Research Article

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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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