



## Evaluation of Acute Hepatitis B Patients Epidemiologically and Clinically

### Akut Hepatit B Hastalarının Epidemiyolojik ve Klinik Olarak Değerlendirilmesi

● Hülya Çaşkurlu, ● Halenur Vural, ● Ravza Gündüz, ● Merve Bozkır Uludağ, ● Yasemin Çağ

*Istanbul Medeniyet University Faculty of Medicine, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey*

#### ABSTRACT

**Objectives:** Hepatitis B virus (HBV) is a DNA virus that can cause acute and chronic hepatitis, liver failure, and liver cancer. It is a widespread public health problem that can be prevented by vaccination. This study aimed to evaluate the demographic, clinical, and laboratory data of patients with acute hepatitis B who were hospitalized in our clinic.

**Materials and Methods:** Twenty-three patients diagnosed with acute hepatitis B who were hospitalized and followed up in the infectious disease service between 2021 and 2023 were included in the study. Our study was designed as a retrospective cohort study.

**Results:** The patients had an average age of  $51.3 \pm 12.6$  years, with 21 (91.3%) being male. Twelve (52.1%) of 23 patients had chronic diseases, which prolonged hospital stays. All patients involved in the study were not vaccinated for HBV. An examination of the transmission routes showed that 3 (13%) patients were infected through intravenous drug use or tattooing, 6 (36%) through dental procedures, and 14 (61%) through sexual contact. Patients who contracted the virus sexually stayed longer in the hospital. Antiviral treatment was started in 7 out of 23 patients (30.4%) because of international normalized ratio elevation (above 1.5) during hospitalization. One patient was referred to a liver transplantation clinic. Other patients were recovered and discharged. All 14 patients who regularly attended outpatient follow-ups had negative hepatitis B core antigen.

**Conclusion:** This study demonstrated that acute HBV infection continues to be observed in individuals over 50 years of age who were not routinely vaccinated in our country. The findings underscore the importance of adult vaccination and the implementation of methods to prevent sexually transmitted infections.

**Keywords:** Acute hepatitis, hepatitis B, vaccination

#### ÖZ

**Amaç:** Hepatit B virüsü (HBV), akut ve kronik hepatite, karaciğer yetmezliğine ve karaciğer kanserine neden olabilen bir DNA virüsüdür. Aşıyla önlenemeyen yaygın bir halk sağlığı sorunudur. Bu çalışma kliniğimizde akut hepatit B tanısıyla yatırılan hastaların demografik, klinik ve laboratuvar verilerini değerlendirmek amacıyla yapıldı.

**Gereç ve Yöntemler:** Çalışmaya 2021-2023 yılları arasında enfeksiyon hastalıkları servisinde yatarak takip edilen akut hepatit B tanısı almış 23 hasta dahil edildi. Çalışmamız retrospektif kohort çalışması olarak tasarlandı.

**Bulgular:** Hastaların ortalama yaşı  $51,3 \pm 12,6$  yıldır ve 21'i (%91,3) erkekti. Yirmi üç hastanın 12'sinde (%52,1) hastanede kalış süresini uzatan kronik hastalıklar mevcuttu. Çalışmaya katılan hastaların tamamı Hepatit B aşısı olmamıştı. Bulaş yollarının incelenmesi, 3'ünün (%13) intravenöz uyuşturucu kullanımı veya dövme yoluyla, 6'sının (%36) diş prosedürleri yoluyla ve 14'ünün (%61) cinsel temas yoluyla enfekte olduğunu gösterdi. Virüsü cinsel yolla kapalı hastalar hastanede daha uzun süre kaldı. Yirmi üç hastanın 7'sine (%30,4) yatış sırasında INR yüksekliği (1,5'in üzerinde) nedeniyle antiviral tedavi başlandı. Bir hasta karaciğer nakli merkezine sevk edildi. Diğer hastalar iyileşip taburcu edildi. Düzenli olarak ayaktan hasta takiplerine katılan 14 hastanın hepsinde hepatit B yüzey antijeni negatifti.

**Sonuç:** Bu çalışma, ülkemizde rutin olarak aşılanmayan 50 yaş üstü bireylerde akut HBV enfeksiyonunun görülmeye devam ettiğini göstermektedir. Bulgular, yetişkin aşılanmasının ve cinsel yolla bulaşan enfeksiyonları önlemeye yönelik yöntemlerin uygulanmasının önemini vurgulamaktadır.

**Anahtar Kelimeler:** Akut hepatit, hepatit B, aşılanma

**Address for Correspondence:** Hülya Çaşkurlu, MD, İstanbul Medeniyet University Faculty of Medicine, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey

**E-mail:** hcaskurlu@hotmail.com **ORCID ID:** orcid.org/0000-0002-6760-2052

**Received:** 13.08.2024 **Accepted:** 24.12.2024 **Epub:** 23.01.2025

**Cite this article as:** Çaşkurlu H, Vural H, Gündüz R, Bozkır Uludağ M, Çağ Y. Evaluation of acute hepatitis B patients epidemiologically and clinically. *Viral Hepat J*.



## Introduction

Hepatitis B virus (HBV) is a DNA virus that causes infection through parenteral, sexual, and vertical (from mother to baby) transmission routes (1). In our country, HBV infection is a common public health issue worldwide, and it is preventable with vaccination. According to World Health Organization 2019 data, there are 296 million HBV carriers worldwide and approximately 1 million deaths per year (2). In addition to causing severe liver damage, it is considered a leading cause of liver cancer.

The incubation period for acute hepatitis B infection ranges from 28 to 180 days, with most infections typically showing symptoms within a period of 60 to 110 days (3). During the incubation period, patients are generally asymptomatic, which increases the risk of transmission (4). Most cases are subclinical, and the course of the disease varies significantly. Although acute hepatitis B usually resolves in immunocompetent individuals, it becomes chronic in 90% of newborns, 30-50% of children under 5 years old, and 5-10% of adults (5).

Hepatitis B surface antigen (HBsAg) and anti-HBs, HBeAg and anti-HBe, and anti-HBc immunoglobulin M (IgM) and IgG are virological biomarkers of hepatitis B infection (6). Biochemical parameters indicating liver damage include aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), gamma glutamyl transpeptidase (GGT), total and direct bilirubin, serum albumin, gamma globulin, complete blood count, and prothrombin time (PT). Increased AST and ALT levels indicate the degree of liver fibrosis. When biochemical parameters are insufficient, invasive and non-invasive methods are preferred to determine the degree of liver damage.

Acute hepatitis B infection is usually managed with supportive therapy, whereas direct antiviral therapy is recommended in the presence of severe liver disease, coagulopathy, and prolonged jaundice (7). The hepatitis B vaccine is a safe and effective vaccine that has been in use worldwide since 1981 (8). In our country, the hepatitis B vaccine has been included in the routine vaccination schedule since 1998 (9).

## Materials and Methods

Our study was designed as a retrospective cohort study. Patients diagnosed with acute hepatitis B who were hospitalized and followed up in the infectious disease department between 2021 and 2023 were included in the study. The demographic data of the patients, routes of transmission, accompanying comorbidities, clinical data, biochemical, microbiological, and serological laboratory parameters, medical imaging, and treatment management were examined. The patient data were scanned retrospectively from

the hospital information database. Our study was reviewed and approved by the Clinical Research Ethics Committee of Istanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital (approval number: 2022/0719, date: 21.12.2022).

## Statistical Analysis

In the case of categorical variables, descriptive characteristics are presented along with frequencies, percentages, means, and standard deviations (SDs). Several statistical techniques, including the t-test, analysis of variance (One-Way ANOVA), and Pearson correlation analysis, were utilized. A p-value 0.05 was considered statistically significant.

## Results

The study included 23 patients. The gender distribution of the patients was as follows: 21 males (91.3%) and 2 females (8.7%). The patients' ages were found to have a mean of 51.3±12.6 years. In total, 12 (52.1%) of the 23 patients had accompanying chronic diseases, while 11 patients (47.9%) did not have any accompanying chronic diseases. All patients were unvaccinated against HBV. Analysis of the transmission routes revealed that 14 patients (61%) acquired the virus through sexual contact, 6 patients (36%) through dental procedures, and 3 patients (13%) through intravenous (IV) drug use or tattooing.

The symptoms at the time of the patients' emergency department admissions were fatigue (61%), jaundice (57%), nausea (43%), dark urine (35%), light-colored stool (17%), and fever (9%) (Table 1).

Regarding the distribution of symptoms, fatigue was the predominant symptom, representing 27% of the cases. The percentage distribution of symptoms at admission is shown in Figure 1.

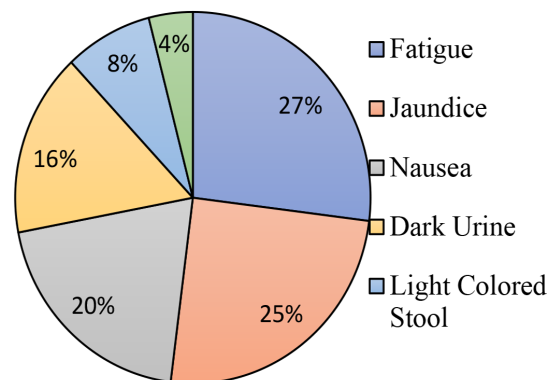


Figure 1. Percentage distribution of symptoms at admission

Symptom duration	Jaundice	Fever	Dark urine	Light-colored stool	Nausea	Fatigue
Acute (0-7 days)	9	1	3	3	7	4
Subacute (7-14 days)	4	1	5	1	2	5
Long-term (14>days)	0	0	0	0	1	5
Total	13	2	8	4	10	14
Percentage	57%	9%	35%	17%	43%	61%

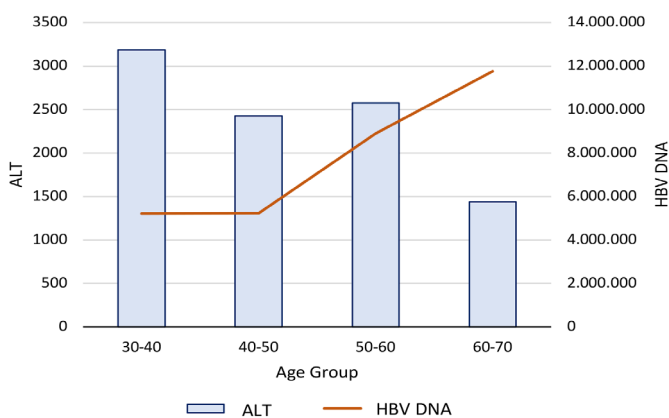
The average HBV-DNA level of the patients at initial admission was determined to be 2719165-3187990 IU/mL. The average AST level was 1664-829 U/L, ALT level was 2332-1151 U/L, ALP level was 289-145 U/L, and GGT level was 272-100 U/L. The mean total bilirubin level is 11.2-6.3 mg/dL; direct bilirubin level is 8.7-5.1 mg/dL. The international normalized ratio (INR) was 1.27 with a SD of 0.1.

Patients' AST and ALT values peaked on the first day of hospitalization. The peak AST value was determined to be an average of 1861-827 SD U/L, and the peak ALT value was an average of 2480-1192 SD U/L. While total bilirubin reached its peak value on the 4<sup>th</sup> day of hospitalization, with a peak value average of 14.7-6.5 SD mg/dL, INR reached its peak value on the 3<sup>rd</sup> day of hospitalization, with an average peak value of 1.38 SD ±0.2.

When patients' age, initial ALT, and HBV-DNA data were examined using descriptive statistical methods, younger patients generally had higher ALT values but lower average HBV-DNA values. Conversely, older patients had higher HBV-DNA levels but lower ALT levels. The correlation between age, HBV-DNA, and ALT levels upon admission is shown in Figure 2.

When examining the correlation between the initial AST-ALT values and the hospitalization duration, we observed that as the liver function test values increased, the hospitalization duration also increased. The correlation between AST, ALT, and length of hospital stay is shown in Figure 3.

All patients had positive anti-Hbc-IgM and anti-IgG antibodies. Five out of 23 patients (21.7%) had positive anti-HBs values. Sixteen patients (70%) had positive HbAg values, whereas 14 patients (61%) had positive anti-Hbe values. All patients tested positive for anti-Hbc-IgM and anti-Hbc-IgG (Table 2).



**Figure 2.** Correlation between age, HBV-DNA, and ALT levels at admission  
HBV: Hepatitis B virus, ALT: Alanine transaminase

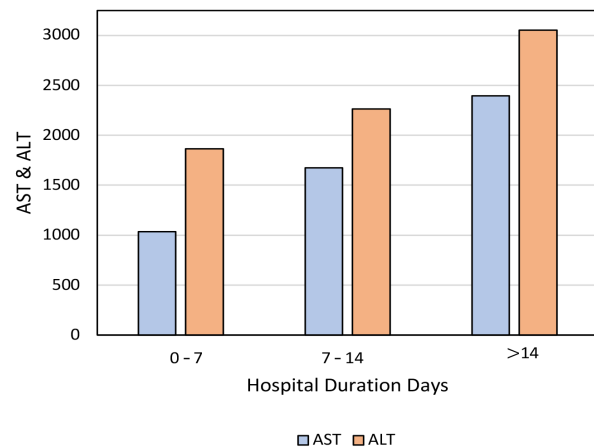
Ultrasonographic examination revealed hepatomegaly in 10 patients (43.4%), grade 1-2 hepatosteatosi in 8 patients (34.7%), and thickening of the gallbladder wall in 11 patients (47.8%). During hospitalization, 30.4% (7 out of 23) of the patients were prescribed antiviral therapy. Specifically, 3 patients were given entecavir and 4 patients were given tenofovir disoproxil fumarate. This treatment was initiated due to an increase in INR levels above 1.5.

The average length of hospital stay was 9.48-4.4 SD days. The number of patients with and without chronic diseases and the average length of hospital stay is presented in Table 3. The t-test indicated that the hospital stay duration was significantly longer for patients with chronic diseases than for those without chronic diseases (p=0.014).

The correlation between patient age and length of hospital stay is presented in Table 4. Pearson correlation analysis showed a significant increase in hospital stay duration with increasing age (p=0.013).

The correlation between hepatitis B transmission routes and length of hospital stay is presented in Table 5. Statistical analysis using the One-Way ANOVA test showed that the mode of transmission had a significant effect on the length of hospital stay, with sexually transmitted infections having the most significant impact (p=0.004).

One patient was referred to a liver transplantation center due to the development of severe liver disease and progression to hepatic failure. The remaining patients recovered and were discharged. During follow-up, 15 patients attended control visits within 1 to 6 months. Among these patients, 6 continued to have positive



**Figure 3.** Correlation between AST, ALT, and length of hospital stay  
AST: Aspartate aminotransferase, ALT: Alanine transaminase

	Anti-Hbs		HbeAg		Anti-Hbe		Anti-Hbc-IgM, IgG	
	Count	Percentage	Count	Percentage	Count	Percentage	Count	Percentage
Positive	6	26%	16	70%	14	61%	23	100%
Negative	17	74%	7	30%	9	39%	0	0%
Total	23	100%	23	100%	23	100%	23	100%

Anti-Hbs: Hepatitis B surface antigen, HbeAg: Hepatitis B e-antigen, anti-Hbe: Anti-hepatitis B e-antigen, IgM: Immunoglobulin M, IgG: Immunoglobulin G

**Table 3.** The number of patients with and without chronic diseases and the average length of hospital stay

Chronic Disease	Count	Average length of hospital stay
Yes	12	11.67
No	11	7.09
Total	23	9.48

**Table 4.** Correlation between patient age and length of hospital stay

Age	Count	Percentage	Average length of hospital stay (days)
30-40	7	36.00	7.29
40-50	5	47.40	7.80
50-60	3	54.33	11.67
60-70	8	66.25	11.63
Total	23	50.21	9.48

**Table 5.** Correlation between hepatitis B transmission route and length of hospital stay

Hepatitis B transmission route	Count	Percentage	Average length of hospital stay (days)
Sexually transmitted	14	61%	11.79
Dental procedures	6	26%	6.33
IV drug use/tattoos	3	13%	5.00
Total	23	100%	9.48

IV: Intravenous

HbsAg levels, while 9 were found to be HbsAg-negative. During the 6-12 month follow-up, seroconversion to negative HbsAg was detected in 5 out of 6 patients who were initially found to be HbsAg-positive at the first outpatient visit, while the HbsAg status of 1 patient could not be determined due to a loss of follow-up. In 6 patients, HBV-DNA was negative during the 1- to 6-month follow-up, while 1 patient continued to have positive HBV-DNA. For the patient with positive HBV-DNA, the 6-12 months data showed that HBV-DNA had become negative.

## Discussion

This study examined the demographic characteristics, clinical findings, transmission routes, laboratory parameters, treatment, and follow-up outcomes of patients with acute hepatitis B infection. In studies conducted in different regions of Turkey, the prevalence of HbsAg positivity is higher in males (10). The majority of the 23 patients included herein were male, suggesting that HBV transmission may be associated with gender and age.

Since 1998, routine vaccination against hepatitis B has been implemented in Turkey. Vaccination coverage has been increasing in recent years, with vaccination rates rising from 64% in 1999 to 98% in 2016. As a result, the incidence of acute HBV infections in the young population has significantly decreased (11). In a study on the epidemiology of acute viral hepatitis conducted by Karacaer et

al. (12) in 2018, it was observed that the ages of patients with acute HBV were mostly between 20 and 40. Considering that hepatitis B vaccination was included in the routine vaccination program in Turkey in 1998, the average age of patients indicates that most of them were not included in Turkey's national vaccination program, suggesting that unvaccinated individuals are at high risk (12).

In a study conducted by Miao et al. (13), a 57.31% decrease in the incidence of acute hepatitis B was observed between 2005 and 2019 in China following the widespread adoption of hepatitis B vaccination. In our study, the high mean age of the patients supported the effectiveness of hepatitis B vaccination in Turkey. The absence of HBV vaccination among the patients we followed also underscores the importance of adult immunization.

When examining transmission routes, we found that most patients acquired the virus through sexual contact and had longer hospitalization periods. These data confirm that unprotected sexual intercourse is a significant risk factor for HBV transmission. In addition, dental procedures and IV drug use/tattooing were identified as contributing factors to transmission routes. In a study conducted by Wu et al. (14) in China, out of 164 patients diagnosed with acute hepatitis B, 33 (20.12%) acquired the virus through sexual transmission and 21 (12.80%) acquired it after dental procedures. The hepatitis B vaccination rate among these patients was only 5.49%.

The most common symptoms of acute viral hepatitis are abdominal pain, nausea, and/or vomiting; dark urine or clay-colored stools; fatigue; fever; jaundice; joint pain; and loss of appetite (15). In our study, when symptoms were examined, patients commonly experienced typical hepatitis symptoms, such as fatigue and jaundice, upon presentation. Looking at the correlation between liver function tests and HBV-DNA according to the age groups of patients at admission, it is observed that liver function tests are high in the younger age group, while HBV-DNA was low, whereas the opposite was true in the older age group. This suggests that inflammation and hepatocyte damage are predominant in young patients, whereas the viral replication burden is higher in older individuals.

Chronicity occurs in 5-10% of individuals who have had acute hepatitis B infection in adulthood, but it is observed in 90% of cases in the newborn period and in 20-50% of cases in childhood (16). In our study, all 14 patients who attended follow-up visits had negative HbsAg values. For patients with severe acute HBV clinical and laboratory findings (INR $\geq$ 1.5 and/or PT longer than 4 seconds above the upper limit of normal and jaundice period >4 weeks), oral antiviral therapy (OAT) is recommended (17). Fulminant hepatitis occurs in less than 1% of jaundiced cases of acute infections. (18).

A meta-analysis to determine the efficacy of nucleoside analogs (NA) compared with placebo or no intervention to treat acute primary HBV infection revealed that there is insufficient evidence to suggest that NA has superior efficacy compared with placebo/standard care in patients with acute viral hepatitis (19). In our study, OAT was preferred for patients with severe liver disease and elevated INR. Among the 7 patients who received OAT, one progressed to liver failure despite antiviral treatment and was referred to a liver transplantation center. The remaining patients were discharged, and follow-up revealed negative HBsAg levels.



When examining the relationship between hospitalization duration and liver function, patients with high liver function values had longer hospital stays.

Upon reviewing the medical histories and vaccination records of the patients, it was found that none had been vaccinated against HBV, highlighting the importance of vaccination for preventing HBV infection. Unprotected sexual contact was the most common route of transmission for acute hepatitis B, emphasizing the importance of safe sexual practices.

### Study Limitations

The limitations of this study include a small number of patients, irregular attendance at follow-up visits, and data obtained from a single center. Future studies with larger sample sizes and data from different centers may provide more comprehensive results.

### Conclusion

In conclusion, this study demonstrated that acute hepatitis B infection continues to occur in individuals over 50 years of age in our country, where routine vaccination is not implemented, emphasizing the importance of adult vaccination and prevention methods against sexually transmitted infections.

### Ethics

**Ethics Committee Approval:** This study was reviewed and approved by the Clinical Research Ethics Committee of İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital (approval number: 2022/0719, date: 21.12.2022).

**Informed Consent:** Informed consents were not obtained due to the retrospective design of the study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: H.Ç., H.V., R.G., M.B.U., Y.Ç., Concept: H.Ç., Design: H.Ç., H.V., Y.Ç., Data Collection or Processing: H.Ç., H.V., R.G., M.B.U., Analysis or Interpretation: H.Ç., H.V., Literature Search: H.Ç., H.V., R.G., M.B.U., Y.Ç., Writing: H.Ç., H.V., Y.Ç.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declare no financial support.

### References

1. Jeng WJ, Papatheodoridis GV, Lok ASF. Hepatitis B. *Lancet*. 2023;401:1039-1052.
2. Kramvis A, Chang K-M, Dandri M, Farci P, Glebe D, Hu J, Janssen HLA, Lau DTY, Penicaud C, Pollicino T, Testoni B, Van Bömmel F, Andrisani O, Beumont-Mauviel M, Block TM, Chan HLY, Cloherty GA, Delaney WE, Geretti AM, Gehring A, Jackson K, Lenz O, Maini MK, Miller V, Protzer U, Yang JC, Yuen M-F, Zoulim F, Revill PA. A roadmap for serum biomarkers for hepatitis B virus: current status and future outlook. *Nat Rev Gastroenterol Hepatol*. 2022;19:727-745.
3. Beasley RP, Hwang LY, Lee GC, Lan CC, Roan CH, Huang FY, Chen CL. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet*. 1983;2:1099-1102.
4. Dekker SE, Green EW, Ahn J. Treatment and prevention of acute hepatitis B virus. *Clin Liver Dis*. 2021;25:711-724.
5. Guvenir M, Arikan A. Hepatitis B virus: from diagnosis to treatment. *Pol J Microbiol*. 2020;69:391-399.
6. Song JE, Kim DY. Diagnosis of hepatitis B. *Ann Transl Med*. 2016;4:338.
7. Tillmann HL, Patel K. Therapy of acute and fulminant hepatitis B. *Intervirology*. 2014;57:181-188.
8. Trépo C, Chan HL, Lok A. Hepatitis B virus infection. *Lancet*. 2014;384:2053-2063.
9. Kılıçaslan Ö, Sav NM, Erişen Karaca S, Sungur MA, Öztürk C, Kocabay K. Adolesan çocuklarda hepatit B belirteçlerinin incelenmesi-Düzce Üniversitesi Hastanesi 5 yıllık sonuçlar. *DÜ Sağlık Bil Enst Derg*. 2021;11:195-199.
10. Ay P, Torunoglu MA, Com S, Çipil Z, Mollahaliloğlu S, Erkoc Y, Dilmen U. Trends of hepatitis B notification rates in Turkey, 1990 to 2012. *Euro Surveill*. 2013;18:20636.
11. T.C. Sağlık Bakanlığı. Türkiye viral hepatit önlem ve kontrol programı 2018-2023. Ankara: Fersa yayıncılık; 2018.
12. Karacaer Z, Tosun S, Batirel A, Şahin S, Altaş İ, Uysal S, Erol S, Ceran N, Albayrak A, Yıldız İE, Kostakoğlu U, Kaçar F, Kuzhan N, Kadanalı A, Karagöz G, Yenilmez E, Bayırlı Turan D, Altunçekiç Yıldırım A, Koçak F, Çetinkaya RA, Parlak M, Aydın Ö, Ergen P, Durmuş G, Öztürk Kaygusuz T, Dağlı Ö, Demir C, Yılmaz Karadağ F. Changes in acute viral hepatitis epidemiology in the Turkish adult population: a multicenter study. *Türk J Gastroenterol*. 2018;29:177-182.
13. Miao N, Zheng H, Sun X, Wang F, Zhang G, Yin Z. Acute hepatitis B - China, 2005-2019. *China CDC Wkly*. 2020;2:559-563.
14. Wu WS, Zhao Y, Chen J, Li C, He HY. Incidence trend of acute hepatitis B and related risk factors in Tianjin. *Dis Surveill*. 2014;29:729-732.
15. Centers for Disease Control and Prevention. Clinical signs and symptoms of hepatitis B I hepatitis B [Internet]. Available from: <https://www.cdc.gov/hepatitis-b/hcp/clinical-signs/index.html> (Accessed on 10.09.2024).
16. Demirtürk N, Köse A, Ural O, Asan A, Barut Ş, Sümer Ş, Şimşek F, Türker N. Management of chronic hepatitis B infection: a consensus report of the Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases-2023 update. 2023. Available from: <https://www.klimikdergisi.org/tr/2023/12/09/khb-takibi-uzlasi-raporu/>
17. VHSD / Türkiye Hepatit B Tanı ve Tedavi Kılavuzu – 2023.
18. Jindal A, Kumar M, Sarin SK. Management of acute hepatitis B and reactivation of hepatitis B. *Liver Int*. 2013;33 Suppl 1:164-175.
19. Henriquez-Camacho C, Hijas-Gomez AI, Risco Risco C, Ruiz Lapuente MA, Escudero-Sanchez R, Cuerda VM. Lamivudine and entecavir for acute hepatitis B: a systematic review and meta-analysis. *Viruses*. 2023;15:2241.