



# An Evaluation of Hepatitis B Virus and Hepatitis C Virus Frequency and the Anti-hepatitis B Surface Seropositivity of Syrian Refugees in the Karabük Province

Karabük İlindeki Suriyeli Sığınmacılarda Hepatit B Virüs, Hepatit C Virüs Sıklığının ve Anti-hepatit B Yüzey Seropozitifliğinin Araştırılması

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## ABSTRACT

**Objectives:** To investigate the frequency of hepatitis B Virus (HBV) and HCV with anti-hepatitis B Surface (HBs) seropositivity using serological and molecular methods in Syrian refugees in the Karabük.

**Materials and Methods:** The study included the HBs Antigen (HBsAg), anti-HBs, anti-HCV, HCV-RNA, HBV-DNA, and HCV genotyping results of Syrian refugees who presented at the Karabük University Training and Research Hospital between January 2016 and March 2019.

**Results:** The 809 patients were comprised of 536 (66.3%) females and 273 (33.7%) males with a mean age of 34 years. HBsAg was found to be positive in 2.3% of patients and in all HBV-DNA were positive. The anti-HBs seropositivity rate was determined as 21.6% and a significant difference was determined between age groups ( $p=0.001$ ). The anti-HCV was positive in 8 (1%) patients and the HCV-RNA viral load was determined in 7/8. In these 7 patients, the HCV genotype was determined as genotype 1b in 3, genotype 3 in 2, and genotype 4 in 2.

**Conclusion:** This study showed that while the frequency of HBV and HCV in Syrian refugees was similar to the data for Turkey, anti-HBs seropositivity was extremely low. Hepatitis B vaccination programs for Syrian refugees should be implemented and regularly followed up.

**Keywords:** Syria, hepatitis, virus

## ÖZ

**Amaç:** Bu çalışmada amacımız Karabük ilindeki Suriyeli sığınmacılarda serolojik ve moleküler yöntemlerle hepatit B Virüs (HBV) ve HCV sıklığı ile anti-hepatit B yüzey (HBs) seropozitifliğini araştırmaktır.

**Gereç ve Yöntemler:** Bu çalışmaya Ocak 2016-Mart 2019 tarihleri arasında Karabük Üniversitesi Eğitim ve Araştırma Hastanesi'ne başvuran toplam 809 Suriyeli sığınmacının HBs antijen (HBsAg), anti-HBs, anti-HCV, HCV-RNA, HBV-DNA ve HCV genotipleme sonuçları dahil edildi.

**Bulgular:** Toplam 809 hastanın 536'sı (%66,3) kadın, 273'ü (%33,7) erkekti. Hastaların yaş ortalaması 34 idi. Hastaların %2,3'ünde HBsAg pozitif bulundu ve bunların tümünde HBV-DNA pozitif idi. Anti-HBs seropozitiflik oranı ise %21,6 olup, yaş grupları arasında anlamlı farklılık gözlemlendi ( $p=0,001$ ). Anti-HCV, hastaların %1'inde ( $n=8$ ) pozitif. Anti-HCV pozitif sekiz hastanın 7'sinde HCV-RNA viral yük saptandı. Yedi hastanın 3'ü HCV genotip 1b, 2'si genotip 3 ve 2'si de genotip 4 olarak tiplendirildi.

**Sonuç:** Bu çalışmada Suriyeli sığınmacılarda HBV ve HCV sıklığı Türkiye verilerine benzer oranlarda iken, anti-HBs seropozitifliği oldukça düşük bulunmuştur. Suriyeli sığınmacılara yönelik hepatit B aşılama programları düzenli olarak takip edilmelidir.

**Anahtar Kelimeler:** Suriye, hepatit, virüs

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## Introduction

The 2011 outbreak of civil war in Syria led to the greatest refugee crisis since World War II, with 4.8 million of Syrians fleeing to neighboring countries, which included Egypt, Jordan, Lebanon, Turkey and Iran. In September 2019, it was reported that there are 3.658 million Syrian refugees in Turkey. This has led to various health problems, one of which is viral hepatitis (1,2). Viral hepatitis can lead to severe health problems such as cirrhosis of the liver and hepatocellular carcinoma (HCC) (3,4). The hepatitis B virus (HBV) and hepatitis C virus (HCV) are transmitted sexually and from infected mothers to newborns vertically, through parenteral contact with infected blood and body fluids (5).

HBV is the most common cause of chronic viral hepatitis worldwide. Approximately 250 million people throughout the world are infected with chronic HBV and it is estimated that on average 887.000 die each year due to cirrhosis or HCC (6). Vaccination against HBV is the most effective method of protection. In 1998, hepatitis B vaccination was included in the national vaccination program in Turkey, and from that time, has been administered in three doses. In Syria, a three-dose vaccination for HBV has been recommended since 1993 and the vaccination rates, especially in young people, increased (7). However, vaccination programs cannot be fully implemented due to the civil war in Syria.

A vaccine for HCV has not yet been developed. More than 71 million people worldwide are infected with HCV, and it is estimated that 399.000 deaths per year are due to HCV infection-related cirrhosis or liver cancer (8). The prevalence of HCV has been reported as <1% in Syria (9).

The aim of this study was to investigate the frequency of HBV and HCV and anti-hepatitis B surface antigen (HBsAg) seropositivity using serological and molecular methods in Syrian refugees in the Karabük province of the western Black Sea region of Turkey.

## Materials and Methods

This study was approved by the Non-invasive Clinical Research Ethics Board of Karabük University (approval number: 77192459-050.99-E.41215). The study included the HBsAg, anti-HBs, anti-HCV, HCV-RNA, HBV-DNA and HCV genotyping results of 809 Syrian refugees who were admitted at the Karabük University Training and Research Hospital between January 2016 and March 2019. Results of repetitive patient results were excluded from the study and the first serological parameters of each patient were evaluated.

The patients were separated into 4 age groups of 0-20 years, 21-40 years, 41-60 years, and 61+ years. The test results of patients were obtained from the hospital laboratory information system.

In the serum samples sent to the microbiology Laboratory, the HBsAg, anti-HBs, and anti-HCV tests were performed using the chemiluminescence method with the ARCHITECT i2000 SR device (Abbott Diagnostics, USA). For HBV-DNA and HCV-RNA, first viral nucleic acid isolation was performed by the quantitative polymerase chain reaction (qPCR) method with a Magnesia 16 device (Anatolia Genework, Turkey). Then, the HBV-DNA and HCV-RNA quantitative tests were performed using the qPCR method with a Montania 4896 device (Anatolia Genework, Turkey)

according to the manufacturer's instructions. In HCV-RNA positive patients, the Bosphore HCV genotype kit (Anatolia Geneworks, Turkey) was used to determine 8 different genotypes of HCV (1, 1a, 1b, 2, 3, 4, 5, and 6). The HCV genotyping test was also applied using the qPCR method with the Montania 4896 device.

## Statistical Analysis

The data obtained in the study were analyzed statistically using SPSS version 22.0 software (SPSS Inc, Armonk, NY, USA). Conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were stated as number (n), percentage (%) and median values. For group comparisons, the Pearson's chi-square test was used. A value of  $p < 0.05$  was accepted as statistically significant.

## Results

The 809 patients were comprised of 536 (66.3%) females and 273 (33.7%) males with a mean age of 34 years (range: 2-94 years). The presence of HBsAg was detected in 19 (2.3%) patients, 10 females and 9 males. In all the HBsAg positive patients HBV-DNA viral load was detected. Anti-HBs seropositivity was determined in 175 (21.6%) patients and a significant difference was determined between age groups in respect to this parameter ( $p=0.001$ ) (Table 1).

No significant relationship was determined between the genders in respect to HBsAg and anti-HBs seropositivity ( $p=0.200$ ). Of the 10 female HBsAg positive patients, eight were of child-bearing age (15-49 years). Anti-HCV was positive in 8 (1%) patients, with HCV-RNA positivity determined in 7. In these 7 patients, the HCV genotype was determined as genotype 1b in 3, genotype 3 in 2, and genotype 4 in 2. The distribution of the serological parameters according to age and gender were shown in Table 2.

## Discussion

Chronic hepatitis B is a global health threat causing high rates of mortality and morbidity. Of patients, 20%-40% are at risk of developing cirrhosis and HCC. Based on the HBV carrier rate, the world can be divided into 3 regions of high, medium, and low endemicity. Turkey is a middle endemic country (2%-8%) for HBV with a prevalence of 2.3% (10,11). Vaccination coverage has increased in Turkey in recent years with vaccination rates increasing from 64% in 1999 to 98% in 2016 (12). While the vaccination rate in Syria was 83% in 2008, it has fallen to 69% due to the outbreak of war (5,7). Also, Syria is one of the middle endemic countries

Age	Anti-HBs negative n (%)	Anti-HBs positive n (%)
0-20 years	62 (62.6)	37 (37.4)
21-40 years	387 (80.8)	92 (19.2)
41-60 years	130 (80.2)	32 (19.8)
>61 years	55 (79.7)	14 (20.3)
<b>Total</b>	<b>634 (78.4)</b>	<b>175 (21.6)</b>

HBs: Hepatitis B surface

**Table 2.** The distribution of the serological parameters of Syrian patients according to age and gender

		HBsAg		Anti-HBs		Anti-HCV	
		%	n	%	n	%	n
Gender	Female (n=536)	10	0.02	116	21.6	5	0.009
	Male (n=273)	9	0.03	59	21.6	3	0.01
Age groups	0-20 (n=99)	2	0.02	37	37.3	-	-
	21-40 (n=479)	12	0.02	92	19.2	1	0.002
	41-60 (n=162)	3	0.02	32	19.7	4	0.02
	>61 (n=69)	2	0.03	14	20.2	3	0.04

HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C Virus

for HBV (13). The results of this study showed that while the rate of anti-HBs seropositivity in Syrian patients in our region was extremely low at 21.6%, HBsAg positivity was determined as 2.3%. All these patients were diagnosed with chronic viral hepatitis and an HBV-DNA viral load was detected in all.

In the current study, HBsAg positivity was not found at a high rate. However, eight of ten HBsAg positive female patients were in the child-bearing age group. İnci et al. (14) also reported HBsAg positivity as 1.1% in 2158 Syrian pregnant women. This constitutes a threat to newborns. The risk of an infant acquiring HBV perinatally from an infected mother is 70%-90%. Therefore active and passive HBV immunoprophylaxis is crucial.

In a study of 140 Syrian children, Köse et al. (5) reported HBsAg positivity at a higher rate (4.2%) than the data for Turkey and anti-HBs seropositivity was determined at a rate of 52.8. This was attributed to Syrian children generally living in poor socio-economic conditions and no follow up vaccinations. In the current study, anti-HBs positivity was found to be 37.4% in the age group <20 years. This rate was higher than that of the other age groups and similar to findings in other studies, indicating that vaccinations were insufficient.

HCV is another important pathogen that leads to viral hepatitis and hepatitis C infections becoming chronic at a rate of 85%. To date, no vaccination has been developed for HCV. In Turkey, the prevalence of HCV has been reported as 1.6% (5,15) and according to Centers for Disease Control and Prevention data, the HCV prevalence in the Syrian population is estimated to be 0.4% (16). The results of this study showed anti-HCV seropositivity in Syrian refugees at a similar rate (1%) to the data for Turkey. In addition to the detection of HCV RNA in anti-HCV positive patients, it is also necessary to identify the HCV genotype to determine the treatment protocol and duration of treatment (17). The most common HCV genotype is genotype 1 worldwide, followed by genotype 3. Studies have reported genotype 1b to be the most frequently seen in Turkey (60%-100%) (18,19,20). However, in a 2015 study by Caliskan et al. (21) of 313 HCV-RNA positive patients, genotype 3 was found at a rate of 46%. This high rate was attributed to the study group being composed of refugees, drug addicts, and prisoners. In Syria, the predominant genotype is genotype 4 (22,23). In the current study, of the seven Syrian refugees found to be HCV-RNA positive, three were determined as genotype 1b, 2 as genotype 3, and 2 as genotype 4, which was similar to the data for Turkey.

## Conclusion

Although the results of the current study did not show a high rate of HBV and HCV prevalence in Syrian patients, anti-HBs seropositivity was found to be extremely low.

This indicates that hepatitis B vaccination is not adequate among the Syrian people. Therefore, hepatitis B vaccination programs for Syrian refugees must be followed up regularly. Furthermore, as the majority of HBsAg-positive females were in the child-bearing age group, this constitutes a risk for hepatitis B infection in newborn infants. Pregnant women must be screened for HBV and for those found to be positive, active, and passive immunoprophylaxis must be applied to the infant in the perinatal period.

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## Ethics

**Ethics Committee Approval:** This study was approved by the Non-invasive Clinical Research Ethics Board of Karabük University (approval number: 77192459-050.99-E.41215).

**Informed Consent:** Retrospective study.

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

## Authorship Contributions

Concept: N.A., Ş.S., Design: N.A., Ş.S., Data Collection or Processing: N.A., Ş.S., Analysis or Interpretation: N.A., Ş.S., Literature Search: N.A., Ş.S., Writing: N.A., Ş.S.

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