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# Evaluation of Risk Factors Associated with HBsAg and Anti-HCV Seropositivity: Results of a Nationwide Population-based Epidemiological Survey Study in Turkey

HBsAg ve Anti-HCV Seropozitifliği ile İlişkili Risk Faktörlerinin Değerlendirilmesi: Ülke Bazında Gerçekleştirilen Epidemiyolojik Çalışmanın Sonuçları

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## Abstract

**Introduction:** In this study, it was aimed to evaluate factors associated with hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) positivity through the "Raising Public Awareness and Determining Epidemiological Changes in Hepatitis" project conducted by the Viral Hepatitis Society of Turkey.

**Materials and Methods:** A total of 61,943 participants (mean age 35±14.1 years, 50.8% males) who volunteered to participate in the study were screened for HBsAg and anti-HCV by primary healthcare centers distributed throughout 78 cities in Turkey. A standard questionnaire form about sociodemographic features and transmission-related risk factors was completed via face-to-face interviews with each participant. A sub-population of 21,473 participants with complete data were analyzed for the presence of risk factors associated with HBsAg and anti-HCV seropositivity.

**Results:** HBsAg and anti-HCV seropositivity were detected in 1,515 (2.5%) and 332 (0.6%) of the 61,943 study population, respectively. By univariate chi-square test, significant associations were found between hospitalization and anti-HCV and between dental treatment in the last five years and HBsAg and anti-HCV seropositivity. In multivariate logistic regression analysis, dental treatment was still associated with HBsAg and anti-HCV seropositivity, while hospitalization was associated with anti-HCV seropositivity.

**Conclusion:** In conclusion, our findings indicate dialysis and history of hospitalization impose significant risks for hepatitis C transmission, and dental treatment is associated with transmission of both hepatitis B and hepatitis C.

**Keywords:** Hepatitis B virus, hepatitis C virus, epidemiology, seroprevalence, risk factors

## Öz

**Giriş:** Çalışma Viral Hepatit Derneği tarafından toplumda hepatit bilincini artırmak ve epidemiyolojik değişkenleri belirlemek projesi kapsamında hepatit B yüzey antijeni (HBsAg) ve anti-hepatit C virüs (HCV) pozitifliği ile ilişkili risk faktörlerinin belirlenmesi amacıyla yapılmıştır.

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**Gereç ve Yöntemler:** Çalışma Türkiye’de 78 ilde birinci basamak sağlık tesislerine başvuran gönüllü 61.943 (yaş:  $35\pm14,1$ , %50,8 erkek) hastada HBsAg ve anti-HCV taraması yapılarak gerçekleştirilmiştir. Sosyo-demografik bilgiler ve olası bulaş risklerini öğrenmeyi amaçlayan standart anket formu yüz yüze görüşme ile doldurulmuştur. Tüm verilerin sağlıklı olarak elde edildiği 21.473 katılımcı dahil edilmiş ve olası bulaş risk faktörleri açısından analiz edilmiştir.

**Bulgular:** HBsAg ve anti-HCV seropozitifliği 61.913 kişiden oluşan çalışma popülasyonunun sırasıyla 1,515 (%2,5) ve 332’sinde (%0,6) saptanmıştır. Tek değişkenli ki-kare testi sonuçlarına göre; hastaneye yatış öyküsü ile anti HCV, son beş yılda dış tedavisi görmüş olmakla HBsAg ve anti-HCV seropozitiflikleri arasında anlamlı ilişki saptanmıştır. Çok değişkenli regresyon analizine göre dış tedavisi ile HBsAg ve anti-HCV ve hastaneye yatış öyküsü ile anti-HCV seropozitiflikleri arasında ilişki bulunmuştur.

**Sonuç:** Bulgular diyaliz ve hastaneye yatış öyküsünün hepatit C, son beş yılda dış tedavisi görmüş olmanın hepatit B ve C bulaşı açısından risk taşıdığına işaret etmektedir.

**Anahtar Kelimeler:** Hepatit B virüs, hepatit C virüs, epidemiyoloji, seroprevalans, risk faktörleri

## Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are among the principal causes of severe liver disease with progressive hepatic fibrosis, cirrhosis, and subsequent complications including hepatocellular carcinoma<sup>[1-4]</sup>. The World Health Organization estimates that there are 285 million people with chronic HBV infection and 170 million people with chronic HCV infection worldwide, resulting in 563,000 and 366,000 deaths each year, respectively<sup>[5]</sup>.

Studies from various centers in Turkey have detected a HBV carrier rate of 4–12% and highly variable rates have been reported in different studies, even within the same province<sup>[6,7]</sup>. Regarding HCV infection, there are marked variations in prevalence in developed countries, ranging from 0.04% in healthy blood donors, 1% in patients presenting to genitourinary clinics, and up to 50% in intravenous drug users<sup>[7]</sup>. In Turkey, the prevalence of HCV varies between 0.5% and 1% in the general population. Anti-HCV seropositivity rate was reported to be 0.05% in blood donors and up to 51.6% in hemodialysis patients<sup>[8-11]</sup>.

Because many chronically infected individuals are asymptomatic and remain unrecognized for many years, conducting population-based studies to determine the prevalence of hepatitis B surface antigen (HBsAg) and anti-HCV among all age groups and the possible risk factors for acquiring these infections might help identify prevention strategies<sup>[12]</sup>. As studies on sero-epidemiology for hepatitis B and hepatitis C infection in Turkey have generally focused on healthy blood donors and health care staff, we conducted this large-scale population-based screening study to determine risk factors associated with HBsAg and anti-HCV positivity. The subject population included blood donors, high risk groups, and healthy subjects from both rural and urban regions of Turkey. This study was part of the national “Raising Public Awareness and Determining Epidemiological Changes in Hepatitis” project carried out by the Viral Hepatitis Society of Turkey.

## Materials and Methods

With permission from the Turkish Ministry of Health, the study was conducted in 2008 among 61,943 participants (mean

age  $35.0\pm14.1$  years, 50.8% males) who presented to primary healthcare centers in 78 cities throughout Turkey. Of these, a sub-population of 21,473 participants with complete medical records was analyzed for the presence of risk factors associated with HBsAg and anti-HCV seropositivity.

The participants were not chosen according to statistical methods but only volunteers from all age groups were included in the study. A standard questionnaire form was applied with each participant in a face-to-face interview and blood samples were collected from each subject for HBsAg, anti-HBs, and anti-HCV analysis. Informed consent was obtained from each subject following a detailed explanation of the study objectives and protocol.

The questionnaire included information about sociodemographic features (age, gender, residence, etc.) and presence of transmission-related risk factors (history of blood transfusion, surgery, hospitalization, dental treatment, unsafe sexual practices, forehead and/or sublingual cuts, dialysis, tattoos, piercings, substance abuse, multiple sexual partners, etc.).

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the Turkish Ministry of Health in Ankara, Turkey (26.02.2008, #B100TSH0005/6363).

### Blood Tests and Further Procedures

Primary screening for HBsAg and anti-HCV was done using 8–10 ml blood samples via immunochromatographic cassette test (Rapid Card test) supplied by the Viral Hepatitis Society, and positive results were confirmed by enzyme immunoassay method (HBsAg Qualitative, Abbott Diagnostics, Ireland) in our reference laboratory.

### Statistical Analysis

Statistical analyses were done using computer software (SPSS version 13.0, SPSS Inc. Chicago, IL, USA). Chi-square test and Fisher’s Exact test were used in comparisons of categorical data. Logistic regression analysis was used to determine correlations between risk factors and serological positivity. Data were expressed as mean and standard deviation, minimum–

maximum, percent (%), odds ratio, and 95% confidence interval where appropriate;  $p < 0.05$  was considered to be statistically significant.

## Results

The mean age of patients was  $35.0 \pm 14.1$  years and 50.8% were males. HBsAg and anti-HCV seropositivities were detected in 1,515 (2.5%) and 332 (0.6%) of the 61,943 study population,

respectively. HBsAg and anti-HCV seropositivity rates in the various regions of Turkey are given in Tables 1 and 2. HBsAg and anti-HCV rates to age groups are given in Tables 3 and 4. In univariate chi-square test, previous history of dental treatment in the last five years was found to be significantly associated with HBsAg ( $p < 0.001$ ) and anti-HCV ( $p < 0.001$ ) seropositivity. History of previous hospitalization was significantly associated with anti-HCV ( $p < 0.001$ ) seropositivity. Results of the univariate chi-square test are summarized in Table 5.

**Table 1. Hepatitis B surface antigen positivity by region**

		Positive	Negative	Total
Mediterranean	Number	305	15252	15557
	%	2.0	98.0	100.0
Eastern Anatolia	Number	28	753	781
	%	3.6	96.4	100.0
Aegean	Number	249	11970	12219
	%	2.0	98.0	100.0
Southeastern	Number	65	1456	1521
	%	4.3	95.7	100.0
Central Anatolia	Number	285	6736	7021
	%	4.1	95.9	100.0
Marmara	Number	354	14011	14365
	%	2.5	97.5	100.0
Black Sea	Number	107	5691	5798
	%	1.8	98.2	100.0
Unknown	Number	122	3702	3824
	%	3.2	96.8	100.0
Total	Number	1515	59571	61086
	%	2.5	97.5	100.0

**Table 2. Anti-hepatitis C virus positivity by region**

		Positive	Negative	Total
Mediterranean	Number	72	15423	15495
	%	0.5	99.5	100.0
Eastern Anatolia	Number	5	786	791
	%	0.6	99.4	100.0
Aegean	Number	84	11856	11940
	%	0.7	99.3	100.0
Southeastern	Number	15	1408	1423
	%	1.1	98.9	100.0
Central Anatolia	Number	51	6606	6657
	%	0.8	99.2	100.0
Marmara	Number	74	14031	14105
	%	0.5	99.5	100.0
Black Sea	Number	22	5698	5720
	%	0.4	99.6	100.0
Unknown	Number	9	3473	3482
	%	0.3	99.7	100.0
Total	Number	332	59281	59613
	%	0.6	99.4	100.0

**Table 3. HBsAg status according to the ages**

		HBsAg		
		Positive	Negative	Total
<15	N/%	18/1.5	1167/98.5	1185
15-17	N/%	25/2.6	929/97.4	954
≥18	N/%	1244/2.5	49176/97.5	50420
Age not documented	N/%	228/2.7	8299/97.3	8527
Total	N	1515	59571	61086
	%	2,5	97,5	100,0

**Table 4. Anti-HCV status according to the ages**

		Positive	Negative	Total
<15	N/%	13/1.2	1100/98.8	1113
15-17	N/%	3/0.3	922/99.7	925
≥18	N/%	295/0.6	49042/99.7	49337
Undocumented	N/%	21/0.3	8217/99.7	8238
Total	N	332	59281	59613
	%	0,6	99,4	100,0

Logistic regression analysis revealed significant correlations: between HBsAg positivity and previous history of dental treatment ( $p<0.001$ ) and between anti-HCV positivity and previous history of dental treatment ( $p<0.001$ ) and hospitalization ( $p<0.001$ ) (Table 6). The presence of other risk factors was not associated with HBsAg or anti-HCV seropositivity.

## Discussion

Herein, we present the first large-scale population-based screening study to determine risk factors associated with HBsAg and anti-HCV seropositivity in a population including risk groups, donors, as well as healthy subjects from both rural and urban regions of Turkey. Our findings revealed 2.5% HBsAg and 0.6% anti-HCV seropositivity rates in the overall study population. Our finding of 2.5% overall HBsAg positivity in our study population supports the claims that Turkey is an intermediate endemic region for HBV (2-7% HBsAg positivity) [6,7,13]. The prevalence of anti-HCV seropositivity (0.6%) was also similar to rates identified in previous studies conducted in Turkey [14,15].

In the present study, univariate analysis revealed that dental treatment was associated with HBV infection and multivariate analysis confirmed dental treatment as an independent risk factor for HBV as well as HCV transmission. A previous study from Poland concerning medical procedures and the risk of iatrogenic hepatitis C infection reported that dental treatment as well as

minor surgical procedures and multiple transfusions contributed to the spread of HCV infection [16]. Although the transmission of HBV and HCV occurs mainly through blood and blood products, saliva has also been implicated as an additional route of infection, with needlestick injury during dental treatment identified as the main risk for exposure to hepatitis viruses.

Moreover, individuals who visited the dentist in the last five years were reported to be twice as likely have HCV infection, primarily due to inadequate sterilization of equipment used in the dental facilities and, more rarely due to an infected dentist [16]. In a previous study related to HBV and HCV seroprevalence in rural areas of the southwestern region of Turkey, factors increasing anti-HCV frequency in univariate analysis were blood transfusion, hospitalization, surgery, low education level, history of contact with a hepatitis C patient, living in the same house with a carrier, and older age. In the same study, multivariate analysis revealed anti-HCV frequency to increase with blood/blood product transfusions [17]. Implementation of control measures in blood transfusion facilities is known to reduce the transmission of HBV and HCV via blood transfusions [18,19]. In a previous study in Turkey, history of blood transfusion was shown to be an important risk factor for HBV and HCV infections [17]. Lack of significant association between blood transfusions and hepatitis in our study may indicate substantial improvement in the transfusion network in recent years.

History of dialysis was not identified as an independent risk factor for HCV and HBV infection in our study cohort. It is important for dialysis patients to receive HBV vaccination and be assessed regularly for anti-HBs titers [17]. Routine HBV vaccination of dialysis patients may explain the low prevalence of HBsAg seropositivity among our patients with history of dialysis [20].

Significant correlation between anti-HCV seropositivity and history of hospitalization was observed in both univariate chi-square test and multivariate logistic regression analysis in our study. Although transfusion of blood or blood products has long been considered a major source of HCV infection, the lack of transfusion history in many HCV-infected individuals suggests that inadvertent exposure to infected blood or body fluids during medical procedures has become a potential source of infection [16]. Apart from blood transfusions, the virus has been reported to spread in medical settings through organ transplantation, from other patients through shared dialysis equipment, colonoscopies, and multi-dose vials, from infected healthcare workers to patients, and from infected patients to healthcare workers, usually as a result of needlestick injuries [16]. In a previous study concerning changes in hepatitis epidemiology in Italy, besides an overall reduction in the incidence of HBV and HCV infection, an increase in the proportion of HBV and HCV infections due to invasive medical procedures like surgery and

**Table 5. Association of risk factors with hepatitis B surface antigen and anti-hepatitis C virus positivity**

	HBsAg		Anti-HCV		
Previous history (in the last 5 years) of	Positive	Negative	Positive	Negative	Total
Blood transfusion	n (%)	n (%)	n (%)	n (%)	n (%)
No	654 (3.1)	20516 (96.9)	153 (0.8)	20247 (99.3)	20400 (100.0)
Yes	32 (2.9)	1063 (97.1)	6 (0.6)	1067 (99.4)	1073 (100.0)
Total	686 (3.1)	21579 (96.9)	159 (0.7)	21314 (99.3)	21473 (100.0)
<b>Operation</b>					
No	632 (3.1)	19902 (96.9)	143 (0.7)	19652 (99.3)	19795 (100.0)
Yes	54 (3.1)	1677 (96.9)	16 (1.0)	1662 (99.0)	1678 (100.0)
Total	686 (3.1)	21579 (96.9)	159 (0.7)	21314 (99.3)	21473 (100.0)
<b>Hospitalization<sup>a</sup></b>					
No	609 (3.0)	19401 (97.0)	130 (0.7)	19151 (99.3)	19281 (100.0)
Yes	31 (3.5)	848 (96.5)	15 (1.7)	846 (98.3)	861 (100.0)
Total	640 (3.1)	20249 (96.9)	145 (0.7)	19997 (99.3)	20142 (100.0)
<b>Dental treatment<sup>b,c</sup></b>					
No	504 (2.8)	17207 (97.2)	106 (0.6)	16929 (99.4)	17035 (100.0)
Yes	136 (4.5)	2905 (95.5)	41 (1.4)	2914 (98.6)	2955 (100.0)
Total	640 (3.1)	20112 (96.9)	147 (0.7)	19843 (99.3)	19990 (100.0)
<b>Unsafe sexual practices</b>					
No	622 (3.1)	19656 (96.9)	141 (0.7)	19406 (99.3)	19547 (100.0)
Yes	10 (3.8)	255 (96.2)	2 (0.8)	254 (99.2)	256 (100.0)
Total	632 (3.1)	19911 (96.9)	143 (0.7)	19660 (99.3)	19803 (100.0)
<b>Forehead/sublingual cuts</b>					
No	630 (3.1)	19871 (96.9)	143 (0.7)	19621 (99.3)	19764 (100.0)
Yes	2 (6.1)	31 (93.9)	0 (0.0)	31 (100.0)	31 (100.0)
Total	632 (3.1)	19902 (96.9)	143 (0.7)	19652 (99.3)	19795 (100.0)
<b>Dialysis</b>					
No	632 (3.1)	19851 (96.9)	143 (0.7)	19601 (99.3)	19744 (100.0)
Yes	0 (0.0)	57 (100.0)	0 (0.0)	57 (100.0)	57 (100.0)
Total	632 (3.1)	19908 (96.9)	143 (0.7)	19658 (99.3)	19801 (100.0)
<b>Tattoo</b>					
No	632(3.1)	19876(96.9)	143(0.7)	19625(99.3)	19768(100.0)
Yes	0(0.0)	30(100.0)	0(0.0)	31(100.0)	31(100.0)
Total	632 (3.1)	19906 (96.9)	143 (0.7)	19656 (99.3)	19799 (100.0)
<b>Piercing</b>					
No	631 (3.1)	19872 (96.9)	143 (0.7)	19621 (99.3)	19764 (100.0)
Yes	1 (3.0)	32 (97.0)	0 (0.0)	33 (100.0)	33 (100.0)
Total	632 (3.1)	19904 (96.9)	143 (0.7)	19654 (99.3)	19797 (100.0)
<b>Substance abuse</b>					
No	632 (3.1)	19893 (96.9)	143 (0.7)	19641 (99.3)	19784 (100.0)
Yes	0 (0.0)	10 (100.0)	0 (0.0)	12 (100.0)	12 (100.0)
Total	632 (3.1)	19903 (96.9)	143 (0.7)	19653 (99.3)	19796 (100.0)
<b>Multiple sexual partners</b>					
No	627 (3.1)	19827 (96.9)	143 (0.7)	19576 (99.3)	19719 (100.0)
Yes	5 (6.0)	79 (94.0)	0 (0.0)	80 (100.0)	80 (100.0)
Total	632 (3.1)	19906 (96.9)	143 (0.7)	19656 (99.3)	19799 (100.0)

<sup>a</sup>p<0.001 for anti-HCV positivity, <sup>b</sup>p<0.001 for HBsAg positivity, <sup>c</sup>p<0.001 for anti-HCV positivity  
HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus



**Table 6. Logistic regression analysis of the correlation between risk factors and serological positivity**

	p value	Odds ratio (95% CI)
<b>HBsAg</b>		
Blood transfusion	0.321	1.316 (0.766-2.262)
Hospitalization	0.180	1.342 (0.873-2.062)
Dental treatment	<0.001	1.604 (1.314-1.957)
Unsafe sexual practices	0.686	1.147 (0.590-2.229)
Forehead/sublingual cuts	0.398	1.864 (0.439-7.906)
Piercing	0.923	1.104 (0.149-8.166)
Multiple sexual partners	0.201	1.855 (0.720-4.778)
<b>Anti-HCV</b>		
Blood transfusion	0.370	1.582 (0.580-4.311)
Hospitalization	<0.001	3.418 (1.902-6.144)
Dental treatment	<0.001	2.050 (1.403-2.996)
Unsafe sexual practices	0.812	0.842 (0.203-3.484)

CI: Confidence interval, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus

dental treatment and a dramatic decrease in infections due to blood transfusion were noted<sup>[21]</sup>.

It is well-documented that risk factors such as intravenous drug use, unsafe sexual practices, and/or multiple sexual partners are important sources of viral hepatitis transmission in Western countries<sup>[18,22,23]</sup>. The limited number of participants using narcotics and/or with multiple sex partners in our patient group may explain the lack of significant association with risk of HBV and HCV infection in our study.

Limitations of our study were possible hesitation among participants to report multiple sexual partners and drug addiction, use of a rapid card test in screening procedure, and inclusion of participants on a volunteer basis without using statistical methods.

## Conclusion

In conclusion, our findings indicate that hospitalization, and dental treatment in the last five years pose significant risk for hepatitis B and C transmission. In this regard, the sterilization and maintenance of instruments used in dental treatment and invasive medical procedures should be carefully monitored, with disposable materials used if possible. Future long-term population-based surveillance studies are needed to better define transmission dynamics and to identify common risk factors for acquiring HBV and HCV infection which could help health care providers and policy makers in designing and initiating effective preventive programs.

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## Ethics

**Ethics Committee Approval:** The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the Turkish Ministry of Health in Ankara, Turkey (26.02.2008, #B100TSH0005/6363).

**Informed Consent:** Informed consent was obtained from each subject following a detailed explanation of the study objectives and protocol.

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

## Authorship Contributions

Surgical and Medical Practices: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Concept: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Design: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Data Collection or Processing: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Analysis or Interpretation: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Literature Search: S.T., İ.B., F.T., N.S., N.Ö., İ.Ş., N.Ö., Y.G., A.I.O., Writing: A.I.O.

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