex as predictors of anti-HBs positivity was applied. Compared with the 1-3-year age group, older age categories showed a stepwise decline in the likelihood of anti-HBs seropositivity. Female sex was also independently associated with higher odds of seroprotection than male sex (Table 2).



Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
n	27	76	123	103	148	114	80	47	43	34	35	35	70	124	78	126	177	255	294	341	393	359

Figure 1. Age-specific distribution of anti-HBs seropositivity and sample size. The proportions of anti-HBs–positive and anti-HBs-negative individuals are shown for each year of age, along with the number of individuals tested in each age group. HB, hepatitis B.

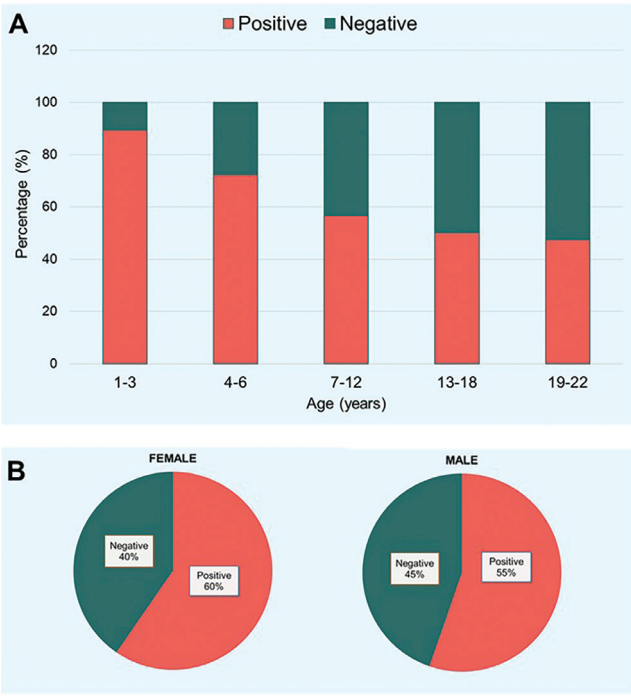


Figure 2. Distribution of anti-HBs serostatus by age group and sex.

(A) Proportions of anti-HBs-positive and anti-HBs–negative individuals according to age group. (B) Distribution of anti-HBs serostatus according to biological sex. HB, hepatitis B.

Discussion

Our findings provide epidemiological insight into age-related patterns of detectable anti-HBs levels among individuals eligible for the national childhood hepatitis B vaccination program. Specifically, they describe the distribution of protective antibodies in a population presumed to have benefited from this childhood immunization program. Moreover, although a substantial proportion of the target population exhibited positive anti-HBs levels during early childhood, seropositivity declined with increasing age. This pattern raises important public health and clinical questions.

One of the key observations among individuals presumed to have been vaccinated under the national immunization program was that the median age of those without protective anti-HBs levels was higher than that of those with protective levels. This finding raises questions about the persistence of measurable antibody levels following childhood vaccination while acknowledging that immunological memory may persist despite declining antibody titers. McMahon et al.[7] investigated individuals aged 6 months and older who received three doses of the hepatitis B vaccine and reported that, after a 22-year follow-up, 60% retained protective antibody levels. A study conducted in Tunisia reported that the overall anti-HBs seropositivity rate among vaccinated students aged 12-17

Table 1. Mann-Whitney U test of median age by initial anti-HBs result.

	Median age (IQR) (years)	Mean rank	Sum of ranks	U	p
Anti-HBs negative (n = 1316)	18.5 (14-21)	1.683.2	2.215.082.5	975.559.5	<0.001
Anti-HBs positive (n = 1766)	17 (6-20)	1.435.9	2.535.820.5		

Anti-HBs, Hepatitis B surface antibody; IQR, Interquartile range.

Table 2. Multivariable logistic regression analysis of factors associated with anti-HBs seropositivity.

Variable	OR	95% CI	p
Age group (years)*			
4-6	0.31	0.19-0.50	<0.001
7-12	0.15	0.10-0.25	<0.001
13-18	0.12	0.08-0.19	<0.001
19-22	0.13	0.08-0.20	<0.001
Sex (female)†	1.26	1.09-1.47	0.002

OR, odds ratio; CI, confidence interval. Nagelkerke R^2=0.079; Hosmer-Lemeshow goodness-of-fit test p=0.877. *Compared with 1-3 years. †Compared with male sex.

years was 68.9%, with seroprotection decreasing significantly with age[8]. Another study found that only 40% of children who received three doses of the hepatitis B vaccine had detectable protective antibodies by week 35, and only 10% remained antibody-positive at 15 years of age[9]. Notably, we observed high antibody response rates in the younger age groups in our study. Once protective antibody levels are achieved following hepatitis B vaccination, long-term immune protection may persist even if measurable antibody levels decline over time[10]. This finding underscores the importance of confirming antibody responses at an early stage after vaccination.

Another factor that may explain the lower anti-HBs seropositivity observed in some older age groups is variation in vaccination coverage over time. In our country, the three-dose hepatitis B vaccination coverage rate was approximately 72% during the early years of the program but increased substantially to 96%-99.3% after 2019[11]. Therefore, the lower seropositivity observed, particularly among individuals aged 19–22 years, may not solely reflect waning detectable antibody levels over time but may also be attributable to lower vaccination coverage during the early years of program implementation. Because individual vaccination records were unavailable, the relative contributions of incomplete vaccination and declining antibody levels could not be distinguished in this cohort. Nevertheless, this finding underscores the importance of maintaining high vaccination coverage to ensure sustained population-level protection across age groups.

Biological sex has an important influence on the immune response[12]. Consistent with our findings, Anticoli et al.[13] reported that female healthcare workers had higher anti-HBs levels than their male counterparts. Another study conducted among vaccinated children reported a higher prevalence of HBV infection in boys than in girls, although the difference was not statistically significant[14]. These findings may be explained by inherent biological differences in immune responses between the sexes.

Based on our findings, we believe that assessing an individual's immune status is more accurate when information from an early post-vaccination antibody test, such as one performed at approximately 1 year of age, is available. However, evidence indicates that antibody levels may decline over time, and many vaccinated individuals lose detectable protective antibody levels after several years[8,15-17]. Bruce et al.[18] reported that a very high seroprotection rate was achieved with a booster dose administered 35 years after completion of the hepatitis B vaccination series. A review suggested that a single booster dose may be beneficial for individuals who fail to develop a protective antibody response following the primary vaccination series[19]. Another review emphasized the importance of incorporating a booster dose into national immunization schedules worldwide[20]. Furthermore, although antibody levels may decline over time, this does not necessarily indicate a loss of protection because immunological memory against HBsAg may persist even when antibodies are no longer detectable[3,10]. In the absence of information on the early antibody response, individuals may be misclassified as non-immune over time. This could result in unnecessary revaccination, increased healthcare costs, and additional workload for healthcare providers. Early confirmation of anti-HBs positivity may help optimize resource utilization and prevent unnecessary interventions by demonstrating vaccine-induced immunity. Establishing national frameworks for the early assessment of antibody responses, particularly in settings with ongoing hepatitis B transmission or intermediate-to-high endemicity, could provide a stronger foundation for developing vaccination strategies. Such an approach may contribute to more efficient resource allocation, reduced healthcare costs, and fewer unnecessary revaccinations, particularly in resource-limited settings.

Study Limitations

Our study has several limitations. First, its retrospective design limited our ability to control for unmeasured confounding factors. Second, the lack of confirmed vaccination history represents an important limitation and prevents direct interpretation of anti-HBs status as evidence of vaccine-induced immunity. Consequently, definitive conclusions regarding the long-term effectiveness of hepatitis B vaccination cannot be drawn, although outcomes were evaluated across age groups targeted by the national vaccination program. Another limitation is that the study was conducted at a single institution, which may limit the generalizability of the findings. However, we believe that our results provide a useful foundation for future studies and may be applicable to other healthcare systems in similar settings.

Conclusion

The high apparent effectiveness observed during early childhood confirms the success of the national hepatitis B vaccination program and underscores the need for more refined post-vaccination monitoring strategies. Although routine post-vaccination testing is not generally recommended for healthy individuals, anti-HBs testing performed between 1 and 3 years of age may be considered in selected high-burden settings to support immunization monitoring, help avoid unnecessary revaccination, and reduce the burden on healthcare systems. However, the cost-effectiveness of such an approach should be evaluated in future studies. These findings highlight the importance of continued evaluation of post-vaccination immunity and support further research to determine optimal follow-up strategies. By informing evidence-based policies and

vaccination strategies, this study provides a useful framework for addressing similar public health challenges globally and promoting a more sustainable and effective approach to hepatitis B vaccination.

Acknowledgment

We express our sincere gratitude to all the physicians whose expertise and efforts contributed to the evaluation of the individuals included in this retrospective study.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Recep Tayyip Erdoğan University (decision no: 2023/237, date: 12.10.2023).

Informed Consent: Informed consent was waived because of the retrospective nature of the study.

Footnotes

Author Contributions

Concept: A.Ö., İ.E.Y., U.K., Y.Y., A.E., Design: A.Ö., İ.E.Y., U.K., Y.Y., A.E., Data Collection or Processing: T.İ., A.Ö., S.M.Ç., Analysis or Interpretation: T.İ., A.Ö., S.M.Ç., M.G.G., Literature Search: T.İ., A.Ö., S.M.Ç., M.G.G., Writing: T.İ., A.Ö., S.M.Ç., İ.E.Y., U.K., Y.Y., M.G.G., A.E.

Conflict of Interest: The authors declare no conflicts of interest.

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References

1. Zhang S, Mak LY, Yuen MF, Seto WK. Mechanisms of hepatocellular carcinoma and cirrhosis development in concurrent steatotic liver disease and chronic hepatitis B. Clin Mol Hepatol. 2025;31(Suppl):S182-95.
2. World Health Organization (WHO). Global hepatitis report 2024: Action for access in low- and middle-income countries, 2024. Geneva, Last accessed date: 01 June 2025. Available from: https://www.who.int/publications/i/item/9789240091672
3. Romano' L, Zanetti AR. Hepatitis B vaccination: a historical overview with a focus on the Italian Achievements. Viruses. 2022;14(7):1515.
4. Langley JM. Adolescent immunization - Protecting youth and preparing them for a healthy future. Int J Pediatr Adolesc Med. 2015;2(1):1-6.
5. Tozun N, Ozdogan O, Cakaloglu Y, Idilman R, Karasu Z, Akarca U, Kaymakoglu S, Ergonul O. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: A fieldwork TURHEP study. Clin Microbiol Infect. 2015;21(11):1020-6.
6. Republic of Türkiye Ministry of Health. Türkiye Viral Hepatitis Prevention and Control Program [Internet]. Ankara: Republic of Türkiye Ministry of Health; 2018-2023 [cited 2025 May 5]. Available from: https://hsgm.saglik.gov.tr/depo/Yayinlarimiz/Programlar/Turkiye_Viral_Hepatit_Onleme_ve_Kontrol_Programi_2018-2023.pdf.
7. McMahon BJ, Dentinger CM, Bruden D, Zanis C, Peters H, Hurlburt D, Bulkow L, Fiore AE, Bell BP, Hennessy TW. Antibody levels and protection after hepatitis B vaccine: results of a 22-year follow-up study and response to a booster dose. J Infect Dis. 2009;200(9):1390-6.
8. Chaouch H, Hachfi W, Fodha I, Kallala O, Saadi S, Bousaadia A, Lazrag F, Bougmiza I, Aouni M, Trabelsi A, Ben Jazia E, Letaief A. Impact and long-term protection of hepatitis B vaccination: 17 years after universal hepatitis B vaccination in Tunisia. Epidemiol Infect. 2016;144(16):3365-75.
9. Bialek SR, Bower WA, Novak R, Helgenberger L, Auerbach SB, Williams IT, Bell BP. Persistence of protection against hepatitis B virus infection among adolescents vaccinated with recombinant hepatitis B vaccine beginning at birth: a 15-year follow-up study. Pediatr Infect Dis J. 2008;27(10):881-5.
10. Banatvala JE, Van Damme P. Hepatitis B vaccine–do we need boosters? J Viral Hepat. 2003;10(1):1-6.
11. Türkiye Cumhuriyeti Sağlık Bakanlığı, Sağlık İstatistikleri Yıllığı 2023. Last accessed date: 05 June 2025. Available from: https://dosyasb.saglik.gov.tr/Eklenti/50500/0/siy202307032025pdf.pdf
12. Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626-38.
13. Anticoli S, Capanna S, Volpin A, Melis P, Ortona E, Vonesch N, Tomao P, Scapellato ML, Ruggieri A. Sex differences in response to HBV vaccination in a cohort of health care workers. Vaccine X. 2024;22:100605.
14. Geta M, Hailu A, Woldeamanuel Y. Breakthrough hepatitis B virus infection and its associated factors among vaccinated children in Northwest Ethiopia. Sci Rep. 2025;15:31704.
15. Sahana HV, Sarala N, Prasad SR. Decrease in anti-HBs Antibodies over time in medical students and healthcare workers after hepatitis B vaccination. Biomed Res Int. 2017;2017:1327492.
16. Gold Y, Somech R, Mandel D, Peled Y, Reif S. Decreased immune response to hepatitis B eight years after routine vaccination in Israel. Acta Paediatr. 2003;92(10):1158-62.
17. Alfaleh F, Alshehri S, Alansari S, Aljeffri M, Almazrou Y, Shaffi A, Abdo AA. Long-term protection of hepatitis B vaccine 18 years after vaccination. J Infect. 2008;57(5):404-9.
18. Bruce MG, Bruden D, Hurlburt D, Morris J, Bressler S, Thompson G, Lecy D, Rudolph K, Bulkow L, Hennessy T, Simons BC, Weng MK, Nelson N, McMahon BJ. Protection and antibody levels 35 years after primary series with hepatitis B vaccine and response to a booster dose. Hepatology. 2022;76(4):1180-9.
19. Yanny B, Konyn P, Najarian LM, Mitry A, Saab S. Management approaches to hepatitis B virus vaccination nonresponse. Gastroenterol Hepatol (N Y). 2019;15(2):93-9.
20. Mironova M, Ghany MG. Hepatitis B vaccine: four decades on. Vaccines (Basel). 2024;12(4):439.