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ORIGINAL ARTICLE

Investigation of Seroprevalence of Viral Hepatitis and Syphilis Co-infection in Individuals Living with HIV: A Single-Center Experience

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Abstract

Introduction: Individuals living with HIV (PLWH) exhibit a higher prevalence of viral hepatitis and syphilis compared to the general population. HIV infection and these co-infections mutually accelerate disease progression. This study aimed to evaluate the seroprevalence of viral hepatitis and syphilis, as well as immunization status against hepatitis, in PLWH.

Methods: The study included 422 PLWH aged >18 years who visited our clinic from 2020 to 2024. Demographic data and the results of HBsAg, Anti-HBc IgG, Anti-HBs, Anti-HCV, Anti-HAV IgG, VDRL, RPR, TPHA, HBV-DNA, and HCV-RNA tests were retrospectively analyzed through the hospital data system. Tests for Treponema pallidum and Hepatitis A/B/C viruses were performed using the ELISA method.

Results: Of the 422 PLWH included in the study, 381 (90.3%) were male, with a mean age of 39.69±12.75 years. When stratified by age, 58.2% of individuals were between 20 and 39 years old. HIV/syphilis co-infection was observed in 149 individuals (35.3%), while 19 individuals (4.5%) had HIV/HBV co-infection. Anti-HCV test results were positive in 7 patients; however, HCV-RNA tests were negative in all cases. The rate of HBV immunity following vaccination was 55.9%, while natural HBV immunity after previous infection was observed in 16.1% of patients. Immunity against HAV was detected in 79.8% (336) of individuals. Co-infected patients with viral hepatitis were statistically significantly older than those infected with HIV alone (p=0.01). A significant difference was found in the male gender among syphilis co-infected individuals (p=0.001). The prevalence of syphilis was significantly higher in individuals positive for Anti-HBc IgG (p=0.002). No significant difference was found between CD4<200 cells/mm^3 and viral hepatitis or syphilis co-infection (p=0.125 and p=0.441).

Discussion and Conclusion: Since syphilis and HBV co-infections are more common in PLWH than in the general population, more effective communication regarding sexually transmitted disease (STD) prevention methods and more frequent screening are necessary in these individuals. Additionally, emphasis should be placed on vaccination programs to improve HBV and HAV vaccination rates in this population.

Keywords: Anti-HBs test; hepatitis B virus; people living with HIV; syphilis.

Human Immunodeficiency Virus (HIV) was isolated in the 1980s and has remained one of the most significant public health concerns globally for over 40 years[1]. With the advent of effective antiretroviral therapy, there has been a radical shift in the natural course of HIV infection, leading to a decrease in the frequency of opportunistic infections

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and an increase in patient survival rates. The reduction in Acquired Immunodeficiency Syndrome (AIDS)-related mortality in people living with HIV (PLWH), along with longer life expectancy, has heightened the importance of other sexually transmitted infections[2,3].

PLWH are at a higher risk of contracting sexually transmitted infections (STIs) compared to the general population. Factors contributing to this increased risk include sexual preferences (e.g., Men Who Have Sex with Men), stigma, multiple sexual partners, casual sex, lack of access to effective preventive tools, and injectable drug use[4].

The World Health Organization's (WHO) 2022-2030 Global Health Sector Strategy report on HIV, viral hepatitis, and sexually transmitted infections emphasizes strategic approaches and inclusive interventions aimed at eliminating AIDS, viral hepatitis B and C, and sexually transmitted infections by 2030[5]. Preventive strategies play a crucial role in the early diagnosis and treatment of viral hepatitis and syphilis, which are more prevalent and tend to have more severe outcomes in PLWH compared to the general population[6].

To develop effective preventive strategies for sexually transmitted diseases such as viral hepatitis and syphilis, the primary requirement is to establish updated epidemiological data for Türkiye.

This study aims to contribute to the epidemiological data in Türkiye by determining the prevalence of Hepatitis B, Hepatitis C, and syphilis co-infections in HIV-positive individuals under follow-up at our hospital

Materials and Methods

This study was conducted with the approval of the Ethics Committee for Scientific Research at Martyr Prof. Dr. İlhan Varank Training and Research Hospital (23.10.2024 - 2024/332). This study was performed in accordance with the Declaration of Helsinki.

This retrospective, cross-sectional, single-center study examined data from 422 PLWH aged 18 years and older, who were followed up at the Infectious Diseases and Clinical Microbiology Clinic of Sultan 2. Abdülhamid Han Training and Research Hospital, Health Sciences University, between March 2020 and August 2024. All participants included in the study had a positive HIV confirmation result, determined using Western blot and HIV RNA tests in conjunction.

The collected data included age, gender, physical examination findings, CD4 T lymphocyte count, and serological markers:

- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (anti-HBc IgG)
- Hepatitis B surface antibody (anti-HBs)
- Hepatitis C virus antibody (anti-HCV)
- Hepatitis A virus antibody (anti-HAV IgG)
- Venereal Disease Research Laboratory (VDRL) test
- Rapid Plasma Reagin (RPR) test
- Treponema pallidum hemagglutination assay (TPHA)
- HBV DNA
- HCV RNA

These data were retrospectively collected from patient files and the hospital's data system.

HBsAg, anti-HBs, anti-HBc, anti-HAV IgG, RPR, and TPHA serological markers were analyzed using the chemiluminescence method (AXSYM Architect kit, Abbott, Germany). Anti-HCV tests were performed using the electrochemiluminescence immunoassay (ECLIA) method with the fourth-generation Elecsys Anti-HCV II kit (Roche Diagnostics, Germany), following the manufacturer's recommendations.

For the detection of HBV-DNA and HCV-RNA, viral nucleic acid isolation was conducted using the QIAsymphony DSP Virus/Pathogen Midi Kit (Qiagen, Germany) on the QIAsymphony SP/AS system. Polymerase chain reaction (PCR) was performed using the Artus QS-RGQ kit (Qiagen, Germany) on the Rotor-Gene Q system, in accordance with the manufacturer's instructions.

A threshold of ≥10 IU/mL for anti-HBs was considered indicative of a vaccine response.

Statistical Analysis

The patient data collected for this study were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) for MacOS 29.0 (IBM Corp., Armonk, NY). Frequency and percentage were used for categorical variables, while mean, standard deviation, median, minimum, and maximum values were provided for continuous variables.

The normality of variables was assessed using the Kolmogorov-Smirnov test. For group comparisons:

- The Mann-Whitney U test was employed for comparisons between two groups.
- Categorical variables were compared using the Chi-square test or Fisher's Exact Test.

Statistical significance was defined as $p<0.05$.

Results

Out of the 422 PLWH included in the study, 381 (90.3%) were male, with a mean age of 39.69±12.75 years. When patients were categorized by age group, 58.2% fell within the 20-39 age range, with the highest proportion (33.6%) in the 30-39 age group (Table 1).

Among the patients, 149 (35.3%) had a co-infection with HIV and syphilis, while 19 (4.5%) had co-infection with HIV and HBV. Seven patients tested positive for anti-HCV; however, their HCV-RNA results were negative (Table 1).

The rate of HBV immunity after vaccination was 55.9%, while the rate of natural HBV immunity following previous infection was 16.1%. The percentage of immunity against HAV was 79.8% (336) (Table 1).

Individuals with viral hepatitis co-infection were found to be statistically significantly older compared to those with HIV infection alone (p=0.01).

A statistically significant gender difference was observed in individuals with syphilis co-infection, with syphilis being more prevalent among males (p=0.001) (Table 2).

Table 1. Demographic and clinical characteristics of the cases, coinfection rates and vaccination rates

Variables	All patients (n=422)	
	n	%
Age group (Year)		
20 - 29	104	24.6
30 - 39	142	33.6
40 - 49	75	17.8
50 - 59	61	14.5
60 - 69	32	7.6
70 - 80	8	1.9
Gender		
Female	41	9.7
Male	381	90.3
CD4+ T lymphocyte, n (%)		
<200 mm^3	88	20.9
≥200 mm^3	334	79.1
HBsAg (+)	19	4.5
HBV Immunity after vaccination	236	55.9
HBV immunity after previous infection	68	16.1
Anti HCV (+)*	7	1.7
TPHA (+)	149	35.3
Anti HBs ≥ 10 IU/mL	304	72
Anti HAV IgG (+)	336	79.8

n: Number of Cases; HBsAg: Hepatitis B surface antigen; Anti-HBc IgG: Hepatitis B core antibody; Anti-HCV: Hepatitis C virus antibody; Anti-HBs: Hepatitis B surface antibody; TPHA: Treponema Pallidum Hemagglutination; Anti-HAV IgG: Hepatitis A virus antibody; * HCV RNA was found to be negative in all anti-HCV positive patients.

Table 2. Comparison of demographic and clinical characteristics of cases coinfected with and without syphilis

Variables	Coinfection with Syphilis, n (%)		p
	Yes 149 (%35.3)	No 273 (%64.7)	
Age (year), Mean±SD	40±13	39±12	<0.429
Gender			
Female	39 (14.3)	2 (1.3)	<0.001
Male	234 (85.7)	147 (98.7)	
CD4+ T lymphocyte, (%)			
< 200 mm^3	60 (22)	28 (18.8)	0.441
≥ 200 mm^3	213 (78)	121 (81.2)	
HBsAg, n (%)			
Positive	11 (4)	8 (5.4)	0.697
Negative	262 (96)	141 (94.6)	
Anti HBc IgG, n (%)			
Positive	52 (19)	48 (32.2)	0.002
Negative	221 (81)	101 (67.8)	
Anti HBs, n (%)			
<10 IU/mL	77 (28.2)	41 (27.5)	0.880
≥10 IU/mL	196 (71.8)	108 (72.5)	
Anti HCV, n (%)			
Positive	4 (1.5)	3 (2)	0.701
Negative	269 (98.5)	146 (98)	
Anti HAV IgG, n (%)			
Positive	212 (77.7)	124 (83.8)	0.135
Negative	61 (22.3)	24 (16.2)	

n: number of cases; SD: standard deviation; HBsAg: Hepatitis B surface antigen; Anti-HBc IgG: Hepatitis B core antibody; Anti-HBs: Hepatitis B surface antibody; Anti-HCV: Hepatitis C virus antibody; Anti-HAV IgG: Hepatitis A virus antibody.

The incidence of syphilis was significantly higher in individuals positive for anti-HBc IgG (p=0.002).

No statistically significant difference was found between viral hepatitis or syphilis co-infection and CD4+ T lymphocyte counts <200 cells/mm^3 (p=0.125, p=0.441, respectively).

Discussion

This study evaluated the prevalence of syphilis, Hepatitis B, and Hepatitis C infections in PLWH followed up in a tertiary hospital in Istanbul between 2020 and 2024. Individuals living with HIV are at an increased risk of contracting sexually transmitted infections (STIs) compared to the general population.

According to Lynn et al.,[7] syphilis increases the likelihood of acquiring HIV by 2.5 times, and HIV/syphilis co-infection exacerbates the progression of both diseases. Another study described the bidirectional relationship between syphilis

and HIV as "epidemiological synergy"[8]. Tumalán-Gil et al.[9] emphasized that the highest seroprevalence of syphilis is observed among men and transgender individuals, with a 37% prevalence in PLWH. The highest incidence of active syphilis was noted in the 20-39 age group.

In a meta-analysis conducted in China, the syphilis co-infection rate was 19.9%, while in Brazil, it was 20.5%. A sub-group analysis of this study highlighted that high-risk behaviors, such as being MSM, having multiple sexual partners, and engaging in unprotected anal intercourse, increase the likelihood of both HIV and syphilis infections[8]. These findings align with the global trend, where a significant proportion of new STI cases occur in younger populations[10].

In our study, the syphilis co-infection rate was 35.3%, which is comparable to the findings of Tumalán-Gil et al.[9] However, studies conducted in Türkiye have reported syphilis co-infection rates of 16.4%, 19.5%, and 17.5%, respectively[3,4,11]. We believe that the high syphilis co-infection rate in our study may be attributed to the fact that 58.2% of our patients were in the 20-39 age range, and 90.3% of them were male.

Additionally, the increasing use of doxycycline for pre-exposure and post-exposure prophylaxis against bacterial STIs in recent years may have led to a reduction in the use of barrier methods, potentially contributing to the rise in syphilis cases. Since sexual orientations were not documented for our patients, we cannot determine whether the MSM group was overrepresented.

Research has demonstrated that a CD4+ T lymphocyte count <200 cells/mm^3 is linked to a higher incidence of syphilis in co-infected patients. Furthermore, the same study suggested that syphilis co-infection may contribute to a reduction in CD4+ T lymphocyte counts[8]. However, other studies have reported that when CD4+ T lymphocyte counts fall below 200 cells/mm^3, the rate of syphilitic reinfection is lower[12]. In contrast, our study did not find any significant correlation between syphilis infection and CD4+ T lymphocyte count.

We did observe a notably higher rate of anti-HBc IgG positivity in syphilis-infected patients, which may be attributed to the increased prevalence of other STIs in PLWH.

Furthermore, no cases of HCV co-infection were observed in our patients. Recent studies suggest that HCV transmission is primarily associated with parenteral routes rather than sexual contact[9]. In the same study, the HBV co-infection rate in PLWH was found to be 4.9%, a relatively high rate that warrants attention regarding sexual transmission.

We believe that the higher HBV rate in our cohort, compared to Türkiye's national data, along with the lower HCV rate, further supports the possibility of sexual transmission in our patient population[13,14].

Patients with viral hepatitis were found to be statistically significantly older. A potential explanation for this could be that the HBV vaccine was incorporated into the national childhood vaccination program in 1998, and 24.6% of our patients were under the age of 29. Additionally, the HBV vaccination rate in our study population was 72%, which is higher compared to the general population[15-17].

Study Limitations

This study has several limitations. First, it was a retrospective study, and data for some patients were inaccessible. Additionally, as a single-center, cross-sectional study, it may not fully represent national data. Since sexual orientation was not accurately documented in patient records, its potential impact on transmission could not be assessed.

In HIV-positive patients, the presence of acute HCV infection may delay the development of anti-HCV antibodies, and HCV RNA testing is required to rule out this diagnosis. However, due to the cross-sectional nature of our study, this was not possible, which may have led to an underestimation of the actual HCV seropositivity rate.

Conclusion

As a result of this study, the seroprevalence of syphilis and HBV among HIV-positive patients followed in our clinic was found to be higher compared to the general population. Given the role of syphilis in increasing the risk of HIV transmission, it is recommended that:

- Identification and targeted screening of at-risk groups,
- Promotion of regular testing, and
- Public education on these issues

be prioritized as key strategies for controlling the HIV epidemic in our country.

Ethics Committee Approval: The study was approved by Martyr Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (No: 2024/332, Date: 23.10.2024).

Informed Consent: We confirm that each participant provided informed consent before participating in the study.

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