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# Viral Hepatitis Journal

## VİRAL HEPATİT DERGİSİ

### RESEARCH ARTICLES



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## AIM AND SCOPE

Viral Hepatitis Journal (Formerly Viral Hepatit Dergisi) is the regular publishing organ of the Viral Hepatitis Society. This periodical journal covers diagnosis, treatment, epidemiology, prevention and information of hepatitis.

Viral Hepatitis Journal is an open-access journal published 3 times per year (April, August and December). In addition, the special issues are published in some periods. It is a periodic national/international journal, published in English language with abstract and title published also in Turkish language and its editorial policies are based on independent peer-review principles.

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PRISMA for preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/),

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/),

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ii. Turkish and English Abstract (max 300 words)
iii. Turkish and English Keywords
iv. Introduction (max 300 words)
v. Materials and Methods (max 400 words)
vi. Results (max 400 words)
vii. Discussion (max 700 words)
viii. Referances (should not exceed 15), all words 2000 not exceed.

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The text file should include the title in Turkish, keywords, the title in English, keywords in English, the text of the article, references, tables (only one table for one page) and figure

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legends (if any), respectively. Within the text file, the names of the authors, any information about the institutions, the figures and images should be excluded.

Abstract: Turkish and English abstracts should be given together with the article title. It should be divided into four sections in the following order: Objectives, Materials and Methods, Results and Conclusion. Abstracts should not exceed 250 words. Abstracts for case reports should be unstructured and shorter (average 100-150 words; without structural divisions in Turkish and English).

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**Discussion:** The study results should be discussed in terms of their favorable and unfavorable aspects and they should be compared with the literature.

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Case reports should present cases which are rarely seen, feature novelty in diagnosis and treatment, and contribute to our current knowledge. The first page should include the title in Turkish and English, an unstructured summary not exceeding 150 words, and keywords. The main text should consist of introduction, case report, discussion, acknowledgment, conclusion and references. The entire text should not exceed 5 pages (A4, formatted as specified above).

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Format for books; initials of author's names and surnames, chapter title, editor's name, book title, edition, city, publisher, date and pages.

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## CONTENTS

### RESEARCH ARTICLES

Research Article

1

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Viral Hepatitis Journal 2021;27(1):1-5

# *Comparison of Liver Histopathology with Non-invasive Inflammation Markers as Neutrophil-lymphocyte Ratio, Platelet-lymphocyte Ratio and Mean Platelet Volume in Chronic Hepatitis B Patients*

## Kronik Hepatit B Hastalarında Karaciğer Histopatolojisi ile Non-invaziv Enflamasyon Belirteçleri Nötrofil-lenfosit Oranı, Trombosit-lenfosit Oranı, Ortalama Trombosit Hacminin Karşılaştırılması

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***ABSTRACT***

**Objectives:** Platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) are commonly studied non-invasive inflammatory markers in cancer patients. There are some studies showing its association with fibrosis in patients with non-alcoholic steatohepatitis and chronic hepatitis B (CHB). The aim of this study is to examine the relationship between liver histopathology and viral load parameters with NLR, PLR and mean platelet volume (MPV) in patients with CHB.

**Materials and Methods:** Two hundred twenty-four CHB patients who admitted to our clinic between 2016 and 2019 and underwent liver biopsy were analysed retrospectively. Study data were obtained from patient files and electronic records.

**Results:** The mean values in complete blood count were MPV: 10.39±1.114 fL, NLR: 2.093±1.048 and PLR: 106.228±37.451. The mean fibrosis score in liver biopsies was 1.38±1.07 and the histological activity index (HAI) was 5.88±2.27. There was a statistical significant relationship between MPV and fibrosis (r=0.244, p=0.005), HBV-DNA and HAI (r=0.296, p=0.001), HBV-DNA and fibrosis (r=0.278, p=0.001) in men. There was no statistical significant difference between the genders in terms of

***ÖZ***

**Amaç:** Trombosit-lenfosit oranı (PLR) ve nötrofil-lenfosit oranı (NLR) kanser hastalarında yaygın araştırılan non-invaziv enflamasyon belirteçleri olup; non-alkolik steatohepatit ve kronik hepatit B'li (KHB) hastalarda fibrozis ile ilişkisini gösteren bazı çalışmalar bulunmaktadır. Amacımız, KHB'li hastalarda karaciğer histopatolojisi ve viral yük parametrelerinin; NLR, PLR ve ortalama trombosit hacmi (MPV) ile olan ilişkisini incelemektir.

**Gereç ve Yöntemler:** İç hastalıkları ve gastroenteroloji polikliniğine 2016-2019 yılları arasında başvuran karaciğer biyopsisi yapılan 224 KHB hastası geriye dönük incelendi. Çalışma verileri, hasta dosyaları ve elektronik kayıtlardan elde edildi.

**Bulgular:** Tam kan sayımında MPV: 10,39±1,114 fL, NLR: 2,093±1,048 ve PLR: 106,228±37,451 idi. Karaciğer biyopside fibrozis skoru: 1,38±1,07 ve histolojik aktivite indeksi (HAİ): 5,88±2,27 olarak saptandı. Erkeklerde MPV ile fibrozis arasında (r=0,244, p=0,005), HBV-DNA ve HAİ arasında (r=0,296, p=0,001), HBV-DNA ve fibrozis (r=0,278, p=0,001) arasında anlamlı bir ilişki saptanmıştır. İki grup arasında fibrozis skorları ve enflamatuvar parametreler açısından anlamlı farklılık gözlenmemiştir. HAİ <6 ve histolojik aktivite indeksi ≥6; fibrosis <2 ve fibrozisf ≥2 ve

**Demiröz H, Bayram M, Irak K, Yıldırım Ö, Kumbasar A, Tabak Ö. Comparison of Liver Histopathology with Non-invasive Inflammation Markers as Neutrophil-lymphocyte Ratio, Platelet-lymphocyte Ratio and Mean Platelet Volume in Chronic Hepatitis B Patients. Viral Hepat J. 2021;27:1-5.**

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***ABSTRACT***

fibrosis scores and inflammatory parameters. Non-invasive markers didn't make a statistical significant difference according to HAI <6 and HAI ≥6, fibrosis <2 and fibrosis ≥2 and HBV-DNA <20,000 and HBV-DNA ≥20,000 (p>0.05).

**Conclusion:** It has been determined that MPV may be a useful marker for predicting fibrosis in patients with CHB, but further studies are needed to replace liver biopsy. Continuous monitoring of MPV will contribute to disease surveillance. NLR and PLR weren't found to be an important marker for evaluating fibrosis.

**Keywords:** Chronic hepatitis B, liver biopsy, non-invasive marker

***ÖZ***

HBV-DNA <20.000 ve HBV-DNA ≥20.000 olma durumuna göre; non-invaziv belirteçler anlamlı bir farklılık oluşturmamıştır (p>0,05).

**Sonuç:** KHB'li hastalarda MPV'nin fibrozis tahmin etmede yardımcı bir belirteç olabileceği, fakat karaciğer biyopsisi yerini tutabilmesi için ek çalışmaya gerek olduğu saptanmıştır. MPV'nin sürekli izlenmesi, hastalık sürveyansına katkıda bulunacaktır. NLR ve PLR fibrozisi değerlendirmede önemli bir belirteç olarak bulunmamıştır.

**Anahtar Kelimeler:** Kronik hepatit B, karaciğer biyopsisi, non-invaziv belirteç

## Introduction

Chronic hepatitis B (CHB) is a disease that affects 240 million people worldwide and progresses from asymptomatic carriage to cirrhosis and hepatocellular cancer. Although antiviral therapy significantly reduces the risk of fibrosis and cirrhosis, some patients may develop advanced fibrosis and cirrhosis. The treatment decision in CHB patients is made according to serum hepatitis B virus (HBV)-DNA levels, alanine aminotransferase levels and the degree of necroinflammation in liver biopsy and the stage of fibrosis. Although biopsy is generally safe, it is invasive, has contraindications, can cause complications, requires hospitalization, causes sampling errors, and has a high cost. Therefore the development of easier, cheaper and non-invasive tests to show liver histopathology has become important (1). Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio PLR and mean platelet volume (MPV) are simple, inexpensive and reproducible non-invasive markers of inflammation that can be easily obtained from hemogram results. Among these markers, studies have shown that NLR guides the prognosis and treatment response of various diseases such as cardiovascular diseases, cancer and postoperative infection (2). NLR is thought to be a guide in predicting mortality when there is liver failure in acute or chronic viral hepatitis, and in determining HCC recurrence after liver transplantation. In compensated cirrhosis, high NLR is an exemplary model, such as Model for End-Stage Liver Disease and Child-Pugh scores, independent of mortality (3). There are many studies on PLR in inflammatory diseases, malignancy, hypertension, diabetes mellitus and autoimmune diseases (4). MPV reflects platelet function and increased platelet activation. It is also an inflammation marker (5). Recently, many studies have been conducted on the role of MPV in the differential diagnosis of familial mediterranean fever and irritable bowel syndrome, its association with coronary artery disease risk factors, and its use as an inflammatory marker in ulcerative colitis, rheumatoid arthritis and ankylosing spondylitis (6). In our study, we retrospectively investigated the relationship between fibrosis, histological activity index (HAI) scores and viral load and NLR, PLR and MPV levels in patients who underwent liver biopsy.

## Materials and Methods

We retrospectively examined 224 patients who admitted to the Clinics of Internal Medicine and Gastroenterology Outpatient, University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital between 2016 and 2019 and underwent liver biopsy with a diagnosis of CHB. According to the Ishak scoring system, fibrosis and HAI scores in the liver biopsies of the patients and NLR, PLR, MPV, hepatitis B surface antigen, hepatitis B e antigen (HbeAg), anti-HBe, HBV-DNA values before biopsy were obtained. Patients were divided into groups with fibrosis score <2 and ≥2 and HAI score <6 and ≥6. This study was approved by the Local Ethical Committee of Haseki Training and Research Hospital (approval number: 2009-49, date: 27.11.2019). Informed consent of patients couldn't obtained due to retrospective design of study.

### Statistical Analysis

SPSS Statistics 15.0 was used for statistical analysis. Parameter distribution was examined with Kolmogorov-Smirnov test and interpreted parametric-non-parametrically. Comparisons of numerical variables between two independent groups were evaluated using the Student's t-test when the normal distribution condition was provided and the Mann-Whitney U test when it was not provided. Relationships between numerical variables were analysed using Pearson correlation analysis when parametric test condition was provided and Spearman correlation analysis when it was not provided. Statistical significance level was accepted as $p<0.05$.

## Results

In our study, 93 of CHB patients were female (41.52%) and 131 were male (58.48%). The mean age of the patients was found to be 42.4 (Table 1).

No statistically significant relationship was found between HAI and fibrosis scores in biopsy results with NLR, MPV and PLR as inflammatory parameters.

There was no significant difference between the groups formed according to HAI <6 and HAI ≥6 in terms of MPV, NLR and PLR variables (p>0.05) (Table 2).

There was no statistically significant difference between the groups formed according to the fibrosis score in terms of MPV, NLR and PLR variables (p>0.05) (Table 3).

A statistically significant relationship was found between MPV and fibrosis (r=0.244, p=0.005), HBV-DNA and HAI (r=0.296, p=0.001), and HBV-DNA and fibrosis (r=0.278, p=0.001) in male patients. There was a positive correlation between MPV value and fibrosis score in male patients. The HAI score in the biopsy results

was found to be statistically significantly higher in the HBeAg positive group compared to the negative group (p=0.012). There was no statistically significant difference between the two groups in terms of fibrosis scores and inflammatory parameters (Table 4).

## Discussion

Starting treatment in CHB is important to prevent complications such as fibrosis and HCC. In our country, after evaluating the liver function tests and viral load of patients in CHB, liver biopsy is required to start antiviral treatment. Liver biopsy is an invasive procedure and complications such as bleeding may occur. For this reason, the efficacy of tests without risk of complications in patients is being investigated to determine liver fibrosis (7). NLR and PLR, which are easily requested, simple and practical values in routine examinations, have become important as markers of liver fibrosis with various studies. In the study of Yeşil et al. (8) it was shown that there was a relationship between NLR and fibrosis and it was thought that NLR could be a cheap fibrosis marker.

**Table 1.** Evaluation of viral load, laboratory and inflammatory parameters

| | Number | Minimum | Maximum | Mean | Standard deviation | Median |
|---|---|---|---|---|---|---|
| Age | 224 | 20 | 79 | 42.4 | 12.3 | 42 |
| AST | 224 | 11 | 659 | 42.7 | 68.4 | 24.5 |
| ALT | 224 | 8 | 1149 | 64.5 | 116.6 | 30 |
| HBV-DNA | 224 | 0 | $2.10^7$ | $9.10^6$ | $1.3.10^6$ | 21165 |
| MPV | 224 | 6.3 | 15.2 | 10.3 | 1.1 | 10.3 |
| NLR | 224 | 0.4 | 7.4 | 2.0 | 1.0 | 10.3 |
| PLR | 224 | 31 | 254 | 106.2 | 37.4 | 101.2 |
| HAI | 224 | 1 | 14 | 5.8 | 2.2 | 6 |
| Fibrosis | 224 | 0 | 6 | 1.3 | 1.0 | 1 |

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HBV: Hepatitis B virus, MPV: Mean platelet volume, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, HAI: Histological activity index

**Table 2.** Evaluation of patients' inflammatory parameters according to the HAI score

| | HAI <6 (n=83) (median) | HAI ≥6 (n=141) (median) | p |
|---|---|---|---|
| MPV | 10.30 | 10.30 | 0.834 |
| NLR | 1.840 | 1.833 | 0.610 |
| PLR | 105.556 | 100.000 | 0.218 |

HAI: Histological activity index, MPV: Mean platelet volume, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

**Table 3.** Evaluation of inflammatory parameters of the patients according to the fibrosis score

| | Fibrosis <2 (n=135) (median) | Fibrosis 2 (n=89) (median) | p |
|---|---|---|---|
| MPV | 10.200 | 10.500 | 0.071 |
| NLR | 1.780 | 1.880 | 0.136 |
| PLR | 102.400 | 100.400 | 0.209 |

MPV: Mean platelet volume, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

**Table 4.** Evaluation of the relationship of inflammatory parameters with biopsy scores by gender

| Female (n=93) | | | | Male (n=131) | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | | **HAI** | **Fibrosis** | **Parameter** | | **HAI** | **Fibrosis** |
| MPV | r | -0.106 | -0.027 | MPV | r | 0.099 | 0.244 |
| | p | 0.314 | 0.798 | | p | 0.261 | **0.005** |
| NLR | r | 0.062 | 0.049 | NLR | r | 0.008 | 0.062 |
| | p | 0.556 | 0.644 | | p | 0.925 | 0.485 |
| PLR | r | 0.008 | -0.199 | PLR | r | -0.038 | -0.017 |
| | p | 0.938 | 0.056 | | p | 0.667 | 0.850 |
| HBV-DNA | r | 0.121 | -0.002 | HBV-DNA | r | 0.296* | 0.278* |
| | p | 0.247 | 0.984 | | p | **0.001** | **0.001** |

HAI: Histological activity index, MPV: Mean platelet volume, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, HBV: Hepatitis B virus

Uluca et al. (9) could not detect a significant relationship between NLR and HAI-fibrosis scores in biopsies in CHB patients. Atay (10) did not detect a statistically significant difference in NLR levels in mild and advanced fibrosis patient groups. Similarly, in the study conducted by Chen et al. (11) there was no statistical significant difference between the CHB group and the control group. In our study, there was no statistically significant relationship between NLR, PLR and MPV values as non-invasive parameters and HAI-fibrosis scores. In the study of Yilmaz et al. (12) a statistically significant relationship was found between NLR and fibrosis stage. Zhao et al. (13) stated in their study of 172 patients that PLR and NLR have an important role in the management of CHB disease. It was shown in the study that NLR can be used to detect disease progression in compensated cirrhotic patients. In our study, we could not find such a result because there were very few patients with advanced fibrosis and compensated cirrhosis.

Lymphomononuclear cells are the main responsible cells for inflammation in CHB (14). Accurate results may not be obtained by evaluating mononuclear inflammation in the tissue with NLR. In the literature, when the relationship between NLR-fibrosis in CHB patients is evaluated, there are studies in which both positive and negative correlations were observed and there were studies in which no relationship was found between the two parameters as in our study. These different results can be explained by the fact that NLR is a variable parameter and is affected by many factors. Therefore, future studies are needed to evaluate the value of PLR and NLR in predicting clinically significant fibrosis in CHB patients with normal liver function test levels. Consequently with the current data, it is thought that NLR and PLR may not be an important test in determining fibrosis in patients with CHB and future studies are needed in this area.

It has been found that there is an association between fibrosis and MPV in patients with chronic hepatitis. In the study conducted by Purnak et al. (15) in 59 patients with CHB, it was argued that there was a correlation between fibrosis level and MPV value and that MPV could be a non-invasive marker in patients with CHB. In the study conducted by Ekiz et al. (16) MPV was found to be higher in CHB patients compared to the control group. Similarly in our study, we found a significant relationship between MPV and fibrosis in male patients. Assuming that iron deficiency anemia is more common in women and MPV is high, this may be the reason why no significant relationship about MPV could be reached in female patients in our study.

### Study Limitations

The limitations of our study were that it was a retrospective study and a single center experience.

## Conclusion

Although liver biopsy in CHB has some disadvantages, it is the gold standard method in the follow-up and treatment of the disease. However in cases where liver biopsy is not possible, there is a need to use non-invasive markers to evaluate fibrosis. Although there was no significant relationship between NLR and PLR and fibrosis in our study, it is thought that MPV may be an important parameter in determining the patient group with advanced fibrosis in CHB. Further studies that are more comprehensive and with larger numbers of patients are needed to evaluate MPV changes in CHB patients.

### Ethics

**Ethics Committee Approval:** This study was approved by the Local Ethical Committee of Haseki Training and Research Hospital (approval number: 2009/49, date: 27.11.2019).

**Informed Consent:** Informed consent of patients couldn't obtained due to retrospective design of study.

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

### Authorship Contributions

Surgical and Medical Practices: A.K., Ö.T., Ö.Y., M.B., K.I., H.D., Concept: A.K., Ö.T., Ö.Y., M.B., K.I., H.D., Design: A.K., Ö.T., Ö.Y., M.B., K.I., H.D., Data Collection or Processing: H.D., Analysis or Interpretation H.D., Literature Search: M.B., K.I., H.D., Writing: A.K., Ö.T., Ö.Y., M.B., K.I., H.D.

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# *Knowledge Level and Risk Perceptions about Hepatitis of Relatives of Patients with Hepatitis B and C Admitted to Erciyes University Hospitals*

## Erciyes Üniversitesi Hastanelerine Başvuran Hepatit B ve Hepatit C'li Hasta Yakınlarının Hepatitler Hakkında Bilgi Düzeyleri ve Risk Algıları

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***ABSTRACT***

**Objectives:** This study was conducted to determine the knowledge, attitudes, behaviours and risk perceptions about the disease of relatives of patients with chronic hepatitis B and C.

**Materials and Methods:** In this cross-sectional study, 121 relatives of patients with chronic hepatitis B and C admitted to Erciyes University Hospital, Infectious Diseases Outpatient Clinic between December 2016 and June 2017 were included.

**Results:** The mean age of the participants was 44.0±14.5 years. Sixty-four participants were male (52.9%) and 83.5% were married. 61.2% of the patients had hepatitis B virus (HBV) infection and 38.8% had HCV infection and 67.8% of the relatives stated that they lived in the same house with the patients. When the relatives of the patients were asked what type of hepatitis they knew, 92.6% stated that they knew HBV, 86.8% said they knew HCV and 79.4% said they knew both HBV-HCV. 26.4% of the participants did not know hepatitis. Approximately one-quarter of the relatives did not know what hepatitis B carrier is. 52.1% of the patient's relatives stated that they felt at risk for hepatitis infection and 69.4% stated that they had hepatitis tests and 48.8% had HBV vaccine. 38.7% of

***ÖZ***

**Amaç:** Bu çalışma Erciyes Üniversitesi Hastanesi, Enfeksiyon Hastalıkları Polikliniği'ne başvuran kronik hepatit B ve C'li hasta yakınlarının hastalıkla ilgili bilgi, tutum, davranış ve risk algılarını belirlemek amacıyla yapılmıştır.

**Gereç ve Yöntemler:** Kesitsel ve tanımlayıcı nitelikteki bu araştırmaya, Erciyes Üniversitesi Hastanesi, Enfeksiyon Hastalıkları Polikliniği'ne 2016 Aralık-2017 Haziran aylarında başvuran kronik hepatit B ve C'li hastaların 121 yakını dahil edilmiştir.

**Bulgular:** Katılımcıların yaş ortalaması 44,0±14,5 yıl olup, 64'ü erkek (%52,9) ve %83,5'i evlidir. Hastaların %61,2'sinde hepatit B virüs (HBV), %38,8'inde ise HCV enfeksiyonu mevcut olup yakınlarının %67,8'i hastalarla aynı evde yaşadığını belirtmiştir. Hasta yakınlarına hangi hepatit türünü bildikleri sorulduğunda %92,6'sı HBV'yi, %86,8'i HCV'yi ve %79,4'ü HBV-HCV'nin her ikisini de bildiklerini belirtmiştir. Katılımcıların %26,4'nün hepatitleri bilmediği görülmüştür. Hasta yakınlarının yaklaşık dörtte biri hepatit B taşıyıcılığının ne olduğunu bilmemektedir. Hasta yakınlarının %52,1'i kendini hepatit bulaşması yönünden risk altında hissettiğini ifade etmiş ve %69,4'ü hepatit testlerini ve %48,8'i HBV aşısını yaptırdığını belirtmiştir. Aşı

**Oral B, Çetinkaya F, Naçar M, Baykan Z, Ulu Kılıç A, Alabay S, Alp Meşe E. Knowledge Level and Risk Perceptions about Hepatitis of Relatives of Patients with Hepatitis B and C Admitted to Erciyes University Hospitals. Viral Hepat J. 2021;27:6-12.**

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***ABSTRACT***

those who did not have vaccination stated that they did not intend to have the vaccination.

**Conclusion:** Although the majority of the patient's relatives knew the basic ways of transmission of hepatitis B and C, their level of knowledge about other risks of transmission in their daily lives was insufficient.

**Keywords:** Hepatitis, patient's relatives, knowledge level, risk perceptions

***ÖZ***

yaptırmayanların %38,7'si ise aşı yaptırmayı düşünmediğini ifade etmiştir.

**Sonuç:** Hasta yakınlarının büyük bir çoğunluğu hepatit B ve C'nin temel bulaşma yollarını bilse de günlük yaşamlarında karşılaşabilecekleri diğer bulaşma riskinin olduğu durumlar hakkındaki bilgi düzeyleri yetersizdir.

**Anahtar Kelimeler:** Hepatit, hasta yakınları, bilgi düzeyi, risk algıları

## Introduction

If the necessary precautions are taken for viral hepatitis, which is an important group of infectious diseases that are related to public health, the infectiousness can be prevented and the disease burden of the disease is prevented. Hepatitis B and C become chronic in addition to acute infection and cause serious morbidity and mortality with the development of liver failure, cirrhosis and liver cancer (1,2,3).

In hepatitis B infection, the transmission of the disease is known as blood pathway, sexual intercourse and perinatal pathway from mother to baby. The disease can be transmitted from contaminated blood and blood products, the use of non-sterilized instruments, dental treatment, joint injectors, razor blades and toothbrushes, and tattooing. The disease may be acute or chronic at an early age and the rate of chronicity in the early period is very high but remains below 5% in adulthood (1,4). According to the World Health Organization (WHO) Global Hepatitis Report published in 2017, 257 million people live with chronic hepatitis B (CHB) (5). Hepatitis B prevalence of a comprehensive study conducted in Turkey was determined to be 4% and it was reported that at least one-third of the country population was faced with hepatitis B (6). Hepatitis C infection like B can be a chronic or acute infection. Similarly, the main ways of transmission are blood and blood products, sexual and perinatal. Again, the use of common injectors and surgical procedures performed with non-sterilized instruments, contaminated manicure and pedicure instruments in hairdressers, shaving blades in barbers, and dental treatments are risky conditions for transmission (7). In the WHO Global Hepatitis Report, 71 million people are reported to have chronic hepatitis (5). It has been shown that the prevalence of hepatitis C in our country is between 0.5 and 1% in various studies (6,8,9).

WHO stated that viral hepatitis caused 1.34 million deaths in 2015 (10). Most of the deaths due to hepatitis (96%) are caused by hepatitis B and C. These two viruses can be chronic cause lifelong infection and cause progressive liver damage such as cirrhosis and hepatocellular carcinoma (1,11). Because of life-long-lasting, becoming chronic, causing serious liver damage, serious health expenses occur. This brings a huge burden for patients, their relatives and the national economy. The cost of new generation drugs developed for hepatitis B and C is also very high (12,13). According to Turkey Viral Hepatitis Diagnosis and Treatment Guide 2017, people live in the same house with Hepatitis infected patients and first degree relative with patients infected with hepatitis B even they don't live in the same house are located primarily in the group that should be examined in terms of hepatitis B infection. Among the risk groups that should be examined for hepatitis C, those with risky contact within the family are also among the priority groups (14).

The relatives of patients with hepatitis, which constitute an important risk group, should be informed adequately and accurately, and their current knowledge and attitudes should be determined. By raising awareness on the subject, disease burden and unnecessary health expenditures will be prevented and this will bring an increase in life quality. The aim of this study is; determine the knowledge, attitude, behavior and risk perceptions of patients with CHB and C.

## Materials and Methods

This cross-sectional and descriptive study was conducted in Erciyes University Hospital between December 2016 and June 2017. 157 relatives (with more than one relative of some patients) of patients with CHB and hepatitis C aged 18 and above admitted to the clinic of infectious diseases outpatient, were informed about the study. The face-to-face interview method was used by a single researcher with a single patient relative.

The questionnaire consisted of a total of 23 questions. The participants were asked about the socio-demographic characteristics such as age, gender, marital status, educational status, social security, and the type of hepatitis in their relatives, the degree of intimacy with the patient and living status in the same home. Patient's relatives were asked what type of hepatitis they knew with an open-ended question, and hearing states of hepatitis A, B, C, D, E, and G were evaluated in later parts of the questionnaire. Those who respond positively to the sentence "Hepatitis is an infectious disease with cell inflammation and jaundice in the liver by various viruses" were considered to be aware of hepatitis. Those who respond positively to the sentence "Patients who carry the germ after HBV disease may be sick again in any time of life-long period and infectiousness of them continues" were also considered to be what is a carriage. Participants' general knowledge about hepatitis, vaccination status and risk perceptions about the disease were also questioned. In addition, their thoughts on the ways of transmission specifically for HBV and HCV and their attitudes and behaviors towards protection were questioned. Behavioural questions were questioned as "always, rarely and never". In order to prevent sexual transmission, condom use was only asked, spouses and sexual partners.

The study was found and approved ethically appropriate by the Erciyes University Clinical Research Ethics Committee (approval

number: 2016/537, date: 07.10.2016). Permission was obtained from the Erciyes University Faculty of Medicine Hospital Head Department. All participants were informed about the study before the study and their verbal consent was obtained.

### Statistical Analysis

Frequency and percentage, mean value, standard deviation, highest and lowest values were used for descriptive statistics. Pearson chi-square test was used for statistical analysis of category data. Statistical significance was considered as $p<0.05$.

## Results

The mean age of the participants was 44.0±14.5 (minimum: 20, maximum: 76) years. 52.9% were male and 83.5% were married. When education levels were evaluated, 40.5% had a primary school and below, 15.7% had secondary, 31.4% had high school and 12.4% had university graduation levels. Most of the participants (80.2%) lived in the city centre. Hepatitis B virus (HBV) infection was present in 61.2% and HCV infection was present in 38.8% of the patient's relatives. Relatives of the patient relatives are 47.1% spouse, 39.7% children or parents and 13.2% distant relatives-friends-neighbours. 67.8% of the patient's relatives lived in the same house, 6.6% of the relatives lived for less than one year, 11.6% for 1-5 years and 81.8% for more than five years. 92.6% of the participants said that they knew hepatitis B, 86.8% hepatitis C, 79.4% knew both hepatitis B and C. In addition, 23.1% of the patient's relatives reported that they knew hepatitis A, 7.4% of them knew hepatitis D and only 4.1% of them knew hepatitis E. When each type of hepatitis was asked separately, the distribution of hearing status of these hepatitis types was given in Table 1.

The majority of the patient's relatives stated that hepatitis can be caused by various viruses that cause cell inflammation in the liver. The rate of those who do not know the hepatitis was 26.4% and 33.1% of the patients' relatives did not know hepatitis carriage. The answers of patient's relatives to some questions about hepatitis were shown in Table 2.

The relationship between the knowledge of hepatitis and its carriage and some socio-demographic characteristics were given in Table 3. The relationship between the knowledge of hepatitis carriage and education level was found to be statistically significant ($p<0.05$). The rate of knowing the carriage of hepatitis was low in the people with primary and lower education level and it was high in the university graduates.

Table 4 shows the responses of the participants to the suggestions about hepatitis B and C transmission ways. When the patient's relatives were asked about the transmission of hepatitis B and C by body secretions, they responded with the highest rated blood, sperm and vaginal fluid (82.6%; 79.3%, 78.5% respectively) and the lowest rate stool, urine and sweat (25.6%, 23.1%, 21.5% respectively). Patient's relatives stated as low rate that breast milk and sputum from body fluids could be infectious (38.8% and 32.2%, respectively).

52.1% of the patient's relatives felt that they were at risk for hepatitis and 19.8% said that they shared this situation with another person. 69.4% of the patient's relatives stated that they

**Table 1.** Hepatitis types hearing status of the patient's relatives in the study group

| Hepatitis types (n=121) | Number | %* |
|---|---|---|
| Hepatitis A | 46 | 38.0 |
| Hepatitis B | 116 | 96.0 |
| Hepatitis C | 113 | 93.0 |
| Hepatitis D | 12 | 10.0 |
| Hepatitis E | 8 | 7.0 |
| Hepatitis G | 2 | 2.0 |

**Table 2.** The distribution of the answers to the questions about hepatitis of the patient's relatives in the research group

| Questions about hepatitis | Yes (n, %) | No (n, %) | I don't know (n, %) |
|---|---|---|---|
| Hepatitis causes inflammation in liver cells | 100 (82.6) | 3 (2.5) | 18 (14.9) |
| Hepatitis can be caused by various viruses | 102 (84.3) | 1 (0.8) | 18 (14.9) |
| Hepatitis can cause jaundice | 104 (86.0) | 0 (0.0) | 17 (14.0) |
| People with hepatitis can infect others | 100 (82.6) | 3 (2.5) | 18 (14.9) |
| People who continue to carry germs after having hepatitis B are called hepatitis B carriers (vector) | 91 (75.2) | 2 (1.7) | 28 (23.1) |
| People with hepatitis B may be ill again for any lifelong period | 94 (77.7) | 1 (0.8) | 26 (21.5) |
| Hepatitis B carriers can infect others | 87 (71.9) | 7 (5.8) | 27 (22.3) |
| Some types of hepatitis may last a lifetime | 100 (82.6) | 0 (0.0) | 21 (17.4) |
| It is possible that can be protected from some types of hepatitis diseases by vaccination | 99 (81.8) | 1 (0.8) | 21 (17.4) |
| Relatives of patients with hepatitis are at risk for disease | 106 (87.6) | 2 (1.7) | 13 (10.7) |
| Family members of patients with hepatitis should be screened | 106 (87.6) | 1 (0.8) | 14 (11.6) |
| Hepatitis can cause liver cirrhosis | 105 (86.8) | 0 (0.0) | 16 (13.2) |
| Hepatitis can cause liver cancer | 101 (83.5) | 0 (0.0) | 20 (16.5) |
| Hepatitis can cause liver failure | 104 (86.0) | 0 (0.0) | 17 (14.0) |
| Hepatitis can cause death | 103 (85.1) | 0 (0.0) | 18 (14.9) |
| Hepatitis B vaccine is given free of charge in groups at risk | 99 (81.8) | 2 (1.7) | 20 (16.5) |

had a hepatitis test and 48.8% stated that they had an HBV vaccine. 38.7% of those who did not have vaccination stated that they did not intend to have a vaccination. In 74 relatives of patients with HBV infection, the rate of vaccination of spouses was 58.8%, while the rate of vaccination of other relatives was 45%. When it was questioned about the ways of obtaining information about hepatitis, it was the highest rate of health personnel with 81.8%. Obtaining information from TV-radio, internet, acquaintance and books were reported at low rates (18.2%; 14.0%; 8.3%; 2.5%, respectively).

Considering their participation in some suggestions about hepatitis, the patient's relatives; 79.3% of those agreed that HBV and 66.9% of those agreed that HCV was curable, 37.2% agreed that HBV and 28.9% agreed that HCV was a self-healing disease. 28.9% of them agreed that herbal remedies may be the solution to the disease, 83.5% of them agreed avoidance of smoking and alcohol, 82.6% of them agreed that balanced and regular nutrition should be.

## Discussion

It is known that there is a serious lack of information about hepatitis which has an important place in infectious diseases. This lack of information is present in patients and their relatives as well

**Table 3.** Hepatitis and carriage knowledge of patient's relatives according to various characteristics- in the research group

| Characteristics | | n | Hepatitis knowledge | | | Hepatitis carriage knowledge | | |
|---|---|---|---|---|---|---|---|---|
| | | | Number | % | $X^2$, p | Number | % | $X^2$, p |
| Whole group | | 121 | 89 | 73.6 | - | 81 | 66.9 | - |
| Gender | Male | 64 | 43 | 67.2 | $X^2$=2.831 p=0.092 | 43 | 67.2 | $X^2$=0.004 p=0.952 |
| | Female | 57 | 46 | 80.7 | | 38 | 66.7 | |
| Education status | Primary school and below | 49 | 32 | 65.3 | $X^2$=4.338 p=0.227 | 25 | 51.0 | **$X^2$=12.932 p=0.005** |
| | Secondary school | 19 | 17 | 89.5 | | 16 | 84.2 | |
| | High school | 38 | 29 | 76.3 | | 26 | 68.4 | |
| | University | 15 | 11 | 73.3 | | 14 | 93.3 | |
| Residence | Provincial center | 97 | 71 | 73.2 | $X^2$=0.032 p=0.858 | 66 | 68.0 | $X^2$=0.267 p=0.605 |
| | Town/village | 24 | 18 | 75.0 | | 15 | 62.5 | |
| Living in same house | Yes | 82 | 58 | 70.7 | $X^2$=1.042 p=0.307 | 51 | 62.2 | $X^2$=2.591 p=0.107 |
| | No | 39 | 31 | 73.6 | | 30 | 76.9 | |

**Table 4.** The distribution of the responses of the patient's relatives to the suggestion of transmission ways of hepatitis B and C

| Transmission ways (n=121) | HBV | | | HCV | | |
|---|---|---|---|---|---|---|
| | Yes (%) | No (%) | I don't know (%) | Yes (%) | No (%) | I don't know (%) |
| Blood transfusion | 87.6 | 0.8 | 11.6 | 87.6 | - | 12.4 |
| Injector stick | 87.6 | - | 12.4 | 86.8 | 0.8 | 12.4 |
| Common injector usage | 87.6 | 0.8 | 11.6 | 86.8 | 0.8 | 12.4 |
| Dental treatment | 86.0 | 0.8 | 13.2 | 83.5 | 1.7 | 14.9 |
| Sexual intercourse | 85.1 | 1.7 | 13.2 | 86.0 | 0.8 | 13.2 |
| Sharing the same toothbrush with the patient | 81.8 | 2.5 | 15.7 | 81.8 | 2.5 | 15.7 |
| Instruments used during acupuncture, tattoo, piercing | 79.3 | 5.0 | 15.7 | 76.9 | 6.6 | 16.5 |
| Barber shears | 77.7 | 3.3 | 19.0 | 76.9 | 4.1 | 19.0 |
| Common instrument use like pedicure manicure | 76.0 | 5.8 | 18.2 | 73.6 | 5.8 | 20.7 |
| From mother to baby during childbirth | 72.7 | 4.1 | 23.1 | 69.4 | 5.8 | 24.8 |
| Using goods like cups, forks and spoons with sick person | 52.1 | 28.9 | 19.0 | 52.1 | 28.9 | 19.0 |
| Living in the same house with the patient | 32.2 | 40.5 | 27.3 | 31.4 | 41.3 | 27.3 |
| Contaminated water and food | 28.1 | 40.5 | 31.4 | 30.6 | 38.0 | 31.4 |
| Coughing-sneezing | 21.5 | 57.9 | 20.7 | 21.5 | 59.5 | 19.0 |
| Eating from the same plate with the patient | 19.8 | 50.4 | 29.8 | 23.1 | 46.3 | 30.6 |
| Mosquito bite | 18.2 | 31.4 | 50.4 | 19.0 | 32.2 | 48.8 |
| Handshake | 14.0 | 61.2 | 24.8 | 16.5 | 57.9 | 25.6 |
| Eating the patient's cooking | 11.6 | 63.6 | 24.8 | 10.7 | 65.3 | 24.0 |

HBV: Hepatitis B virus, HCV: Hepatitis C virus

**Table 5.** Knowledge and application of patient's relatives who participated in the research related to some issues to consider about hepatitis (%)

| Some issues to consider | Knowledge status (n=121) | Application status (n=121) | | |
|---|---|---|---|---|
| | | Always | Rarely | Never |
| Condoms should be used for sexual intercourse* (n=57) | 86.0 | 61.4 | 22.8 | 17.6 |
| The toothbrush of patients with hepatitis does not be used | 88.4 | 90.9 | 1.7 | 7.4 |
| The nail clippers of the patient with hepatitis do not be used | 76.9 | 65.3 | 10.7 | 24.0 |
| In case of any injury, the wound is not treated with bare hands | 82.6 | 70.2 | 10.7 | 19.0 |
| It should be protected from sick people's blood and body fluids | 85.1 | 73.6 | 8.3 | 18.3 |
| It should be careful about visiting a dentist that disease can be transmitted from | 86.0 | 66.9 | 9.9 | 23.1 |
| It should be careful about visiting barber-hairdresser that disease can be transmitted from | 77.7 | 58.7 | 10.7 | 30.6 |
| Foods should be washed with plenty of water | 84.3 | 76.9 | 8.3 | 14.9 |

as in many segments of society (15,16,17,18,19,20). In our study, awareness rates of hepatitis types B, C, A, D and E were 92.6%, 86.8%, 23.1%, 7.4%, 4.1% respectively (Table 1). In a similar study conducted by Poyrazoğlu et al. (21) In 2009, they found hepatitis B to be 99.1%, hepatitis C to 98.2%, and hepatitis A to be 86.6% with higher rates than our study. In another study conducted by Güner et al. (15) related to the level of knowledge in patients with hepatitis B, they found hepatitis D and E low similar to our study. Although the participants were asked by saying the name of each type of hepatitis in our study, the rate of awareness of hepatitis A, D and E was very low. This can be explained by the fact that the people in the research group had a higher awareness of hepatitis types B and C because they were relatives of patients with hepatitis B and hepatitis C.

Instead of our study, it was observed that 26.4% of the participants did not know hepatitis and 33.1% did not know the carriage (Table 2). According to Poyrazoğlu et al.'s (21) study, the rate of incomplete or incorrect knowledges of hepatitis and hepatitis carriage were 58.9%, 96.4% respectively and the rates were higher than our study. Over a decade of time between the two studies, increased knowledge of patient's relatives about hepatitis can be attributed to the higher educational level of our study group and to the change in socio-demographic characteristics, such as residence in the provincial centre. In our study, the majority of the patient's relatives stated that hepatitis can cause liver failure, cirrhosis and liver cancer (86.0% 86.8%, 83.5%, respectively) (Table 2). Güner et al. (15) respectively, 61.9%, 85.7% and 65.7% were found to be low compared to our study. In a society-based study aiming at the level of knowledge about hepatitis in Brazil, it was reported that hepatitis may cause cirrhosis and liver cancer as 80.8% and 84.6% respectively (22). Having such high rates indicates that societies including in our country are aware of the serious diseases that hepatitis can cause.

The main ways of transmission of hepatitis B and C are the perinatal, sexual, and parenteral/percutaneous ways, which are the route of transmission from mother to infant; It is known that the same cutlery and plate can be transmitted in barbers and beauty centres, and there is no transmission by water and food, vectors and air (23,24). Hepatitis viruses can be found in all fluids in the human body, especially in the blood, semen and vaginal fluid, in the vagina, semen and saliva are found relatively low concentrations (25). It has been shown in several studies that infected blood and blood products and genital secretions, pericardium, peritoneum, pleura, cerebrospinal, synovial and amniotic fluid, such as body fluids can also be passed through the mucosa contact. However, in the case of stool, urine, saliva, sweat, sputum, and vomiting, there is no risk of transmission unless it contains a significant amount of blood (24). There are publications showing that hepatitis B and C are not infected with vectors such as handshaking with the patient, eating from the same container, coughing, and mosquitoes. At the same time, in a review published in 2015, it was stated that transmission by vectors was suspicious (21,26).

In our study, although the majority of the participants knew the three basic transmissions ways correctly, they did not have enough information about the transmission ways of hepatitis. The participants stated that the most common transmission ways of hepatitis B were blood transfusions, stinging, the use of a common syringe, dental treatment, and sexual intercourse (87.6% 87.6%, 86.0% 85.1%, respectively). They stated that the transmission ways of hepatitis C were blood transfusions, stinging-joint injectors, sexual intercourse and dental treatment (87.6% 86.8%, 86.0% 83.5%, respectively) (Table 4). In addition, the rate of those who know that hepatitis B and C will not be transmitted by contaminated water and food is around 40%. These rates indicate that patients' relatives should be informed about the ways of transmission. In the study, more than three-quarters of the participants knew that the using the same toothbrush with the patient, barber scissors, manicure pedicure instruments, and the use of acupuncture, tattoos, and piercings could make the transmission of the disease. The reason why there is not enough information about the seriously contamination in the use of social areas can be because of lack of information, low awareness, and the fact that our study group is quite older than the age range that will perform procedures such as tattoos and piercings. About one-fifth of the participants thought that hepatitis can be transmitted by mosquito bites, coughing and sneezing, and eating from the same dish with the patient. This suggests that the transmission routes of hepatitis may be confused with other respiratory diseases.

There are many publications in the literature about the transmission of hepatitis in the family and during sexual intercourse between spouses is well known (27,28,29). Intra-family transmission is likely to occur during sexual intercourse between

spouses (30). However, the use of common living space and the use of personal belongings may be involved in the transmission of children. In addition to taking preventive measures, family members who carry a serious risk for hepatitis infection should also have some examinations in terms of disease. In the study, 87.6% of the participants stated that their relatives are at risk and that they should have a screening test. 71.9% of the participants stated that HBV carriers can infect the disease. Approximately 30% of the participants think that the disease can be transmitted by living in the same house. The instead of our study, 52.1% of the patient's relatives felt that they were at risk for disease transmission and 69.4% stated that they had a test. These rates were similar to the results of previous studies conducted at the same university (21). Despite a decade of time between these two studies, living at home with the patient was a risk factor, but at low rates, almost no difference was observed between the rate of those testing for the disease. The lack of information about the transmission ways of the disease is thought to continue.

In our study, 81.8% of the participants stated that some types of hepatitis can be prevented by vaccination and a free hepatitis B vaccine is given to individuals at risk (Table 2). In a previous study by Poyrazoğlu et al. (21), the rate of knowing free vaccination was reported as 26.8%. This makes us think that the awareness of vaccination programs has increased in our country. In our country, it is given free of charge to adults in hepatitis A and B risk groups who are in routine vaccines in the childhood vaccination program (31). In our study, 48.8% of the patient's relatives stated that they had an HBV vaccine, and 58.8% of the other patient's relatives had HBV vaccination. 38.7% of those who did not have vaccination stated that they did not intend to have the vaccination. The fact that spouses are vaccinated at a higher rate than other relatives can be attributed to the high level of knowledge about the sexual transmission of the disease and to the awareness of the spouses. However, vaccination rates are still well below expectations.

In our study, the participants stated that 81.8% of the patients were informed about the disease from health personnel. This was followed by TV-radio and the Internet. Güner et al. (15) in their study, physicians are the primary source of information in patients with hepatitis B. In another study evaluating the level of knowledge about hepatitis in Korean American parents, physicians were the reliable source of information with 40.2% (32). These rates show that healthcare professionals are a very important group for a reliable source of information.

In this study, various suggestions about the transmission of hepatitis were given to the patient's relatives and their knowledge and application status were questioned. The use of condoms during sexual intercourse, the toothbrush and nail scissors of the patient with hepatitis will not be used, no bare-handed intervention to open injuries, visiting the dentist and barber-hairdresser should be careful are the cases which are known by the participants at higher rates. Although participants' knowledge rates were high their application rates about the cases were relatively low (Table 5). In our study, it was found that the knowledge of these propositions was higher than that of Güner et al.'s (15) study. According to Poyrazoğlu et al. (21), their knowledge s was lower, but their application status was higher than our study. Although the ways of transmission of the disease are known, low rates in applications shows that the behavioral transformation of information is insufficient. A remarkable point in our study is that the food should be washed with plenty of water to respond to a high rate and some herbal remedies may have a place in the treatment of the disease that is close to 30%. In the study of Güner et al. (15), while the rate of those who think that herbal remedies can be a solution to the disease was 13%, higher rates in our study suggest that traditional and alternative medicine has become widespread in recent years in our country and may cause some misperceptions in the society.

### Study Limitations

The fact that the study was conducted in a single center, that it could not be generalized to other patients, the number of patients attending a tertiary hospital and their relatives did not represent the population are among the limitations of the study.

## Conclusion

In our study, it was found that the participants did not have enough knowledge about hepatitis and some wrong and incomplete applications. In particular, there was a serious deficiency in converting some knowledge into behaviour. For this reason, the training to be given to this group as well as to the whole society is of great importance. There can be achieved awareness about facilitating access to information, the importance of vaccination, and ways of protection from disease with the help of providing accurate and sufficient information. For this purpose, first of all, training should be provided for health workers and this information should be transferred to patients and their relatives by means of correct communication. It is recommended to establish counselling units for the patients and their relatives in the hospital. In addition, the importance of vaccination with public spots can be emphasized and the benefits of vaccination and negative attitudes towards vaccination can be prevented.

### Ethics

**Ethics Committee Approval:** The study was found and approved ethically appropriate by the Erciyes University Clinical Research Ethics Committee (approval number: 2016/537, date: 07.10.2016).

**Informed Consent:** All participants were informed about the study before the study and their verbal consent was obtained.

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

### Authorship Contributions

Consept: F.Ç., E.A.M., Desing: Z.B., Supervision: F.Ç., E.A.M., Data Collection or Processing: B.O., S.A., Analysis or İnterpretation: B.O., S.A., Literature Search: Z.B., Writing: B.O., M.N., Critical Review: Z.B., A.U.K.

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Research Article

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# *Genotype Distributions and Hepatitis B Coinfection in Hepatitis C Patients at a University Hospital*

## Bir Üniversite Hastanesinde Hepatit C ile Enfekte Hastalarda Genotip Dağılımları ve Hepatit B Koenfeksiyonu

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***ABSTRACT***

**Objectives:** Hepatitis C virus (HCV) infection is a major cause of chronic liver disease. Comorbidity with the hepatitis B virus (HBV) leads to progressive fibrosis and severe liver disease. Our study aimed to determine HBV coinfection rates in HCV patients.

**Materials and Methods:** This single-center study retrospectively examined anti-HCV-positive patients monitored at our center in January 2015-June 2020. The patients' hepatitis B surface antigen, anti-hepatitis B core antigen immünoglobulin (anti-HBc IgG), anti-HBs, anti-delta, anti-human immunodeficiency virus (HIV), HCV-RNA, HBV-DNA and HDV-RNA test results were analyzed.

**Results:** Among 602 anti-HCV-positive patients, 462 (76.7%) with positive HCV-RNA values were included. The median age was 55.27 (18-88), while 279 (60.4%) were female. The most prevalent genotype was 1b 60.7%. HCV/HBV coinfection was found as 1.8%. HBV exposure was in 27.7%, isolated anti HBc IgG positivity was in 4.4%, and 21% were naturally immune to HBV. HBV-DNA was <2000 IU/mL in all patients.

**Conclusion:** Due to their similar route of contagion, HCV patients need to be screened for HBV serology. Patients with negative HBV serology should be vaccinated.

**Keywords:** Genotype, hepatitis B, hepatitis C

***ÖZ***

**Amaç:** Hepatit C virüsü (HCV) enfeksiyonu kronik karaciğer hastalığının majör nedenidir. Hepatit B virüsü (HBV) ile birlikteliği ilerleyici fibrozis ve ciddi karaciğer hastalığına yol açmaktadır. Çalışmamızda kronik HCV ile enfekte hastalarda HBV koenfeksiyonu oranlarını saptamayı amaçladık.

**Gereç ve Yöntemler:** Bu tek merkezli kohort çalışmasında Ocak 2015-Haziran 2020 tarihleri arasında merkezimizde izlenen anti-HCV pozitif hastalar retrospektif olarak tarandı. Hastaların hepatit B yüzey antijen, anti-hepatit B çekirdek antijen immünoglobulin (anti-HBc IgG), anti-HBs, anti-delta, insan bağışıklık yetmezliği virüsü (anti-HIV), HCV-RNA ve HBV-DNA, HDV-RNA test sonuçları istatistiksel olarak analiz edildi.

**Bulgular:** Anti-HCV pozitif 602 hastanın, HCV-RNA değeri pozitif 462'si (%76,7) çalışmaya dahil edildi. Olguların yaşları medyan 55,27 (18-88), 279'u (%60,4) kadındı. En sık genotip, 1b %60,7 idi. HCV/HBV koenfeksiyonu %1,8 olarak bulundu. HBV maruziyeti olguların %27,7'sinde, izole anti HBc IgG pozitifliği %4,4'ünde tespit edilirken, %21'i HBV'ye doğal bağışıktı. HBV-DNA hastaların tümünde <2000 IU/mL idi.

**Sonuç:** Benzer bulaş yolları sebebiyle HCV ile enfekte hastalar HBV serolojisi açısından taranmalıdır. HBV serolojisi negatif hastalar aşılanmalıdır.

**Anahtar Kelimeler:** Genotip, hepatit B, hepatit C

**Aydın Ö. Genotype Distributions and Hepatitis B Coinfection in Hepatitis C Patients at a University Hospital. Viral Hepat J. 2021;27:13-18.**

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## Introduction

Hepatitis B and hepatitis C infections are among the most prevalent causes of chronic liver (CL) disease in the world (1). It is estimated that more than 250 million people in the world are infected with hepatitis B virus (HBV), and more than 70 million are infected with HCV (1,2,3). According to the current report of World Health Organization, the annual number of deaths related to viral hepatitis is 1.34 million, and this rate is higher in comparison to tuberculosis and the human immunodeficiency virus (HIV). Hepatitis B and hepatitis C infections are responsible for 96% of deaths related to viral hepatitis, and they are a major public health problem. Most deaths take place in relation to end-stage liver disease and hepatocellular carcinoma (HCC) (2,3). It is estimated that HCC develops by 1-3% in HCV-infected patients in 30 years (4).

Dual HCV/HBV infection is not a surprise due to their similar route of contagion. Coinfection is seen in regions that are endemic for HCV or HBV. The risks of viruses to be transmitted through the parenteral route is high in specific groups such as hemodialysis patients, intravenous drug users, those who have organ transplantation, HIV-infected individuals and beta thalassemia patients (5).

It is determined that, in coinfected patients, the HCV prevents HBV replication, and while HCV is involved in viremia, the HBV-DNA levels are suppressed. The interaction between the two viruses is a complex clinical picture, while it is mostly characterized by HBV inhibition applied by HCV. When clinical observational studies are compared to HCV and HBV infections in coinfected cases, they show that CL disease is more progressed (6).

While direct-acting antiviral agents (DAA) that are used during treatment of chronic HCV achieve HCV clearance, the suppressed HBV has a risk of replication. Reactivation may occur without observation of a picture of hepatitis, whereas it may be seen on a broad spectrum to include development of CL failure on a level requiring transplantation. Patients infected with chronic HCV need to be monitored closely and carefully in terms of the serological markers of HBV infection (7,8,9,10).

In this study, we aimed to retrospectively determine the genotype distributions, HBV infection exposure and coinfection prevalence of patients with chronic HCV infection being monitored at our clinic.

## Materials and Methods

This single-center retrospective cohort study was carried out at the İstanbul Medeniyet University, Göztepe Training and Research Hospital. The ethical approval for the study was obtained from the İstanbul Medeniyet University, Göztepe Training and Research Hospital on the date of 22.07.2020 and with the decision number of 2020/0461.

In our study, the patients with anti-HCV positivity between January 2015 and June 2020 were retrospectively searched and determined from the hospital database, and those with a positive HCV-RNA value were included in the study. The sex, age and nationality of the patients were recorded, and their anti-HCV, as well as diagnosis hepatitis B surface antigen (HBsAg), anti-hepatitis B core antigen (HBc) immunoglobulin (IgG), anti-HBs, anti-HIV and anti-delta values were studied with the enzyme linked immunosorbent assay (ELISA) method and recorded. The HCV-RNA, HCV genotypes, HBV-DNA and HDV-RNA values were measured by the polymerase chain reaction method.

### Statistical Analysis

For the statistical analysis, the Number Cruncher statistical System 2007 (Kaysville Utah, USA) software was used. While analyzing the data of the study, descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were utilized. The compatibility of the quantitative data with normal distribution was tested by Kolmogorov-Smirnov test, Shapiro-Wilk test and graphical assessments. In the comparison of the qualitative data, Pearson's chi-squared test, Fisher-freeman-halton exact test and Fisher's exact test were used. The level of statistical significance was accepted as $p<0.05$.

## Results

Among the 602 anti-HCV positive cases, the study included 462 (76.7%) cases with positive HCV-RNA measurements. 279 (60.4%) of the patients were female, and 183 (39.6%) were male. The median age of the patients was 55.27 (18-88) years. The patients were most frequently infected with the genotype 1b (240/399, 60.7%).

In 433 patients with positive HCV-RNA; HBsAg, anti-HBc IgG and anti-HBs were examined. HBsAg was positive in 8 (1.8%) of 433 patients, and HCV/HBV coinfection was determined. One hundred twenty of the patients (27.7%) showed anti HBc-IgG positivity, and there was HBV exposure. Ninety-three patients (21.5%) with anti HBc-IgG and anti-HBs positivity were naturally immune to HBV infection. Isolated anti HBc-IgG positivity was found in 19 (4.4%) patients. One hundred fourty-seven patients with anti-HBs positive values (33.9%) were vaccinated against HBV. In 8 coinfected patients and 8 of the isolated anti HBc IgG positivity patients (42%), HBV-DNA was <2000 IU/mL, and hepatitis B e antigen (HBeAg) was negative. In 2 (25%) patients where dual HCV/HBV infection was determined, HBsAg clearance was determined during follow-ups. One of the patients (50%) developed anti HBs. Anti-delta was positive in 1 patient (1/16, 6.3%), and the HDV-RNA value was negative. One of the patients (1/461, 0.2%) had anti-HIV positivity, whereas this case also showed isolated anti HBc IgG positivity (Table 1, Figure 1).

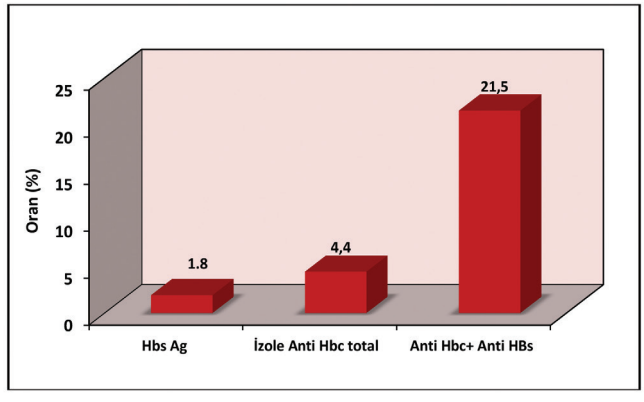


**Figure 1.** Assessment of HBV exposure rates in HCV-RNA positive cases

HBV: Hepatitis B virus, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen

| **Table 1.** Distribution of descriptive characteristics | | | |
|---|---|---|---|
| | | n | % |
| Age (years) | Min-max (median) | 18-88 (58) | |
| | X ± SD | 55.27±14.58 | |
| | <35 years | 49 | 10.6 |
| | 35-44 years | 66 | 14.3 |
| | 45-54 years | 80 | 17.3 |
| | 55-64 years | 133 | 28.8 |
| | ≥65 years | 134 | 29.0 |
| Sex | Female | 279 | 60.4 |
| | Male | 183 | 39.6 |
| Nationality | TC | 413 | 89.4 |
| | Foreign nationality | 49 | 10.6 |
| Genotype (n=399) | 1 | 71 | 17.8 |
| | 1a | 40 | 10.0 |
| | 1b | 242 | 60.7 |
| | 2 | 7 | 1.8 |
| | 2a/c | 7 | 1.8 |
| | 3 | 18 | 4.5 |
| | 3a | 7 | 1.8 |
| | 4 | 2 | 0.5 |
| | 4a | 2 | 0.5 |
| | 4c/d | 3 | 0.8 |
| HCV-RNA | Min-max (median) | 276-98756321 (1698075) | |
| | X ± SD | 5710202.73±11201601.20 | |
| Anti-HIV (n=461) | Negative | 460 | 99.8 |
| | Positive | 1 | 0.2 |
| HBsAg (n=433) | Negative | 425 | 98.2 |
| | Positive | 8 | 1.8 |
| Anti-HBc IgG (n=433) | Negative | 313 | 72.3 |
| | Positive | 120 | 27.7 |
| Anti-HBs (n=433) | Negative | 193 | 44.6 |
| | Positive | 240 | 55.4 |
| Anti-HBc IgG + anti-HBs (n=433) | Negative | 340 | 78.5 |
| | Positive | 93 | 21.5 |
| Isolated anti-HBc IgG (n=433) | Negative | 414 | 95.6 |
| | Positive | 19 | 4.4 |
| HBsAg clearance | Negative | 6 | 75 |
| | Positive | 2 | 25 |
| Isolated anti-HBs (n=433) | Negative | 286 | 66.1 |
| | Positive | 147 | 33.9 |
| HBV-DNA (n=16) | Negative (<2000) | 16 | 100 |
| HBeAg (n=16) | Negative | 16 | 100 |
| Anti-delta (n=16) | Negative | 15 | 93.8 |
| | Positive | 1 | 6.3 |

Min: Minimum, Max: Maximum, SD: Standard deviation, TC: Republic of Turkey, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, HBsAg: Hepatitis B surface antigen, HBc: Hepatitis B core antigen, IgG: Immunoglobulin, HBeAg: Hepatitis B e antigen

In the analysis of the qualitative data, no significant difference was found between the ages of the cases based on their sexes (p>0.05). The HBsAg, anti-HBc IgG, anti-HBs, anti-HIV, anti-delta positivity rates also did not show a significant difference based on sex (p>0.05). The ratio of the female cases being of foreign nationality was significantly higher (p=0.001, p<0.01) (Table 2).

There was a significant difference among the genotypes of the patients based on their nationalities (p=0.048; p<0.05). The genotype 1 rate in the citizens of the Republic of Turkey (TC) nationals and the genotype 3 rate in the foreign nationals were found higher (Table 3).

## Discussion

In our study, we determined the HBV coinfection rate in the chronic HCV infected patients being monitored at our clinic to be 1.8%. Studies conducted worldwide have shown the HCV/HBV dual infection rate was determined as 7.2% in Taiwan, 2.4-6% in Turkey, 1.4% in the USA, 8.4% in China, 0.8% in Brazil and 6.6% in Pakistan (10,11,12,13,14,15,16,17,18,19). The prevalence differences in studies may be explained by the differences in the HCV and HBV mono-infection rates in geographical regions. If the mono-infection is endemic in that region, the prevalence of dual infection increases in parallel to this.

**Table 2.** Assessment of patients based on sex

| | | Sex | | p |
|---|---|---|---|---|
| | | Female | Male | |
| | | n (%) | n (%) | |
| Age (years) | <35 years | 31 (11.1) | 18 (9.8) | [a]**0.170** |
| | 35-44 years | 37 (13.3) | 29 (15.8) | - |
| | 45-54 years | 40 (14.3) | 40 (21.9) | - |
| | 55-64 years | 82 (29.4) | 51 (27.9) | - |
| | ≥65 years | 89 (31.9) | 45 (24.6) | - |
| Nationality | TC | 232 (83.2) | 181 (98.9) | [a]**0.001**** |
| | Foreign nationality | 47 (16.8) | 2 (1.1) | - |
| Anti-HIV | Negative | 278 (100) | 182 (99.5) | [b]**0.397** |
| | Positive | 0 (0) | 1 (0.5) | - |
| HBsAg | Negative | 259 (98.1) | 166 (98.2) | [b]**1.000** |
| | Positive | 5 (1.9) | 3 (1.8) | - |
| Anti-HBc IgG | Negative | 190 (72.0) | 123 (72.8) | [a]**0.854** |
| | Positive | 74 (28.0) | 46 (27.2) | - |
| Anti-HBs | Negative | 115 (43.6) | 78 (46.2) | [a]**0.596** |
| | Positive | 149 (56.4) | 91 (53.8) | - |
| Anti-HBc IgG + anti-HBs | Negative | 204 (77.3) | 136 (80.5) | [a]**0.429** |
| | Positive | 60 (22.7) | 33 (19.5) | - |
| Isolated anti-HBc IgG | Negative | 255 (96.6) | 159 (94.1) | [a]**0.214** |
| | Positive | 9 (3.4) | 10 (5.9) | - |
| Isolated anti-HBs | Negative | 175 (66.3) | 111 (65.7) | [a]**0.896** |
| | Positive | 89 (33.7) | 58 (34.3) | - |
| Anti-delta | Negative | 6 (85.7) | 9 (100) | [b]**0.438** |
| | Positive | 1 (14.3) | 0 (0) | - |

[a]: Pearson's chi-squared test, [b]: Fisher's exact test, **p<0.01, HIV: Human immunodeficiency virus, HBsAg: Hepatitis B surface antigen, HBc: Hepatitis B core antigen, IgG: Immunoglobulin

**Table 3.** HCV genotype and nationality relationship

| | | Genotype | | | | | | p |
|---|---|---|---|---|---|---|---|---|
| | | Genotype 1 | Genotype 1a | Genotype 1b | Genotype 2 | Genotype 3 | Genotype 4 | |
| | | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | |
| **Nationality** | **TC** | 68 (19.2) | 35 (9.9) | 214 (60.5) | 12 (3.4) | 18 (5.1) | 7 (2.0) | [c]**0.048*** |
| | **Foreign** | 3 (6.7) | 5 (11.1) | 28 (62.2) | 2 (4.4) | 7 (15.6) | 0 (0) | |

[a]: Pearson's chi-squared test, [c]: Fisher freeman halton exact test, *p<0.05, **p<0.01, TC: Republic of Turkey, HCV: Hepatitis C virus

Approximately two thirds of the HCV-RNA positive patients who were included in the study were 55 years old or older. In various studies, the rate of 50 years old or older patients among those with HCV positivity varied in the range of 72-75% (20,21). This situation may be explained by that patients and physicians do not have a sufficient level of awareness on screening for HCV.

89.4% of our patients were TC nationals, while 10.6% were mostly women of foreign nationality coming from Turkic Republics. The genotype 1b was determined in 60.7% of the cases. The genotype 1 rate in the TC national cases and the genotype 3 rate in the foreign national cases were found to be significantly higher. The finding that the foreign national patients were mostly women may be explained by the migration of women to Turkey to work in childcare and household jobs. Studies have supported the finding that genotype 1 infection is the most frequently seen genotype in Turkey (21,22,23).

The prevalence of HCV and HBV is not exactly known due to the absence of studies covering a large population of patients and occult HBV infection in most patients. This picture that is defined as an occult hepatitis B picture carries a high risk of CL fibrosis and HCC (3). In HCV-positive cases, serological markers of hepatitis B are observed to be positive by 25% (24,25). In our study, there was HBV infection exposure in approximately a third of the patient. Similarly, Tozun et al. (26) determined HBV exposure in one third of patients in Turkey infected with HCV. Different studies have reported this rate as 24-39.1% (10,15,18). Isolated anti HBc IgG positivity was determined in 4.4% of our cases. Previous studies conducted in Turkey reported this rate as 5.4-17% (12,13,15). Determination and monitoring of isolated HBc IgG are important in terms of the risk of HBV reactivation. The HBV vaccination rate in our cases was determined as 33.9%. While Yılmaz-Karadag (15) reported that HBV immunization was not encountered in any of their cases, this rate was determined as 60% in the study by Tahmaz et al. (12). The most effective method of preventing HBV coinfection development is to vaccinate seronegative individuals.

In coinfected patients, while hepatitis C is active, it may lead to suppression of HBV-DNA, HBeAg seroconversion or HBsAg clearance (5). While the HCV infection was dominant in all cases of ours, HBV-DNA was <2000 IU/mL and suppressed. HBsAg clearance developed in 2 of 8 coinfected patients of ours, and anti-HBs formation was observed in 1 of these patients. In their study where they applied HCV treatment on 28 coinfected patients, Uyanikoglu et al. (27) determined HBsAg loss in 2 patients, while they reported anti-HBs development in 1 of these patients. Potthof et al. (28) determined HBsAg clearance and anti-HBs seroconversion during the follow-up of a patient coinfected with HBV for whom they provided HCV treatment.

While HCV clearance is observed during antiviral treatment in dual infection patients, reactivation of hepatitis B which is inactive before treatment may be observed. Today, reactivation is also determined DAA treatments that have replaced interferon-based treatments. Reactivation may result in a broad range of outcomes from alanine aminotransferase (ALT) exacerbation to CL failure or even death. This situation reveals the importance of making sure to investigate HBV serological markers in cases infected with HCV. In HCV patients planned for DAA treatment, HBsAg, anti HBc IgG and anti-HBs should be checked, and if necessary, the ALT and HBV-DNA parameters should be monitored. In suitable cases, it is recommended to use nucleoside analogues for HBV treatment (7,8,9,10). As our data were retrospectively collected, we were not able to determine whether or not there was HBV infection exacerbation in our patients. In their study involving 82 coinfected patients during their chronic HCV treatment, Aygen et al. (29) reported that HBV reactivation developed in 33.3% of the cases while they were receiving pegylated interferon and ribavirin treatment, and HBV-DNA values turned negative by oral antiviral treatment. Likewise, Lee et al. (10) observed HBV reactivation in 28.6% of their cases during DAA treatment, while they did not determine HBsAg clearance in any of the cases.

Among the HCV/HBV coinfected cases, anti-delta positivity was determined in 1 case, anti-HIV positivity was determined in 1 of the isolated anti HBc IgG positive cases, and as HBV, HCV, HIV and HDV have similar parenteral transmission route especially in risky patient populations, this shows the necessity of simultaneous serological screenings. Prevention and/or early diagnosis of coinfections and determination of treatment principles are highly important in preventing progressive CL damage.

### Study Limitations

As our study was retrospective, it had limitations due to the missing data on the infection risk factors of our patients, some serological parameters and treatment information.

## Conclusion

Consequently, we determined the HCV/HBV dual infection prevalence in chronic HCV infected patients as 1.8%. It should be kept in mind that progressive CL damage in coinfected patients is more frequent in comparison to mono-infections, and hepatitis B serological parameters should be determined in HCV-infected patients. Patients that show positivity in terms of HBV serology should be closely monitored in terms of HBV reactivation during hepatitis C treatment, and they should be assessed in terms of treatment. It should be ensured that patients with negative hepatitis B serological tests are vaccinated in the shortest possible time.

### Ethics

**Ethics Committee Approval:** This study was approved by İstanbul Medeniyet University, Göztepe Training and Research Hospital (approval number: 2020/0461, date: 22.07.2020).

**Informed Consent:** Retrospective study.

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

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Research Article

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# *Frequency of HBV, HCV and HIV Infections and Determination of HCV Genotype Distribution in People who Inject Drugs*

## Damaryolu ile Madde Kullanımı Olan Kişilerde HBV, HCV ve HIV Enfeksiyonlarının Sıklığı ve HCV Genotip Dağılımının Belirlenmesi

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***ABSTRACT***

**Objectives:** The aim of this study was to determine the frequency of blood-borne infections [hepatitis B virus (HBV), HCV, and human immunodeficiency virus (HIV)] and the genotype distribution retrospectively in people who inject drugs (PWID).
**Materials and Methods:** A total of 150 PWID were investigated retrospectively. HBV, HCV, HIV serologies and viral load information were recorded.
**Results:** The mean age was 27.0±4.89 and 13 (8.7%) patients were female. One hundred and twenty six (84.0%) patients had shared injectors at least once in their lives. Anti-HCV positivity was detected in 91 (60.6%) of 150 patients, hepatitis B surface antigen positivity in 3 (2.0%) and anti-HIV positivity in 1 patient. HCV-RNA was detected in 61 of the patients with anti-HCV positivity and 48 (67.6%) of them were positive for HCV-RNA. Genotype was studied in 38 patients with HCV-RNA positivity. Genotype 1a was detected in 20 patients, genotype 3a in 12 patients, genotype 4c/d in 5 patients and 2b in 1 patient.
**Conclusion:** In PWID, HCV infection was found to be in high ratio in PWIDs and the most common HCV genotype was 1a. It was concluded that injector sharing caused infectious diseases in PWID and that some HCV genotypes were dominant in these patients. Genotype determination will be a guide for individualized treatments in these patients.
**Keywords:** Hepatitis C virus, genotype, people who inject drugs

***ÖZ***

**Amaç:** Bu çalışmanın amacı, damar içi madde kullanıcılarında (DİMK) kan yoluyla bulaşan enfeksiyonların [hepatit B virüs (HBV), HCV ve insan bağışıklık yetmezliği virüsü (HIV)] sıklığını ve genotip dağılımını geriye dönük olarak belirlemektir.
**Gereç ve Yöntemler:** Geriye dönük olarak toplam 150 DİMK incelendi. HBV, HCV, HIV serolojileri ve viral yük bilgileri kaydedildi.
**Bulgular:** Ortalama yaş 27,0±4,89 olup, 13 (%8,7) hasta kadındı. Yüz yirmi altı (%84,0) hasta hayatında en az bir kez enjektör paylaşmıştı. Yüz elli hastanın 91'inde (%60,6) anti-HCV pozitifliği, 3'ünde (%2,0) hepatit B yüzey antijen pozitifliği ve 1 hastada anti-HIV pozitifliği saptandı. Anti-HCV pozitifliği olan hastaların 61'inde HCV-RNA tespit edildi ve bunların 48'inde (%67,6) HCV-RNA pozitifti. Genotip tayini, 38 HCV-RNA pozitif hastada yapıldı. Yirmi hastada genotip 1a, 12 hastada genotip 3a, 5 hastada genotip 4c/d ve sadece bir hastada genotip 2b tespit edildi.
**Sonuç:** DİMK'de HCV enfeksiyonu yüksek oranda bulundu ve en yaygın HCV genotipi 1a olarak tespit edildi. Enjektör paylaşımının DİMK'de bulaşıcı hastalıklara neden olduğu ve bu hastalarda bazı HCV genotiplerinin baskın olduğu sonucuna varıldı. Genotip tespiti, bu hastalarda bireyselleştirilmiş tedavilerin planlanmasında yol gösterici olacaktır.
**Anahtar Kelimeler:** Hepatit C virüsü, genotip, damar içi madde kullanıcıları

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## Introduction

Blood-borne pathogens are microorganisms, such as bacteria and viruses, that can cause disease in humans. These pathogens are transported through the blood. There are many blood-borne pathogens such as malaria, syphilis, brucellosis, hepatitis B virus (HBV), HCV and human immunodeficiency virus (HIV). Studies show that less than half of people who inject drugs (PWID) use a sterile syringe (46.9%) and 38.5-61% of them share syringe/needle or drug solutions with someone else over the past 6 months (1,2).

Due to the common use of contaminated needles and injection equipment, PWID are an important risk group for HCV infection (3,4,5). HCV seropositivity rate increases to 50-90% in PWID (6). In a study conducted in the UK, 428 PWID under the age of 30 were found to encountered 4% HIV and 44% HCV in the initial evaluation (7). In a systematic review of 11 studies from five European Union Countries, the proportion of undiagnosed HCV infections among those using intravenous drug varies between 24-76% (8).

Among PWID, the prevalence of hepatitis B surface antigen (HBsAg) carriers ranges from 5% to 10% in 21 countries and exceeds 10% in 10 countries (9). The prevalence of hepatitis B infection was found to be 0.8% in a study in Bosnia and Herzegovina, but it was found to be as high as 21.5% in another study in China (10,11). In a study conducted in 2077 patients using intravenous drug in Germany, HIV seroprevalence was found to be 0-9.1% compared to cities (12).

There are six genotypes of HCV. Determination of HCV genotypes is important in the treatment and course of the disease. HCV genotype distribution was investigated in different groups in the world geography. In the general population, genotype 1 is the most common in North America, Northern and Southern Europe, Japan, and Eastern Europe including our country (13,14,15). Genotype 3 is common in PWID in the Middle East and North Africa (16); In a Chinese study, genotype 3b and genotype 6a were more common (17). In our country, the most common genotype was found to be 1a in HCV-infected adolescents using intravenous drug (18,19).

The aim of this study is to investigate the sociodemographic characteristics of PWID who applied to Akdeniz University Alcohol and Substance Addiction Research and Application Center (AMBAUM) and to determine the frequency of blood-borne infections (HBV, HCV, and HIV) in this patient group. We also aimed to determine genotype distribution in patients with HCV infection.

## Materials and Methods

This study was planned retrospectively in PWID who applied to AMBAUM between August 2017 and March 2018. Age, sex, education, heroin use, age of initiation of heroin use, drug use other than heroin, possible blood-borne agent serology and HCV genotype distribution were evaluated in PWID. Anti-HBs, anti-HCV and anti-HIV antibodies were analysed by EIA method (Advia Centaur HP, Siemens Healthcare Diagnostics, USA). HCV-RNA determination was performed by a commercial real time-polymerase chain reaction (RT-PCR) test (COBAS AmpliPrep/COBAS TaqMan HCV, Roche Diagnostics, Roche Molecular Systems, Pleasanton, CA). A commercial reverse hybridization (line probe-based assay; GEN-C RT-PCR, Italy) was carried out for HCV genotyping. The ethics committee approval of the study was given by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (approval number: 352, date: 30/07/2018).

### Statistical Analysis

The data obtained in the study were analyzed by a computer using SPSS 20 software package program. Mean ± standard deviation was used for descriptive continuous variables and number and percentage were used for median categorical variables. The suitability of continuous variables to normal distribution was examined by Shapiro-Wilk test. The difference in percentages of categorical variables was analyzed by Pearson chi-square test, if more than 20% of expected frequencies were less than 5, Fisher's exact test was used. Due to lack of parametric test assumptions, difference between two independent group averages was analyzed by Mann-Whitney U test. Spearman's rho correlation analysis was used to determine the relationship between the two variables. When comparing continuous data of three or more groups, One-Way ANOVA was used when parametric test assumptions were met, and where parametric test assumptions were not met, Kruskal-Wallis test was used. $\alpha$=0.05 error margin (or 95% significance level) was used to determine differences in the analyzes.

## Results

A total of 150 patients with intravenous drug use were included in the study. The mean age of the patients was 27.0±4.89 and the sociodemographic characteristics including gender, education, and clinical characteristics such as smoking, cannabis, cocaine and stimulant use in addition to heroin are shown in Table 1.

**Table 1.** Sociodemographic characteristics and use of substances other than heroin

| | (n=150) | % |
|---|---|---|
| **Gender** | | |
| Female | 13 | 8.7% |
| Male | 137 | 91.3% |
| **Education status** | | |
| Primary school | 15 | 10.0% |
| Middle school | 101 | 67.3% |
| High school | 23 | 15.3% |
| University | 11 | 7.3% |
| **Smoking** | | |
| Yes | 142 | 94.7% |
| No | 8 | 5.3% |
| **Cannabis use** | | |
| Yes | 106 | 70.7% |
| No | 44 | 29.3% |
| **Cocain use** | | |
| Yes | 95 | 63.3% |
| No | 55 | 36.7% |
| **Use of stimulant** | | |
| Yes | 72 | 48.0% |
| No | 78 | 52.0% |

The mean age at onset of drug use was 19.04±3.85 years, the amount of use was 2.12±1.79 gram/day and the mean drug use time was 7.71±3.95 years. The number of drug users in the last 1 month was 122 (81.9%). The number of patients using drug intravenously in the last 1 month was 113 (75.8%). In addition, 84.0% (126) of the patients reported that they shared injectors at least once in their lives. The number of patients admitted to any treatment clinic before admission to our clinic was 104 (69.3%). Thirty-six patients reported that they had never received treatment at a substance abuse center before. Hepatitis markers and HCV genotype distribution were shown in Table 2. Anti-HCV positivity was detected in 91 (60.6%) of 150 patients with intravenous drug use. HCV-RNA was studied in 61 patients with anti-HCV positivity. HCV-RNA was positive in 48 (67.6%) of these patients. Genotype was determined in patients with HCV-RNA positivity. In some patients, genotype detection could not be performed due to the low number of HCV-RNA copies or the patient not coming back to the control. Genotype was detected in 38 patients. Genotype 1a in 20 patients, genotype 3a in 12 patients, genotype 4c/d in five patients and 2b in one patient were detected. No statistically significant difference was found between serum HCV-RNA levels and the mean age of the patients according to genotype distribution (p=0.332, p=0.457) (Table 2). In addition, the mean age of patients with anti-HCV positive and anti-HCV negative was 28 and 25.53, respectively. The mean age of anti-HCV positive patients was higher and it was found to be statistically significant compared to anti-HCV negative patients (p=0.03).

Of the 91 patients with anti-HCV positivity, 67 (73.6%) who were regularly followed up were consulted to the infectious diseases outpatient clinic. However, only 38 (56.7%) of these patients applied to the related unit. Of the 48 patients with positive HCV-RNA levels, 23 patients (47.91%) received treatment. The remaining patients did not apply, so treatment could not be given.

The prevalence of HBV seropositivity was 2.0% (3/150). HCV co-infection was not detected in three patients. Seventeen (11.3%) of the 150 patients developed immunity to HBV either naturally or by vaccination. HBV-DNA was found high in two of the HBsAg positive patients, the levels were $3x10^5$ and $98x10^7$ copies/mL. The other one's HBV-DNA value was negative. Treatment could not be given because none of them admitted to us again.

Anti-HIV seropositivity was detected in 1 of 150 patients. As a result of detailed examination, false seropositivity was found in this patient.

## Discussion

In our study, in PWID, genotype 1a was found to be the most common in patients who came to AMBAUM from Antalya and the surrounding provinces, and genotype 3a was detected in the second frequency. The distribution of HCV genotypes in the world generally varies according to geographical regions (20). In a study conducted in China, genotype 1b was dominant in the general population, whereas genotype 6a was the most common in PWID (11). 1b and 2a/2c have been identified among HCV genotypes in PWID in Korea (21). In studies conducted in Italy and Brazil, genotypes 1 and 3 were similarly detected at a higher rate (22,23). In Romania, non-1b genotypes were detected in 54.8% of cases; The most common of these are 1a and 3a (24). In South Africa the most common HCV genotype was genotype 1a in PWID (73%, 270/368) (25). In our country, the number of studies on the detection of HCV genotype in PWID is limited. Similar to our study, 1a was found to be the most common genotype in studies İstanbul and Mersin regions (18,19). In a study conducted in Çukurova region, 52 (58.6%) of 87 patients had genotype 3 (26). As a result of the comparisons, although the regional variability is seen among PWID in our country, the most common genotype is 1a.

In our study, HCV-RNA was detectable in 52.3% (48/91) of the patients with anti-HCV positivity. In a Korean study, 154 patients had anti-HCV positivity and HCV-RNA was found 98.1% (151/154) in patients who were anti-HCV positive. In 151 patients with detectable serum HCV-RNA, 90 (59.6%) patients showed high levels of viremia (HCV-RNA level above 400,000 IU/mL) (21). In Italy, HCV-RNA was found in 68.3% of patients who were anti-HCV positive. High levels of viremia (HCV-RNA level above 600,000 IU/mL) were found in approximately 50% of these patients (22). In Romania, active HCV viral replication was detected in 104 patients (80%) (24). In studies among PWID, In Myanmar HCV prevalence was 68-76% and in South Africa HCV seroprevalence was 55% (513/937) (25,27). A meta-analyse suggest that based on 118 HCV antibody prevalence measures, the pooled mean prevalence in PWID for all Middle East and North Africa was 49.3% (28).

**Table 2.** Hepatitis markers, HCV genotype distribution

| Viral marker | n | % | HCV-RNA count (median) (IU/mL) |
|---|---|---|---|
| Anti-HCV positive | 91 | 60.6 | - |
| HCV-RNA positive* | 48 | 67.6 | - |
| HCV genotype** | | | |
| 1a | 20 | 52.6 | $9.5x10^5$ |
| 2b | 1 | 2.6 | $43.3x10^5$ |
| 3a | 12 | 31.6 | $1.48x10^5$ |
| 4c/d | 5 | 13.2 | $1.9x10^5$ |
| HBsAg positive | 3 | 2.0 | - |
| Anti-HBs positive | 17 | 11.3 | - |

*Measured at detectable level in anti-HCV positive patients. **In patients with genotype determination.
HCV: Hepatitis C virus, RNA: Ribonucleic acid, HBsAg: Hepatitis B surface antigen, anti-HBs: Hepatitis B surface antibody

According to these results, we can say that HCV has high viremia levels in PWID. In addition, in our study, genotype 4c/d was found to be 13.2% among all genotypes. Kandemir and Gültekin. (18) found this rate to be 6.3%, and it was observed that genotype 4 could not be detected in two other studies on genotype determination in our country (19,26). According to these results, genotype 4 may be increasing between PWID. Considering that the mean age of this patient group is lower than the general population; genotype 4 may be highly prevalent in the general population in the near future. In addition, it is thought that one of the most important reasons for this genotype to be seen at a higher rate in PWID compared to other genotypes is the injector sharing of the patients. A study in Korea reported that 51.3% of patients shared injectors (21). In Romania, the injector sharing rate was 86.9%, which is similar to our study (24). Injector sharing is one of the most powerful predictors for increasing the likelihood of HCV (29).

Seven (8.7%) of the patients who participated in our study were female and this rate was higher than other studies conducted in our country (19,26). This data makes us think that the incidence of intravenous drug use and blood-borne infectious diseases is increasing among women in our country.

HBV markers (HBsAg, HBcAb, HBeAb and HBV-DNA) were found to be significantly higher in PWID than in the general population but HBsAb positivity in PWID was lower than in the general population (21). While the prevalence of HBV in PWID is 6.2% in our country, this rate is 5.9% in those who have injected intravenously within the last 30 days (29). We observed that these rates were lower in the province of Antalya (the prevalence of HBsAg positivity was 2.0% and immunity to HBV was 11.3%). In addition, HCV co-infection was not detected in any of HBsAg positive patients. With this result, it can be said that HBV and HCV coinfections between PWID are low.

HIV is expected to be seen at higher rates among PWID (12). While anti-HIV positivity was found in 3.1% in Italy (22), 80.8% of 130 patients with HCV in Romania were found to be HIV-infected (24). In contrast to these studies, anti-HIV seropositivity was detected in only 1 out of 150 patients in our study. Detailed investigations of this patient revealed false seropositivity. HIV infection is very rare among PWID in our country with a prevalence of 0.34% (29). These results show that HIV is still not common among PWID in our country.

Patients with intravenous drug use who were found to be HCV positive were referred to ınfectious diseases outpatient clinic, but only 56.7% of them went to related unit and most patients did not come to the check examination. This suggests that most patients choose to refuse treatment after learning about HCV positivity. This low treatment compliance can be considered as an important factor in the spread of infections in PWID.

In HCV infected PWID group, the rate of reinfection is high despite the treatment. Among PWID treated for hepatitis C were reported higher rates of re-infection than existing estimates (30). In our study, only 47.91% of patients with positive HCV-RNA levels received HCV therapy. The reason for this low rate was that patients did not apply for HCV treatment. These data highlight the importance of substance use therapy in PWID patients, along with HCV therapy. Thus, compliance of patients to HCV treatment can be increased.

### Study Limitations

Our study has limitations such as low number of patients, being a retrospective study, being performed in a single center and low number of patients applying to the infection department.

## Conclusion

Our study reveals the frequency and HCV genotype distribution of blood-borne pathogens in PWID. The most common genotype in patients was 1a and 3a was the second most common genotype. HCV infection is an important health problem among PWID. Determining HCV genotype distribution among PWID will be a guide for future individualized treatments. In addition, it is important that our study is the first study conducted in Antalya region and it is one of the limited number of studies in our country.

### Ethics

**Ethics Committee Approval:** The ethics committee approval of the study was given by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (approval number: 352, date: 30/07/2018).

**Informed Consent:** Retrospective xstudy.

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

### Authorship Contributions

Concept: H.K., D.İ., Design: H.K., D.İ., Data Collection or Processing: Ö.Ö., D.Ç., G.Ö., Analysis or Interpretation: H.K., D.İ., Ö.Ö., A.E., D.Ç., G.Ö., Literature Search: H.K., D.İ., Ö.Ö., A.E., D.Ç., G.Ö., Writing: D.Ç., G.Ö.

**Conflict of Interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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# *Seroprevalence of HBsAg and Anti-HCV among HIV Positive Patients*

## HIV Enfeksiyonu Olan Bireylerde HBsAg ve Anti-HCV Seroprevlansının Araştırılması

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***ABSTRACT***

**Objectives:** The study aimed to investigate the seroprevalence of hepatitis B surface antigen (HBsAg) and hepatitis C virus (anti-HCV) in human immunodeficiency virus (HIV) infected patients and to evaluate the results according to risk factors in our hospital in İstanbul, which was one of the centers where HIV-infected patients were followed up the most in our country.

**Materials and Methods:** The medical files of 611 HIV-infected patients who were followed up in our infectious diseases and clinical microbiology outpatient clinic between 1999 and 2016, were analyzed to determine the seroprevalence of HBsAg and anti-HCV retrospectively. HIV-monoinfected patients, HIV+HBV-coinfected patients, and HIV+HCV-coinfected patients were examined separately in terms of demographic characteristics and risk factors, and compared with each other.

**Results:** Of the patients 86.6% were male. The mean age of the patients was 37.0±11.2 (16-83). More than one-third of patients were 30-39 years old. Of the patients 43.7% were men who had sex with men (MSM). Of the patients, 5.8% were HBsAg-positive and 14.7% (236) of patients were positive for isolated anti-HBc IgG. The HBV-DNA positivity ratio was determined as 8.7% in the isolated anti-HBc IgG positive group. Of the patients 2% were anti-HCV positive, and 0.9% were HCV-RNA positive. The prevalence of HIV/HCV coinfection was statistically significantly higher in intravenous (IV) drug users than HIV-monoinfected patients (p<0.001).

**Conclusion:** It is not sufficient to evaluate HBsAg alone in HIV-infected individuals. Anti-HBc IgG and HBV-DNA should also be evaluated. Anti-HCV antibody must be tested especially in patients with IV drug addiction.

**Keywords:** Hepatitis B virus, hepatitis C virus, human immunodeficiency virus

***ÖZ***

**Amaç:** Çalışmamızda, ülkemizde en çok HIV enfekte hasta takibi yapılan merkezlerden biri olan İstanbul'daki hastanemizde, insan bağışıklık yetmezliği virüsü (HIV) enfekte bireylerde hepatit B yüzey antijen (HBsAg) ve anti-HCV seroprevalansının araştırılması ve risk faktörlerine göre değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Mart 1999-Mart 2016 yılları arasında enfeksiyon hastalıkları ve klinik mikrobiyoloji polikliniğimizde takip edilen HIV/AIDS hastalarının dosyalarında kayıtlı olan veriler retrospektif olarak incelenerek HBsAg ve anti-HCV seroprevalansı araştırılmıştır. HIV ile monoenfekte, HIV/HBV koenfekte ve HIV/HCV koenfekte hastalar; demografik özellikleri ve risk faktörleri açısından ayrı ayrı incelenmiş ve birbiri ile kıyaslanmıştır.

**Bulgular:** Çalışmaya alınan 611 hastanın 529'u (%86,6) erkek idi. Hastaların yaş ortalaması 37,0±11,2 (16-83) olup 1/3'ünden fazlası 30-39 yaş arasında saptanmıştır. Hastaların 236'sında (%43,7) erkek homoseksüel temas öyküsü vardır. Hastaların %5,8'inde HBsAg pozitifliği, %14,7'sinde izole anti-hepatit B çekirdek antijen immünoglobulin (anti-HBc IgG) pozitifliği tespit edilmiştir. İzole anti-HBc IgG pozitif bulunanlarda HBV-DNA pozitifliği %8,7 olarak saptanmıştır. Hastaların 11'inde (%2) anti-HCV pozitif iken 5'inde (%0,9) HCV-RNA pozitif bulunmuştur. Damar içi uyuşturucu madde kullananlarda HIV/HCV koenfeksiyonu, HIV monoenfekte hastalara kıyasla istatistiksel olarak anlamlı düzeyde yüksek saptanmıştır (p<0,001).

**Sonuç:** HIV ile enfekte bireyleri sadece HBsAg açısından taramak yeterli değildir, anti-HBc IgG ve HBV-DNA açısından da taramak gerekir. Özellikle damar içi uyuşturucu madde kullanıcıları anti-HCV antikoru açısından test edilmelidirler.

**Anahtar Kelimeler:** Hepatit B virüsü, hepatit C virüsü, insan immün yetmezlik virüsü

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## Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infections are more prevalent among the human immunodeficiency virus (HIV) infected patients, due to common transmission routes (1). Mortality due to HIV infection and classical HIV related opportunistic infections have been reduced with the use of highly active antiretroviral therapy. However, the incidence rate of deaths due to HBV and HCV infections and non-AIDS causes remain to be considerably high. Age, geographical region, and having risky behavior for the infection affect the rates of co-infection, as well as routes of transmission (2,3).

HIV infection has an adverse impact on the course of HBV infection. Progression of HBV is rapid in HIV/HBV co-infected individuals due to high HBV replication and the risk of cirrhosis increases by 4.2 times. There is a correlation between viral replication control and immunosuppression degree, and HBV reactivation can occur in HIV infected individuals that anti-HBs positive. Reactivation of HBV may occur in case of not treating with an antiviral agent which efficient against HIV and HBV. However, HBV is considered to have no effect on HIV progression (4,5). It is stated that conditions which cause immunosuppression may be associated with occult hepatitis and the rate of occult hepatitis B is higher in HIV infected patients than the general population (3).

The clinical course in HIV/HCV co-infection is associated with HIV related immunosuppression. HCV infection progresses more quickly if the degree of immunosuppression is high. There is an interval of 30-40 years before the development of hepatocellular carcinoma in HCV monoinfected cases have liver failure, while the time interval is 10-20 years in HIV co-infected cases. There is no effect of HCV on HIV infection in co-infected patients (6).

İstanbul is preferred by HIV infected patients due to its cosmopolitan society structure, advanced examination treatment facilities, and easy transportation, especially those who are exposed to stigma. Therefore, it is thought that our centrally located hospital in which the follow-up of HIV infected individuals has been performed since the first HIV/AIDS case in İstanbul reflects the general profile of Turkey. This study aimed to investigate the prevalence of HBV and/or HCV co-infection and evaluate the findings according to risk factors in HIV infected patients.

## Materials and Methods

The data was obtained through the retrospective review of the medical files of HIV infected patients aged more than 16 years and followed up for at least six months. The patients that were followed up for less than six months and those whose medical records were not complete were excluded from the study. Thus, a total of 611 patients diagnosed with HIV/AIDS and confirmed by the Western blot test between March 1999 and March 2016 were included in the further evaluation.

The data on age distribution, gender, intravenous (IV) drug use, marital status, sexual orientation, transfusion information, family history of infectious diseases (HIV, HBV, HCV infections), condom use, number of partners within the last two years, and place of residence was recorded from the patient files. The results of hepatitis B surface antigen (HBsAg), anti- hepatitis B core antibody (HBc) immunoglobulin (IgG), anti-HBs, anti-HCV, and HBV-DNA with HBsAg positivity or isolated anti-HBc IgG positivity (HBsAg and anti-HBs negative, anti-HBc IgG positive) and HCV-RNA with anti-HCV positivity were evaluated based on the laboratory findings using the Murex HIV Ag/Ab combination kit for anti-HIV (Diasorin S.p.A., Italy), Murex HBsAg version 3 kit for HbsAg (Diasorin S.p.A., Italy), and Murex anti-HCV version 4 kit for anti-HCV (Diasorin S.p.A., Italy) by the ELISA method.

The levels of HIV-RNA, HBV-DNA, and HCV-RNA were examined by the real-time polymerase chain reaction method using the Cobas AmpliPrep/COBAS TaqMan HIV-1 test (Roche Molecular Systems, USA), Cobas AmpliPrep/COBAS TaqMan HBV test (Roche Molecular Systems-ABD), and Cobas AmpliPrep/COBAS TaqMan HCV test (Roche Molecular Systems-ABD), respectively.

The HBsAg-positive patients were defined as HIV/HCV co-infection, anti-HCV and HCV-RNA positive patients were defined as HIV/HCV co-infection, and isolated anti-HBc IgG-positive patients were considered as occult HBV infection in HIV infected patients if HBV DNA is positive.

HIV monoinfected patients, HIV/HBsAg positive patients, and HIV/anti-HCV positive patients were analyzed respectively according to features of patients and risk factors. These groups were compared to each other.

The Ethical Committee of Haseki Training and Research Hospital approved the study and the required institutional permission was obtained (approval number: 320, date: 20.01.2016).

### Statistical Analysis

SPSS 15.0 for Windows was used for statistical analysis and descriptive statistics were obtained as numbers and percentages for categorical variables. The comparison of ratios in independent groups was undertaken with the chi-square analysis. When the number of cells with chi-square expected count less than 5 was greater than 20%, Fisher's exact test was used in 2 by 2 table statistics, and Monte Carlo simulation with Fisher's exact test results were used for table statistics which were larger than 2 by 2. The statistical significance level of alpha was accepted as $p<0.05$.

## Results

The mean age of the patients was 37.0±11.2 (16-83) years. The general characteristics of the patients are presented in Table 1. More than one-third of the patients were in the age range of 30-39 years. Furthermore, 43.7% of the patients reported that they were homosexual or bisexual.

Examining the serological findings of HBV and HCV infections in HIV infected cases, 33 patients (5.8%) were HBsAg positive and 11 (11%) were anti-HCV positive despite the lack of a previous record of an HCV infection or treatment. The HCV-RNA results were available in eight of the anti-HCV positive cases, of which five (0.9%) were found to be HIV/HCV coinfected. HIV/HCV/HBV co-infection was not found in any of our cases.

Considering anti-HBc IgG positivity, more than one-third of the cases (171 patients: 36.5%) were infected with HBV and 14.7% (69/469) were positive for anti-HBc IgG but negative for HBsAg and anti-HBs. HBV-DNA was found positive in 8.7% (4/46) of the patients with isolated anti-HBc IgG positivity.

It was found that HBsAg, anti-HBc IgG, and anti-HBs results were entered complete in 135 of the patients' files and 47.4% of

the immunizations were achieved with recombinant HBV vaccine at 0, 1, and 6 months.

HBsAg seroprevalence was determined as 7.7% (9/117) in the HIV infected bisexual group, 3.7% (4/108) in the male homosexual group, and 5.1% (15/289) in the heterosexual population. There was no statistically significant difference between the groups concerning HBsAg positivity according to some features like age, gender, relationship status, residence, and sexual orientation (Table 2).

Anti-HCV positivity was found to be statistically significantly higher in the patients with a history of IV drug use (p<0.001), who all reported to be heterosexual. When the characteristics of age, gender, and sexual orientation were examined in HCV co-infected patients, no significant difference was found between the groups (Table 3).

## Discussion

HBsAg positivity was detected as 5.7%, and the prevalence of HBV (anti-HBc) and HCV (anti-HCV) infections in HIV infected cases was 36.5% and 2%, respectively. Exposure to HCV infection was similar to that of the general population in Turkey, but exposure to HBV infection was found to be higher. It is estimated that the prevalence of chronic HBV infection in HIV infected people in the world is between 5% and 20% (7). In a study conducted in 12

**Table 1.** General features of HIV/AIDS patients

| Patient features | | n | % |
|---|---|---|---|
| Gender | Female | 82 | 13.4 |
| | Male | 529 | 86.6 |
| Age groups | <30 | 175 | 28.6 |
| | 30-39 | 217 | 35.5 |
| | 40-49 | 126 | 20.6 |
| | >49 | 92 | 15.1 |
| | Unknown | 1 | 0.2 |
| IV drug use | No | 578 | 98.8 |
| | Yes | 7 | 1.2 |
| Marital status | Married | 287 | 47.8 |
| | Never married | 256 | 42.7 |
| | Divorced/widowed | 57 | 9.5 |
| Sexual orientation | No sexual intercourse | 1 | 0.2 |
| | Heterosexual | 304 | 56.2 |
| | Homosexual | 115 | 21.3 |
| | Bisexual | 121 | 22.4 |
| Transfusion information | No | 430 | 91.9 |
| | Yes | 38 | 8.1 |
| Infectious diseases in the family (HIV/HBV/HCV) | No | 568 | 98.6 |
| | HIV | 1 | 0.2 |
| | HBV | 3 | 0.5 |
| | HCV | 4 | 0.7 |
| Condom using | No | 253 | 54.8 |
| | Sometimes | 173 | 37.4 |
| | Yes | 36 | 7.8 |
| Number of partners within the last two years | 0 | 28 | 6.2 |
| | 1 | 141 | 31.0 |
| | 2-5 | 112 | 24.6 |
| | >5 | 174 | 38.2 |
| Features of partners | HIV-positive | 72 | 16.9 |
| | Bisexual/homosexual | 95 | 22.2 |
| | Random partner or sex worker | 259 | 60.7 |
| Place of residence | İstanbul | 455 | 92.1 |
| | Other provinces in Turkey | 39 | 7.9 |

HIV: Human immunodeficiency virus, IV: Intravenous HBV: Hepatitis B virus HCV: Hepatitis C virus

**Table 2.** Comparison of HBsAg and anti-HIV-positive patients with HIV monoinfected patients according to risk groups

| Patient features | | HBsAg negative | | HBsAg positive | | p |
|---|---|---|---|---|---|---|
| | | n | % | n | % | |
| Gender | Female | 68 | 12.7 | 2 | 6.1 | 0.411 |
| | Male | 466 | 87.3 | 31 | 939 | |
| Age groups | <30 | 159 | 29.5 | 7 | 21.2 | 0.498 |
| | 30-39 | 189 | 35.1 | 12 | 36.4 | |
| | 40-49 | 110 | 20.4 | 10 | 30.3 | |
| | >49 | 81 | 15.0 | 4 | 12.1 | |
| IV drug use | No | 517 | 98.7 | 28 | 100.0 | 1.000 |
| | Yes | 7 | 1.3 | 0 | 0.0 | |
| Marital status | Married | 254 | 47.8 | 17 | 53.1 | 0.775 |
| | Never married | 228 | 42.9 | 13 | 40.6 | |
| | Divorced/widowed | 49 | 9.2 | 2 | 6.3 | |
| Sexual orientation | Heterosexual | 274 | 56.4 | 15 | 53.6 | 0.403 |
| | Homosexual | 104 | 21.4 | 4 | 14.3 | |
| | Bisexual | 108 | 22.2 | 9 | 32.1 | |
| Transfusion information | No | 386 | 92.1 | 23 | 95.8 | 1.000 |
| | Yes | 33 | 7.9 | 1 | 4.2 | |
| Infectious diseases in the family (HIV/HBV/HCV) | No | 511 | 98.8 | 28 | 96.6 | 0.170 |
| | HBV | 2 | 0.4 | 1 | 3.4 | |
| | HCV | 4 | 0.8 | 0 | 0.0 | |
| Condom use | No | 230 | 54.9 | 10 | 43.5 | 0.331 |
| | Sometimes | 158 | 37.7 | 10 | 43.5 | |
| | Yes | 31 | 7.4 | 3 | 13.0 | |
| Number of partners within the last two years | 0 | 25 | 6.1 | 1 | 4.3 | 0.401 |
| | 1 | 127 | 31.1 | 5 | 21,7 | |
| | 2-5 | 97 | 23.7 | 9 | 39.1 | |
| | >5 | 160 | 39.1 | 8 | 34.8 | |
| Features of partners | HIV-positive | 66 | 16.9 | 2 | 10.0 | 0.816 |
| | Bisexual/homosexual | 85 | 21.8 | 4 | 20.0 | |
| | Random partner or sex worker | 238 | 61.0 | 14 | 70.0 | |
| Place of residence | İstanbul | 415 | 93.0 | 19 | 86.4 | 0.209 |
| | Other provinces in Turkey | 31 | 7.0 | 3 | 13.6 | |

HBsAg: Hepatitis B surface antigen, HIV: Human immunodeficiency virus, IV: Intravenous HBV: Hepatitis B virus HCV: Hepatitis C virus

countries in the Asian Continent, HBsAg positivity in HIV infected people was found to be 10.4%, higher than the prevalence of HBV in the general population (the highest rate was 8.6% in East Asia) (8,9). The prevalence of HBV infection in HIV infected individuals was 8.7% in a study conducted in 72 different centers in various countries in Europe (10). In Kenya and Brazil, these rates were found as 6% and 3.8%, respectively (11,12). In these studies, the prevalence of HBV infection was higher in HIV infected subjects compared to the general population in the region (10,11,12). Turkey is a moderate endemic area for HBV infection, and the HBsAg positivity is around 4-5%, with regional differences (13). In two different studies undertaken in Turkey, HBsAg positivity in the HIV infected population was reported to be 4% and 5% (14,15). In light of this information, compared to the general population in Turkey and the world, it can be stated that the frequency of encountering HBV in HIV infected individuals is higher.

In the present study, 43.7% of the patients (21.3% homosexual, 22.4% bisexual) were MSM, while in two previous studies conducted in different provinces in Turkey, the homosexuality ratio was reported to be 3% and 4.3%, respectively in HIV infected patients (16,17). The ratio of HIV infected homosexual men in Turkey was found to be lower than in the USA. Although when compared to cities of Anatolia, it is seen that there is an accumulation of homosexual men in İstanbul. This difference

**Table 3.** Comparison of anti-HCV and anti-HIV positive patients with HIV monoinfected patients according to risk groups

| Patient features | | Anti-HCV negative | | Anti-HCV positive | | p |
|---|---|---|---|---|---|---|
| | | n | % | n | % | |
| Gender | Female | 69 | 12.8 | 2 | 18.2 | 0.461 |
| | Male | 471 | 87.2 | 9 | 81.8 | |
| Age groups | <30 | 160 | 29.4 | 2 | 18.2 | 0.242 |
| | 30-39 | 185 | 33.9 | 7 | 63.6 | |
| | 40-49 | 116 | 21.3 | 2 | 18.2 | |
| | >49 | 84 | 15.4 | 0 | 0.0 | |
| IV drug use | No | 525 | 99.2 | 6 | 66.7 | <0.001 |
| | Yes | 4 | 0.8 | 3 | 33.3 | |
| Marital status | Married | 258 | 48.0 | 5 | 45.5 | 1.000 |
| | Never married | 229 | 42.6 | 5 | 45.5 | |
| | Divorced/widowed | 50 | 9.3 | 1 | 9.1 | |
| Sexual orientation | Heterosexual | 274 | 56.4 | 8 | 72.7 | 0.156 |
| | Homosexual | 97 | 20.0 | 3 | 27.3 | |
| | Bisexual | 115 | 23.7 | 0 | 0.0 | |
| Transfusion information | No | 389 | 92.2 | 9 | 90.0 | 0.563 |
| | Yes | 33 | 7.8 | 1 | 10.0 | |
| Infectious diseases in the family (HIV/HBV/HCV) | No | 514 | 98.7 | 10 | 100.0 | 1.000 |
| | HBV | 3 | 0.6 | 0 | 0.0 | |
| | HCV | 4 | 0.8 | 0 | 0.0 | |
| Condom use | No | 236 | 55.9 | 2 | 25.0 | 0.112 |
| | Sometimes | 153 | 36.3 | 6 | 75.0 | |
| | Yes | 33 | 7.8 | 0 | 0.0 | |
| Number of partners within the last two years | 0 | 25 | 6.1 | 1 | 11.1 | 0.141 |
| | 1 | 127 | 30.9 | 2 | 22.2 | |
| | 2-5 | 102 | 24.8 | 0 | 0.0 | |
| | >5 | 157 | 38.2 | 6 | 66.7 | |
| Features of partners | HIV positive | 68 | 17.5 | 0 | 0.0 | 0.594 |
| | Bisexual/homosexual | 78 | 20.1 | 2 | 25.0 | |
| | Random partner or sex worker | 242 | 62.2 | 6 | 75.0 | |
| Place of residence | İstanbul | 412 | 92.6 | 9 | 90.0 | 0.544 |
| | Other provinces in Turkey | 33 | 7.4 | 1 | 10.0 | |

HIV: Human immunodeficiency virus, IV: Intravenous HBV: Hepatitis B virus HCV: Hepatitis C virus

is thought to be due to people with homosexual tendencies preferring to live in crowded and cosmopolitan cities like İstanbul as they can live a more comfortable life and express their sexual orientation. HIV/HBV co-infection is more common in homosexual men than in the general population. In Brazil, the USA, and China, the seroprevalence of HBV in HIV infected individuals was found to be 2.3%, 7.6%, and 12.6%, respectively. When the HIV infected homosexual men were examined in the same patient groups, the rates of HBV infection were 4.4%, 9.2%, and 14.3%, respectively (18,19,20). In the present study, the HBsAg seroprevalence was 7.7% in the HIV infected bisexual men, whereas it was 3.7% among homosexual men and 5.1% among heterosexual men. When the bisexual and homosexual groups were considered as a common group, the rate of HBV co-infection appeared to be higher in those with a history of homosexual contact. In this study, the HIV infected patients with a history of homosexual contact were found to have a higher rate of HBV, similar to studies conducted in various parts of the world. But there is no statistically significant difference. This may be related to the low number of HBV co-infected patients.

Occult hepatitis and isolated anti-HBc IgG positivity are more frequent in patients with immunosuppression, hepatocellular carcinoma, hemodialysis, HCV infection, and HIV infection because of HBsAg clearance (21,22). In a study conducted in New York, the incidence of occult hepatitis was found as 13% in HIV infected patients, and in another study conducted in Nigeria, it was found as 11.2% (23,24). In previous studies conducted in Turkey, the

incidence of occult hepatitis was found to be 12-21% among HIV infected patients (14,15,25). In our study, the isolated anti-HBc IgG positivity ratio was 14.7%, and among these patients, the HBV-DNA positivity ratio, where available, was 8.7%. In Turkey, the isolated anti-HBc IgG positivity ratio in blood donors was reported to be 0.91%, and the rate of isolated anti-HBc IgG was higher in HIV infected patients than the general population in the present study and other studies conducted in Turkey (14,15,25).

HCV infection in HIV infected individuals is also seen at a higher rate than in the general population due to common transmission routes and the fact that viral passage is easier in co-infection (26). Although rates of anti-HCV positivity are high among HIV infected patients worldwide, these rates vary according to the region and patient group. The seroprevalence of anti-HCV in HIV infected patients was found to be 7.6% in Slovenia, 16.1% in the USA, 4.2% in West Africa, and 2.2% in India (27,28,29,30). Seroprevalence of HCV in the general population in Turkey was reported to be 1% in the TURKHEP study (31). Two studies that investigated HIV infected patients in Turkey calculated HCV prevalence as 0.9% and 6% (14,31). In the present study, the prevalence of HIV/HCV co-infection was similar to the general population in Turkey (0.9%) probably due to the low rate of homosexual contact history and IV drug use in our patient group. Furthermore, IV drug use was significantly higher ($p<0.001$) and appeared to be a risk factor for HCV infection similar to the previous reports in the literature. However, the number of patients evaluated was low; therefore, there is a need for further studies with wider patient groups in Turkey.

## Conclusion

The prevalence of HCV co-infection in HIV infected was similar to that of the general population of Turkey. HBV infection was detected at a higher rate in HIV infected patients. The HIV/HCV co-infection rate was significantly higher only in the group that used IV drugs; however, no significant difference was found between other risk groups in terms of HBV or HCV co-infection. Moreover, we found that homosexual contact wasn't a risk factor for HBV and HCV co-infections.

### Ethics

**Ethics Committee Approval:** The Ethical Committee of Haseki Training and Research Hospital approved the study and the required institutional permission was obtained (approval number: 320, date: 20.01.2016).

**Informed Consent:** Since our study was retrospective, informed consent was not used.

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

### Authorship Contributions

Surgical and Medical Practices: M.Ş., Ö.A.A., H.K.K., Consept: Ö.A.A., Desing: Ö.A.A., M.Y., Data Collection or Processing: M.Ş., Analysis or İnterpretation: M.Y., Literature Search: M.Ş., M.Y., Writing: M.Ş.

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

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Research Article

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# *Investigating Hepatitis C, D and HIV Prevalance in Cases with Positive Hepatitis B Virus Antigen in a Tertiary Hospital and Examining Anti-HDV Positive Cases*

## Üçüncü Basamak Bir Hastanede Hepatit B Virüsünün Yüzey Antijeni Pozitif Olgularda Hepatit C, D ve HIV Sıklığının Araştırılması ve Anti-HDV Pozitif Olguların İrdelenmesi

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***ABSTRACT***

**Objectives:** Hepatitis B infection has a faster and more progressive course in the presence of hepatitis C virus (HCV), HDV and human immunodeficiency virus (HIV) infections. The aim of this study was to determine anti-HCV, anti-HDV and anti-HIV prevalance in hepatitis B surface antigen (HBsAg) (+) positive patients and to examine patients with positive anti-HDV.

**Materials and Methods:** Data were obtained through scanning hepatitis B patient follow-up files and the hospital automation system. Descriptive data was expressed in numbers and percentages (%).

**Results:** Mean age of 1829 HBsAg positive patients was 42.65±14.83 (7-95) and 1099 (60.1%) were male and 730 (39.9%) were female. 30 patients (1.64%) had anti-HCV and 28 patients (1.53%) had anti-HDV while 1 patient (0.055%) had positive anti-HIV. The mean age of the patients with positive anti-HDV was 53.16±15.46 and 12 of these (42.9%) were female and 16 (57.1%) were male. Fifteen HDV positive patients were given peginterferon and 10 patients had relapse and 4 patients had hepatocellular cancer during the follow-up. A patient died due to the quick progression of the disease after deciding upon transplantation.

**Conclusion:** Patients should also be scanned for hepatitis C, D and HIV in the presence of hepatitis B infection and the patient should be followed up and treated accordingly if coinfection is detected.

**Keywords:** Hepatitis B, hepatitis C, hepatitis D, HIV, coinfection

***ÖZ***

**Amaç:** Hepatit B enfeksiyonu, hepatitis C virüs (HCV), HDV, insan bağışıklık yetmezliği virüsü (HIV) enfeksiyonu varlığında daha hızlı ve progresif seyreder. Bu çalışmada hepatit B yüzey antijen (HBsAg) pozitifliği saptanan hastalarda anti-HCV, anti-HDV, anti-HIV sıklığının belirlenmesi ve anti-HDV pozitifliği saptanan hastaların irdelenmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Veriler hepatit B hasta takip dosyaları ve hastane otomasyon sistemi üzerinden taranarak elde edildi. Tanımlayıcı veriler sayı ve yüzde (%) olarak belirtildi.

**Bulgular:** HBsAg pozitif 1829 hastanın yaş ortalaması 42,65±14,83 (7-95) olup 1099'u (%60,1) erkek, 730'u (%39,9) kadındı. Thirty anti-HCV (%1,64), 28 (%1,53) anti-HDV, 1 (%0,055) anti-HIV pozitifliği saptandı. Anti-HDV pozitif olan hastaların yaş ortalaması; 53,16±15,46 olup 12'si (%42,9) kadın, 16'sı (%57,1) erkekti. HDV pozitif 15 hastaya peginterferon verilmiş olup takipte 10 hastada relaps, 4 hastada hepatoselüler kanser gelişti. Nakil kararı verilmiş olan bir hastada, hastalık hızlı progresyon gösterdiğinden hasta kaybedildi.

**Sonuç:** Hepatit B enfeksiyonu varlığında hastalar hepatit C, D ve HIV yönünden de taranmalı ve koenfeksiyon saptandığında, hasta buna yönelik de takip ve tedavi edilmelidir.

**Anahtar Kelimeler:** Hepatit B, hepatit C, hepatit D, HIV, koenfeksiyon

**Kepenek Kurt E, Bulut R, Kandemir B, Erayman İ, Bitirgen M, Esenkaya Taşbent F. Investigating Hepatitis C, D and HIV Prevalance in Cases with Positive Hepatitis B Virus Antigen in a Tertiary Hospital and Examining Anti-HDV Positive Cases. Viral Hepat J. 2021;27:31-35.**

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## Introduction

With an epidemiology affected by different factors such as vaccine and immigration, hepatitis B virus (HBV) infection is a global public health problem (1). The number of HBV-infected individuals around the world is estimated as nearly two billion. Many people die due to HBV-related diseases every year. A positive change is observed globally in hepatitis B surface antigen (HBsAg) positivity. Thus, while global number of chronic HBV cases was considered to be around 400 million until the last few years, this number is estimated to decrease approximately down to 240-257 million. Coinfection of other viral factors may also accompany HBV (2). Delta hepatitis or HDV was first discovered by Rizzetto et al. (3) in 1977. HDV can be seen as a coinfection with HBV or a superinfection in individuals infected with HBV (4). HDV can not form its own envelope protein since it is a defective hepatotropic virus affecting patients only with HBV infection and needs HBV for virion production and disease formation (3,5). Although seen rarely among chronic viral hepatitis, chronic delta hepatitis is the type with the severest course. HDV causes a more severe course in hepatitis B infection-caused acute and chronic liver diseases and also a significant increase in becoming chronic (6). These two viruses share the same transmission ways as parenteral, sexual and maternal (3). Nearly 5% of HBV carriers are also HDV-infected (7). Although the prevalence changes according to regions, nearly 15-20 million people are estimated to be infected with HDV around the world (8).

In patients with chronic HBV infection, HCV coinfection fastens liver disease progression and increases hepatocellular carcinoma (HCC) risk (1). Although hepatitis B and C viruses have different life cycles and gene sequences, they follow the same common path in disease progression. Anti-HCV positivity is 3-20% in HBsAg positive individuals and HBsAg positivity is 2-10% in anti-HCV positive individuals (9). HBV and HCV concurrence was shown to be high especially in places where HBV and HCV infections are endemic and also in intravenous drug addicted individuals (10). HCV coinfection rate was found as 10-15% in chronic HBV patients (2).

Nearly 36.7 million individuals have human immunodeficiency virus (HIV) worldwide and 2.7 million of these cases are coinfected with HBV (2). Liver fibrosis progression, cirrhosis and HCC risk increases in patients with HIV/HBV coinfection (1). The aim of this study was to determine anti-HCV, anti-HDV and anti-HIV prevalence in HBsAg (+) positive patients and to evaluate patients with anti-HDV positivity.

## Materials and Methods

After taking the consent of university Ethics Board for the study (approval number: 2019/1921), the demographic characteristics and anti-HCV, anti-HDV and anti-HIV results of the patients detected to have HBsAg positive result and aspartate aminotransferase (AST), alanine aminotransferase (ALT), hepatitis B e antigen (HBeAg), anti-HBe, HBV-DNA, HDV-RNA values, biopsy results, treatments and prognoses of patients detected to have anti-HDV (+) between 2000 and 2018 in our clinic were scanned through hepatitis B patient follow-up files and hospital automation system and were analyzed through recording on Excel form.

### Statistical Analysis

Data were stated in number, percentage (%), mean, median and standard deviation.

## Results

Mean age of a total of 1829 HBsAg (+) patients was 42.65±14.83 (7-95) and 1099 of them (60.1%) were male and 730 (39.9%) were female. Anti-HCV, anti-HDV and anti-HIV were checked in all patients and their test results were provided on Table 1.

Mean age of 28 patients detected to have both HBsAg and anti-HDV positive was 53.16±15.46 (minimum: 29, maximum: 72) and 12 of these were female (42.9%) and 16 were male (57.1%). Mean HBV-DNA of the patients was $64.4x10^6$ copy/mL (minimum: 0, maximum: $288.2x10^6$ copy/mL) and ALT (minimum: 15 u/Lt, maximum: 1650 u/Lt) was detected in 16 patients and high AST was detected in 14 patients (minimum: 17 u/Lt maximum; 917 u/Lt). Initial HDV-RNA was negative for two patients and mean HDV-RNA of the other eight patients with accessible HDV-RNA information was found as $40x10^6$ copy/mL (minimum: 1240, maximum: $18.2x10^6$ copy/mL). Biopsy could not be performed in four patients since it was contraindicated and the biopsy results of 21 patients were reachable. Epidemiological data, biopsy results and laboratory findings of the patients detected to have positive anti-HDV were shown in Table 2. Treatment information of fifteen patients was reachable and it was found that peginterferon-alpha (PegIFN-$\alpha$) treatment was given to these patients for 1 year. 10 patients had relapse and 4 patients had HCC in the follow-ups. A patient whose transplantation was decided upon died due to the quick progression of the disease. As anti-HBc IgM was detected negative in all patients, they were all considered to have superinfection. Delta antigen results were reachable for 14 cases detected to have positive anti-HDV and 12 of these results were negative and 2 were positive. Anti-HCV and anti-HIV positivity wasn't detected in any of these patients.

## Discussion

Increased HCC risk was validated and shown in the epidemiological studies made in patients with HBV/HCV coinfection (11,12). While HCC risk was 6.4 for 100 patients with coinfection

**Table 1.** Hepatitis C, D and HIV* seroprevalence in HBsAg** (+) patients

| Serology | Antibody studied | Number | Percentage (%) |
|---|---|---|---|
| Hepatitis C (n=1829) | Anti-HCV*** | 30 | 1.64 |
| Hepatitis D (n=1829) | Anti-HDV**** | 28 | 1.53 |
| HIV (n=1829) | Anti-HIV | 1 | 0.055 |

*HIV: Human immunodeficiency virus, **HBsAg: Hepatitis B surface antigen, ***Anti-HCV: Anti-hepatitis C virus, ****Anti-HDV: Anti-hepatitis D virus

**Table 2.** Epidemiological and laboratory findings of anti-HDV* (+) patients

| | |
|---|---|
| **Age (years) mean** | **53.16±15.46** |
| Gender (female/male) (n, %) | 12 (42.9), 16 (57.1) |
| HBeAg (-) anti-HBe (+) (n=28) (%) | 23 (82.1) |
| HBeAg** anti-HBe*** (-) (n=28) (%) | 3 (10.7) |
| HBeAg (+) anti-HBe (-) (n=28) (%) | 2 (7.2) |
| Mean HBV-DNA (n=28) | 64.4x10$^6$ copy/mL |
| Mean AST**** (n=28) | 27.5 u/Lt |
| Mean ALT***** (n=28) | 144.6 u/Lt |
| Mean HDV-RNA (n=8) | 40x10$^6$ copy/mL |
| Biopsy result stage 0-2<br>(n=21) (%) 3-4<br>5 | 13 (61.9)<br>7 (33.3)<br>1 (4.8) |
| Biopsy result HAI****** 1-7<br>n=21(%) 8-11<br>≥12 | 6 (28.6)<br>10 (47.6)<br>5 (23.8) |

*Anti-HDV: Anti-hepatitis D virus, **HBeAg: Hepatitis B e antigen, ***Anti-HBeAg: Anti-hepatitis B e antigen, ****AST: Aspartate aminotransferase, *****ALT: Alanine aminotransferase, ******HAI: Histological activity index

in another study, it was detected as 2 in HBV mono infection and as 3.7 in HCV mono infection (13). In a study made in Egypt, HBV/HCV coinfection prevalence was reported as 0.7% (14). Coinfection rate was detected as 5.8% in another study made in USA (15). İnci et al. (16) evaluated 1339 CHD patients in a study made in İstanbul in 2012 and detected anti-HCV positive in 26 (1.9%) patients. Anti-HCV positivity was detected in 1.64% of HBsAg (+) patients in our study. In general, this rate is lower than other studies and this condition may be related to the attention paid to sterilization and disinfection in hemodialysis and other invasive operations, use of disposable injectors and scanning of hepatitis analyses before blood and blood products transfusion.

Değertekin et al. (17) evaluated studies on delta hepatitis between 1980 and 2005 and showed that there was a decrease in delta hepatitis in Turkey between 1980 and 2005 (4.1% and 2.9%) and delta hepatitis was mainly a problem in Southeastern region. Delta positivity rate was found 20% (5961 cases) in chronic HBV cases and 32.5% in cirrhotic cases in the same study and it was detected as 3% in 1416 acute viral hepatitis cases, 8.1% in 766 acute HBV infections, 4.9% in 6613 inactive HBV carrier cases, 32.52% in cirrhosis patients (11,264 cases) and as 23% in HCC cases (17). In the Bus Project made by Viral Hepatitis Society in 2009, positive results were acquired in 43 cases (2.39%) when anti-delta immunoglobulin G (anti-HDV IgG) was also checked in 1805 HBsAg positive individuals among a total of 29960 individuals aged between 0 and 103 (18). In the study made by Eser-Karadağ (19) in Elazığ between 2017 and 2019, anti-HDV positivity was detected in 8.8% out of 455 chronic HBV infection diagnosed patients. Güdücüoğlu et al. (20) found anti-HDV positivity in the serums of 36 out of 184 HBsAg positive soldiers (19.5%) in Van Military Hospital in 2006. Prevalence of HDV coinfection (anti-HDV IgM positive in 3 patients) in addition to acute HBV infection (anti-HBC IgM positive in 39 patients) was 7.69%. Prevalence of HDV superinfection (anti-HDV total "IgM+IgG" positive in 145 patients) prevalence in addition to chronic HBV infection (anti-HBc total "IgM+IgG" positive in 36 patients) was 24.8% (20). In a study covering some cities of Eastern Anatolia including Van, anti-HDV was found positive in 55 out of 955 HBsAg positive cases (5.8%) (21). Doğan et al. (22) found anti-HDV prevalence as 7.3% in patients with chronic HBV infection in Ağrı in 2012. Kart Yaşar et al. (23) found positive anti-HDV results in 49 out of 692 HBsAg positive cases in İstanbul (7%). İzmirli et al. (24) found anti-HDV positive in 4.5% of HBsAg positive cases and 4.4% of chronic hepatitis B (CHB) patients in the study they made in İstanbul in 2011. Anti-HDV positivity was detected in 1.9% out of 1829 HBsAg positive patients in Konya region in our study. This rate was found lower compared to other studies made in different regions of our country at different times. Since HDV occurs in the presence of HBV, this condition may be related to hepatitis B vaccination condition, application of injection and other invasive operations in sterile conditions, improvement of socioeconomic condition and public training on hepatitis B and vaccine in our region.

It was reported that HDV infection could affect all age groups (24). In a study made in our country and covering central regions of Black Sea including Samsun, the mean age of HDV positive patients was found 45.63 years (16-74 years) higher (25). Mean age of HDV positive patients was 53.16±15.46 years higher in our study and this condition may be related to the fact that young individuals are vaccinated in our country since hepatitis B was included in routine vaccine program in 1998.

Although hepatitis D positivity is not statistically significant in literature, it was found to be more common in males (26). Parlak et al. (27) also found this infection more common in males (66%). 57.1% of the patients with positive anti-HDV were males in our study and this may be explained by higher rate of risky behaviors in males in line with literature.

HDV infection suppresses HBV replication in general and HBeAg negative, anti-HBe positive CHB and low titrated HBV causes DNA positivity (27). Mean HBV-DNA of the patients was 64.4x10$^6$ copy/mL (minimum: 0, maximum: 288.2x10$^6$ copy/mL)

in our study. In the study by Parlak et al. (27), mean HBV-DNA was found 3449908.09±29928971.38 IU/mL in HBsAg positive patients.

İzmirli et al. (24) found superinfection rate more than coinfection. Superinfection was found in all patients in our study.

EASL 2017 suggests PegIFN-α for minimum 48 weeks in patients with HDV/HBV coinfected compensated liver disease. PegIFN-α is the only drug with proven antiviral efficiency against chronic HDV infection now (28). Treatment information of 15 patients could be reached in our study and it was determined that PegIFN-α treatment was provided for 48 weeks in these patients. Ten patients had relapse and 4 patients had HCC formation and one patient whose transplantation was decided died due to the quick progression of the disease.

Course of HBV infection is faster in individuals coinfected with HIV. Cirrhosis, final stage liver disease and/or HCC formation may be much faster. HBV is observed in 5-10% of HIV infected individuals globally. Although effective antiretroviral treatment (ART) decelerates progression to cirrhosis, it is interesting that the risk remain high when compared to individuals without coinfection (29). Positive anti-HIV was detected in 0.055% of the patients in our study. Although a HBsAg positive patient was anti-HIV negative at the beginning, the result became anti-HIV positive during the follow-up. This condition brings along the question "Should anti-HIV be checked at certain intervals in individuals with positive HBsAg?" due to the similarity of transmission ways for HBV and HIV.

Regardless of CD4 cell count, ART should be started in all patients with HIV-HBV coinfection (1). It is suggested that HIV/HBV coinfected and ART scheme should cover two drugs affected on the two viruses (30). Tenofovir is the most important antiviral agent effective for both HIV and HBV in HIV/HBV coinfection today. Although a HBsAg positive had a negative anti-HIV test result at the beginning in our study, anti-HIV result became positive in the follow-up and tenofovir containing ART was started after a detailed examination.

## Conclusion

HCV, HDV and HIV infection rates were found low in hepatitis B diagnosed cases in our region in our study. Due to similar transmission ways and since the liver damage would be high in the presence of coinfection, HCV and HDV should be scanned in HBV presence and treated in a suitable way if detected positive. Although PegIFN is used as the only agent in hepatitis D in our country, new treatment agents are needed for HDV treatment since the disease may relapse.

### Ethics

**Ethics Committee Approval:** Ethics committee approval for this study was obtained from the Necmettin Erbakan University, Meram Faculty of Medicine, Non-Invasive Clinical Studies Ethics Committee (approval number: 2019/1921, date: 21.06.2019).

**Informed Consent:** It wasn't obtained.

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

### Authorship Contributions

Surgical and Medical Practices: E.K.K., Consept: E.K.K., İ.E., B.K., Desing: E.K.K., İ.E., B.K., Data Collection or Processing: E.K.K., R.B., F.E.T., Analysis or İnterpretation: E.K.K., R.B., Literature Search: E.K.K., R.B., İ.E., M.B., Writing: E.K.K., B.K., İ.E., M.B.

**Conflict of Interest:** The authors of this article declare that they have no conflict of interest.

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