



# Retrospective Investigation of Hepatitis B and Hepatitis C Virus Infections in Patients Evaluated Preoperatively

Preoperatif Değerlendirilen Hastalarda Hepatit B ve Hepatit C Virüs Enfeksiyonlarının Retrospektif Olarak İncelenmesi

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## ABSTRACT

**Objectives:** This study aimed to determine the seroprevalence of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and anti-hepatitis C virus (anti-HCV) in preoperative patients and to discuss whether preoperative tests for hepatitis B virus HBV and HCV should be performed in light of new treatments and changing current information.

**Materials and Methods:** Patients were divided into three groups according to age groups: 18-44 years old, 45-64 years old and over 65 years old. Pre- and post-seropositivity medical records of patients with seropositivity in HBsAg and anti-HCV serological test results were obtained from the data processing center and analyzed using anonymized data.

**Results:** The mean age of 26,855 patients was 40.7±17.4 (18-98 years). It was observed that 57.4% (15,426) of the patients were between the ages of 18 and 44, 29.8% (8,008) were 45 and 64, and 12.7% (3,421) were over the age of 65. HBsAg seropositivity was highest in the 18-44 age group (49.5%). HBsAg reactivity in 569 (2.1%) patients; anti-HCV reactivity was determined in 50 (0.2%) patients. The highest reactivity rate for HBsAg (3.9%) was in the 45-64 age group; for anti-HCV, the highest reactivity rate (0.6%) was found in the group over 65 years old.

**Conclusion:** Secondary prevention of patients is now possible with early detection of HBV and HCV infections. It is thought that HBV and HCV screenings to be performed during the pre-operative preparation phase will contribute to this issue.

**Keywords:** Hepatitis, anesthesia, pre-operative evaluation

## ÖZ

**Amaç:** Bu çalışmanın amacı preoperatif hastalarda hepatit B yüzey antijeni (HBsAg), hepatit B yüzey antikorunu (anti-HBs) ve anti-hepatit C virüsü (anti-HCV) seroprevalansını belirlemek ve yeni tedaviler ve değişen güncel bilgiler ışığında hepatit B virüsü (HBV) ve HCV için preoperatif testlerin yapılıp yapılmaması gerektiğini tartışmaktır.

**Gereç ve Yöntemler:** Hastalar yaş gruplarına göre üç gruba ayrıldı: 18-44 yaş, 45-64 yaş ve 65 yaş üstüdür. HBsAg ve anti-HCV serolojik test sonuçları seropozitif olan hastaların seropozitiflik öncesi ve seropozitiflik sonrası tıbbi kayıtları bilgi işlem merkezinden elde edilmiş ve anonimleştirilmiş veriler kullanılarak analiz edilmiştir.

**Bulgular:** Yirmi altı bin sekiz yüz elli beş hastanın yaş ortalaması 40,7±17,4 (18-98 yıl) idi. Hastaların %57,4'ünün (15,426) 18-44 yaş arasında, %29,8'inin (8,008) 45-64 yaş arasında ve %12,7'sinin (3,421) 65 yaş üzerinde olduğu görülmüştür. HBsAg seropozitifliği en yüksek 18-44 yaş grubundaydı (%49,5). HBsAg reaktivitesi 569 (%2,1) hastada; anti-HCV reaktivitesi ise 50 (%0,2) hastada tespit edilmiştir. HBsAg için en yüksek reaktivite oranı (%3,9) 45-64 yaş grubunda; anti-HCV için ise en yüksek reaktivite oranı (%0,6) 65 yaş üstü grupta bulunmuştur.

**Sonuç:** HBV ve HCV enfeksiyonlarının erken teşhisi ile hastaların sekonder korunması artık mümkündür. Ameliyat öncesi hazırlık aşamasında yapılacak HBV ve HCV taramalarının bu konuda katkı sağlayacağı düşünülmektedir.

**Anahtar Kelimeler:** Hepatit, anestezi, preoperatif değerlendirme

**Cite this article as:** Kılınc G, Kula AC, Çetin Duran A, Kula Atik T. Retrospective Investigation of Hepatitis B and Hepatitis C Virus Infections in Patients Evaluated Preoperatively. *Viral Hepatitis Journal* 2023;29(1):15-21

## Introduction

One of the most important occupational risks that healthcare professionals are exposed to in their working environment is infections. During healthcare delivery, many infectious agents can be transmitted by percutaneous or mucosal contact of healthcare professionals with the blood or body fluids of infected patients (1). Hepatitis B virus (HBV) and hepatitis C virus (HCV) are among the factors transmitted through blood and other body fluids and cause serious consequences such as long-term illness, disability, and death (1,2,3,4).

Worldwide, HBV and HCV infections are important health problems. The World Health Organization (WHO) estimates that 296 million people were living with chronic HBV infection in 2019. In 2019, an estimated 820,000 deaths were caused by HBV, mostly from cirrhosis and hepatocellular carcinoma. By 2019, 30.4 million people (10.5% of all people estimated to be living with hepatitis B were aware of their infection, while 6.6 million (22%) of those diagnosed were receiving treatment (2). Turkey is among the middle endemic countries with a rate of 2-7% in terms of HBV infection (2,4,5,6). It is estimated that approximately 71 million people worldwide are infected with chronic HCV infection. It is predicted that some of them will develop cirrhosis or liver cancer. Approximately 399,000 people died due to HCV in 2016 (4). The prevalence of HCV in our country is approximately 1% (3,7).

In the diagnosis of HBV infections, it is essential to demonstrate HBV-specific serological markers and HBV-DNA, which is a replication, using molecular diagnostic methods. Hepatitis B surface antigen (HBsAg) is the first antigen detected at diagnosis (5). Detection of hepatitis C surface antibodies (anti-HBs) (anti-HCV) are the most common method used in the serological diagnosis of HCV infections. It is important that the HCV-RNA test follows a positive HCV antibody test to identify people with current (chronic) HCV infection, as a positive HCV antibody test cannot distinguish between someone who has been previously infected and someone who has a current infection (5). Because HCV infections are often subclinical, there may be delays in the diagnostic process. The diagnosis is made incidentally during blood donation, pregnancy, premarital, or pre-operative screening. Although preoperative anti-HCV screening is still a controversial issue in terms of cost and patient rights, these screenings are performed in most hospitals today (8). The Centers for Disease Control and Prevention (CDC) recommends that HCV screening tests be performed for people living in areas with high HCV prevalence or who are in the HCV risk group. It aims to increase the number of HCV tests performed to increase the chance of diagnosis and treatment and recommends expanding the screening to include individuals born between 1945 and 1965 (9). In our clinic, preoperative serological tests for HBV and HCV screenings are performed in every adult patient for whom elective surgery is indicated under general anesthesia.

This study aims to determine the seroprevalence of HBsAg, anti-HBs, and anti-HCV in preoperative patients and to discuss whether preoperative tests for HBV and HCV should be performed considering new treatments and changing current information.

## Materials and Methods

### Study Design and Patients Included in the Study

After the approval of the Balikesir University Faculty of Medicine Local Ethics Committee (approval number: 2020/235, date: 09.12.2020, anti-HBs, HBsAg, and anti-HCV serological test results of the patients who were referred from different outpatient clinics for preoperative preparation to our hospital anesthesia polyclinics between 2017 and 2019 were retrospectively evaluated. Our study was conducted in accordance with the principles of the Helsinki Declaration. The first result determined for each patient was included in the study, and other recurrent results of the same patient were excluded from the study. Patients were divided into three groups according to age groups: 18-44 years old, 45-64 years old, and over 65 years. Patients were divided into three main groups as young, middle-aged, and elderly patients. No further grouping was made to avoid confusion.

Pre- and post-seropositivity HBV and HCV records of patients with seropositivity in HBsAg and anti-HCV serological test results were analyzed using patient files and anonymized data obtained from the hospital information system.

### Serological Studies

Anti-HBs, HBsAg, and anti-HCV tests were performed with the i2000SR device (Abbott Diagnostics Division, Germany) used in routine diagnosis in the laboratory according to the manufacturer's instructions. Threshold values of 10 mIU/mL, 1.0 mIU/mL, and 1.0 mIU/mL were used for anti-HBs, HBsAg, and anti-HCV reactivity, respectively.

### Molecular Studies

HBV-DNA and HCV-RNA tests were performed with the real-time polymerase chain reaction method (Bosphore HBV Panel Kit; Bosphore HCV Panel Kit, Anatolia Geneworks, Turkey) used in routine diagnosis in the laboratory.

### Statistical Analysis

The data obtained in the study were recorded in the SPSS 22.0 (SPSS INC, Chicago, IL, USA) program and statistical analyzes were performed. Numerical data were given as percentage and mean  $\pm$  standard deviation. Categorical data are given as percentages. The chi-square test was used to compare the distribution of categorical variables such as serological test results and demographic characteristics by age groups. Cases where the p-value was below 0.05 were considered as statistically significant results.

## Results

The mean age of 26,855 patients included in the study was determined to be  $40.7 \pm 17.4$  (18-98 years). It was observed that 57.4% (15,426) of the patients were between the ages of 18 and 44, 29.8% (8,008) were between the ages of 45 and 64, and 12.7% (3,421) were over the age of 65. Nineteen thousand four hundred forty-nine (72.4%) of the patients were female and 7,406 (27.6%) were male. The patients included in the study mostly applied to obstetrics and gynecology outpatient clinic (n=11,983, 44.6%). Other polyclinic distributions are shown in Table 1.

While 59.33% (15,883) of 26,773 patients whose anti-HBs test was studied were found to be negative, 40.67% (10,890) were found to be positive. It was determined that the highest rate of reactivity (49.5%) was observed in the 18-44 age group. HBsAg reactivity was observed in 569 (2.1%) patients; anti-HCV reactivity was determined in 50 (0.2%) patients. The highest reactivity rate for HBsAg (3.9%) was in the 45-64 age group; for anti-HCV, the highest reactivity rate (0.6%) was found in the group over 65 years old. It was observed that the female/male ratio, anti-HBs, HBsAg, and anti-HCV reactivity ratios showed statistically significant differences according to age groups ( $p < 0.001$ ) (Table 2).

One hundred thirty three (23.4%) of the HBsAg seropositive patients were under control and treated in the past. HBsAg seropositivity was detected for the first time in 436 (76.6%) patients. Molecular methods have also shown that 119 (27.3%) of 436 patients whose first seropositivity was detected, aged between 20 and 77 years (mean age:  $48.59 \pm 13.42$  years) were under regular control for HBsAg carriage. The HBV-DNA results of the patients under control ranged from  $10^1$  to  $10^7$  IU/mL (Table 3).

Fourteen (28.0%) of the anti-HCV seropositive patients were control and treated patients. It was observed that 36 (72.0%) were seropositive for the first time. It has also been shown by molecular methods that 5 (13.9%) of 36 patients with reactivity detected for the first time, aged between 26 and 73 years (mean age:  $59.4 \pm 16.95$  years) were under regular control after this date. The HCV-RNA values of these patients ranged from  $10^5$  to  $10^6$  IU/mL (Table 3).

## Discussion

The global prevalence of HBV infections, which is an important public health problem, varies. Turkey is a medium-endemic country for HBV infection (2,7). It has been shown in different multicenter meta-analysis studies in our country that HBsAg seropositivity rates vary between 4.0 and 6.0% and anti-HBs seropositivity rates vary between 31.9 and 43.2% (7,10,11). In different studies conducted in our country, it was reported that preoperative HBsAg seropositivity rates ranged between 0.2 and 7.7% (Table 4). With the effective Hepatitis B Control Program implemented over the years, this rate has decreased over the years (12,13,14,15).

Similar to these rates in our study, the HBsAg seropositivity rate was 2.1% and the anti-HBs seropositivity rate was 40.6%. In our study, the age group with the highest HBsAg seropositivity rate (3.9%) was 45-64 years; it was determined that the age group with the highest anti-HBs seropositivity rate (49.5%) was 18-44 years ( $p < 0.001$ ). It is thought that this situation is related to the fact that the HBV vaccine is included in the childhood compulsory vaccination scheme in our country and that adults born before the vaccination scheme are at higher risk for HBV infections. In different studies, it has been shown that while anti-HBs seropositivity rates decrease with age, HBsAg seropositivity rates increase (16,17).

The chronic HCV infection is the leading cause of liver cirrhosis. Liver failure and hepatocellular carcinoma observed in these patients cause serious increases in the risk of early death (3,4,18). In studies conducted in different regions of our country, preoperative anti-HCV seropositivity rates were found to vary

**Table 1.** The number of patients by clinic

	n (%)
<b>Patient</b>	<b>26,855</b>
Male	7,406 (27.6%)
Female	19,449 (72.4%)
<b>Clinic</b>	
Gynecology and obstetrics	11,983 (44.6)
Cardiovascular surgery	4,020 (15.0)
Thoracic surgery	1,903 (7.1)
Otolaryngology	1,892 (7.0)
Plastic surgery	1,674 (6.2)
Urology	1,545 (5.8)
General surgery	1,263 (4.7)
Ophthalmology	1,173 (4.4)
Neurochirurgie	795 (3.0)
Orthopaedics and traumatology	607 (2.3)

**Table 2.** Female/male ratio, anti-HBs, HBsAg, and anti-HCV reactivity ratios by age groups

	18-44 years (n=15426)	45-65 years (n=8008)	65-year $\leq$ (n=3421)	p-value
Female/male ratio	4.5	1.9	0.8	<0.001
Anti-HB reactivity rate	49.5%	27.2%	32.3%	<0.001
HBsAg reactivity rate	1.1%	3.9%	2.7%	<0.001
Anti-HCV reactivity rate	0.04%	0.3%	0.6%	<0.001

Anti-HBs: Hepatitis B surface antibody, HBsAg: Hepatitis B surface antigen, anti-HCV: Hepatitis C surface antibody

<b>Table 3. Demographic data of newly diagnosed patients</b>				
	<b>HCV</b>		<b>HBV</b>	
Newly diagnosed patient (n)	36		436	
HCV-RNA (IU/mL)	10 <sup>5</sup> -10 <sup>6</sup>		-	
HBV-DNA (IU/mL)	-		10 <sup>1</sup> -10 <sup>7</sup>	
Age (mean ± SD)	61.2±13.9		50.1±14.1	
<b>Age group distribution</b>				
18-44 (n)	3		120	
45-65 (n)	15		246	
65≤ (n)	18		70	
<b>Gender</b>				
Male (n)	20		189	
Female (n)	16		247	
Patient under follow-up (n)	5		119	
Age (mean ± SD)	59.4±16.9		48.5±13.4	
<b>Age group distribution</b>				
18-44 (n)	1		32	
45-65 (n)	1		72	
65≤ (n)	3		15	
<b>Gender</b>				
Male (n)	1		46	
Female (n)	4		73	
	<b>HBV</b>		<b>HCV</b>	
<b>Clinic</b>	<b>New diagnosis</b>	<b>Patient under follow-up</b>	<b>New diagnosis</b>	<b>Patient under follow-up</b>
Obstetrics and gynecology	86	27	2	1
Ear, nose and throat disorders	30	9		
Neurochirurgie	13	6	1	
General surgery	122	27	10	1
Thoracic surgery	16	7	3	
Eye disease	20	4	4	1
Cardiovascular surgery	63	20	4	
Orthopedics and traumatology	44	8	8	1
Plastic and reconstructive surgery	16	3	1	
Urology	26	8	3	1

HBV: Hepatitis B virus, HCV: Hepatitis C virus, SD: Standard deviation

<b>Table 4. Preoperative HBsAg and anti-HCV reactivity ratios</b>				
<b>Reference</b>	<b>Year</b>	<b>Patient</b>	<b>HBsAg</b>	<b>Anti-HCV</b>
Karaayak Uzun et al. (15)	2013	4,367	7.7%	2.3%
Sayhan (14)	2015	994	1.5%	0.1%
Onerci Celebi et al. (13)	2018	3,731	3.6%	0.3%
Akpınar et al. (12)	2018	2,440	0.2%	0.1%
Erbay et al. (8)	2019	25,424	-	0.6%

HBsAg: Hepatitis B surface antigen, Anti-HCV: Hepatitis C virus

between 0.1-2.3% (Table 4) (9,13,14,15,16). Similar to these rates in our study, the rate of anti-HCV reactivity was found to be 0.2%. In our study, it was determined that the age group with the highest rate of anti-HCV seropositivity (0.6%) was patients over the age of 65 ( $p < 0.001$ ). Similarly, in different studies conducted in our country, it has been shown that the rate of anti-HCV seropositivity increases with age (16,17).

The CDC emphasized that HBV infections can be easily diagnosed even before symptoms appear with inexpensive, reliable, and easy-to-apply tests, and thus patients can be saved for many years with early initiation of treatment. Considering the expected benefits in the diagnosis of HBV infections, which is a serious health problem, the costs of screening tests have been reported to be reasonable (19). In our study, it was determined that 23.4% of patients with HBsAg reactivity were registered patients from the past, and 76.6% were patients with reactivity detected for the first time. It was shown in our study that 27.3% of patients (mean age:  $48.5 \pm 13.4$  years; minimum-maximum: 20-77 years) in whom reactivity was detected for the first time were followed up regularly for HBsAg carriers after this date.

Since individuals infected with HCV are usually asymptomatic until a late stage, it is thought that nearly half of infected individuals are unaware of their condition. Diagnosis in the early stages of the disease and rapid initiation of strong direct-acting antiviral treatments are critical in preventing late complications associated with HCV (3,4,20,21). Antiviral drugs can cure more than 95% of people with HCV infection and reduce the risk of death from cirrhosis and liver cancer. However, low diagnostic rates for HCV infections unfortunately reduce the rates of access to treatment (22). Since there is currently no effective vaccine against HCV, early diagnosis of HCV infections and thus the initiation of treatment as soon as possible is very important. In our study, it was determined that 28.0% of the patients with anti-HCV reactivity were registered patients from the past, and 72.0% were patients with reactivity detected for the first time. It was found that 13.9% (mean age:  $59.4 \pm 16.9$  years; minimum-maximum: 26-73) of the patients who were found to have reactivity for the first time were under regular follow-up and control after this date. In a study conducted in Germany by Winkelmann et al. (23), anti-HCV seropositivity was found in 21 (1.5%) of 1,373 patients screened before surgery, but it was reported that 7 (33%) of 21 patients were not aware of HCV infection before. Erbay et al. (8) found 21 (26.9%) people who did not know that they were anti-HCV positive before surgery. The current approach to the prevention and control of HCV infections is focused on testing people with risk factors. Recent studies have shown that screening of the general population is cost-effective compared with risk-based screening. In the new treatment environment with highly effective and well-tolerated direct-acting antiviral therapies, many countries are reconsidering their testing strategies (24,25). There is also a need to establish a universal HCV screening program to reach WHO's goals for HCV eradication by 2030 (24,26). In a study conducted in Europe examining the prevalence and cost-effectiveness of HBV and HCV, it was stated that HBV and HCV infections were generally asymptomatic and 40-80% of people with chronic hepatitis were not aware of their infection. Therefore, it has been emphasized that screening programs for chronic HBV and HCV infection can

contribute significantly to the primary and secondary prevention of these infections (27).

The risk of percutaneous injury in healthcare workers in Turkey is higher than in developed countries. The risk of exposure in healthcare workers involved in surgical procedures is even higher than in other healthcare workers (28). Screening for HCV and HBV warns the surgeon about high-risk patients, provides a reconsideration of the surgical procedure, and provides an opportunity for the surgical team to take more intensive measures in the operating room to reduce the risk of infection (29). Universal screening for HCV is recommended for patients undergoing orthopedic surgery, especially since HCV-positive patients have a high risk of transmission in orthopedic surgeries, and these screening programs are applied in many surgical disciplines in high-risk areas (30). In fact, in countries with low seroprevalence rates, preoperative testing is uncommon because it is considered not cost-effective. However, preoperative screening is a very cost-effective strategy for patients living in areas with high HCV and HBV seroprevalence, and preoperative testing is recommended (31). With the widespread use of direct-acting antiviral agents in recent years, it has been emphasized that screening programs should not only be limited to high-risk populations but also be applied to the general population. Because the cost-effectiveness of these screenings was stated to be quite good compared to the costs of delayed viral hepatitis treatment (24,26).

Negative serological tests do not mean that the patient is not infected. The patient may be in the window period. Universal precautions must be taken. All the health staff must take preventive measures and consider as if the patients are potentially infected. Hepatitis B core antigen (anti-HBc) immunoglobulin M (IgM) can be checked to identify patients in the window period. However, it does not need to be examined unless there is a clinical suspicion.

Retrospective planning, anti-HBc IgG not checked, and questioning of the patients included in the study only through the system are limitations of our study. However, the fact that 27.3% of patients with HBsAg reactivity and 13.9% of patients with anti-HCV positivity are under regular follow-up and control after the pre-operative screening suggests that preoperative HBV and HCV screening should be performed in our country.

### Study Limitations

Our study has some limitations. First, it is a single-center, retrospective study and includes a specific follow-up period. Secondly, since it includes a certain follow-up period, it contains limited information about the processes of the patients after the diagnosis.

### Conclusion

The diagnosis of HBV and HCV infections should be established before cirrhosis and cirrhosis-related complications develop in asymptomatic infected individuals. Thus, early treatment will improve clinical results, reduce the risk of transmission, and provide significant savings in health costs. Now that secondary prevention of HBV and HCV infections is possible, there is a need to develop a strategy to identify chronic carriers who may benefit from treatment. It is thought that HBV and HCV screenings during

preoperative preparation will contribute to this issue. At the same time, it is predicted that this practice will increase awareness and attention and reduce the risk of transmission for healthcare workers who are at a high risk of transmission.

### Ethics

**Ethics Committee Approval:** This study was approved by the Ethics Committee of Balikesir University Faculty of Medicine (approval number: 2020/235, date: 09.12.2020).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: G.K., A.C.K., A.Ç.D., T.K.A., Concept: G.K., A.C.K., A.Ç.D., T.K.A., Design: G.K., A.C.K., A.Ç.D., T.K.A., Data Collection and Processing: G.K., A.C.K., A.Ç.D., T.K.A., Analysis or Interpretation: G.K., A.C.K., A.Ç.D., T.K.A., Literature Search: G.K., A.C.K., A.Ç.D., T.K.A., Writing: G.K., A.C.K., A.Ç.D., T.K.A.

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

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

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