ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 30(1): 44-48, 2025
DOI: 10.5505/ejm.2025.58259

Frequency of Syphilis and Hepatitis in HIV Patients

Hacer Özlem Kalaycı[1*], Huseyin Erdal[2], Ahmet Burak Gürpınar[3], Mustafa Kerem Calgin[1]

[1]*Department of Medical Microbiology, Ordu University, Faculty of Medicine, Ordu, Türkiye*
[2]*Department of Medical Genetics, Aksaray University, Faculty of Medicine, Aksaray, Türkiye*
[3]*Department of Medical Biochemistry, Ordu University, Faculty of Medicine, Ordu, Türkiye*

ABSTRACT

Understanding the frequency and impact of syphilis and hepatitis in HIV patients is crucial for optimizing clinical management strategies. Early diagnosis and treatment of these co-infections are vital to mitigate their detrimental effects on HIV progression and overall patient health. This study aims to elucidate the frequency of syphilis and hepatitis co-infections in individuals with HIV.

The outcomes of serological tests for syphilis, HBsAg, anti-HBs, HBV-DNA, and anti-HCV, which were conducted simultaneously with or after the anti-HIV test, along with the patients' demographic data, were retrospectively reviewed and assessed. Statistical analyses were performed using the MedCalc (version 20.009; Ostend, Belgium) statistical package program.

Of the anti-HIV test results examined between May 2021 and 2024, 72 were found to be reactive. Of these, 12 (18.8%) were found to be reactive for Treponema pallidium total antibody. HIV/Syphilis/HBV coinfection was observed in only 1 patient. In logistic regression analysis, individuals with syphilis were 40 times more likely to contract HIV, while individuals with HBV were 2.18 times more likely to contract HIV. HIV reactivity was 14.3 times less common in women than in men. A significant association was found between genders in terms of HIV reactivity.

Since the main transmission route of syphilis, as in HIV infection, is known to be sexual contact, we found a very high rate of syphilis in HIV-infected individuals in our study. Early diagnosis by performing serological tests for both syphilis and viral hepatitis in all HIV-infected patients will be beneficial in reducing transmission.

Keywords: Syphilis, HIV, Coinfection

Introduction

The interplay between syphilis, hepatitis, and human immunodeficiency virus (HIV) infection represents a critical public health concern, meriting comprehensive investigation due to the synergistic effects of these infections on patient morbidity and public health (1–3). Syphilis and hepatitis, both of which can be sexually transmitted, are prevalent co-infections in individuals with HIV, significantly influencing clinical outcomes and complicating the management of HIV (4). HIV, a retrovirus that targets the immune system, continues to pose a significant global health burden. According to the World Health Organization (WHO), approximately 38 million people were living with HIV at the end of 2022 (5). The virus compromises the immune system by destroying CD4+ T cells, leaving individuals susceptible to opportunistic infections and other comorbidities, including syphilis and hepatitis B and C viruses (HBV and HCV). Syphilis, caused by the spirochete Treponema pallidum, progresses through distinct stages, with varying clinical presentations from primary lesions to systemic involvement in later stages (6). Despite the availability of effective antibiotics, the incidence of syphilis has resurged globally over the past two decades, often in conjunction with HIV, especially among men who have sex with men (MSM) and other high-risk populations. Hepatitis, encompassing HBV and HCV, affects the liver and can lead to chronic liver disease, cirrhosis, and hepatocellular carcinoma. Co-infection with HIV is common, given shared routes of transmission, particularly sexual contact and intravenous drug use. HIV-HBV and HIV-HCV co-infections are associated with more rapid progression to liver disease and a higher incidence of hepatotoxicity, complicating antiretroviral therapy (ART). The co-infection rates of syphilis and hepatitis in HIV-positive individuals are notably higher than in the general population. Studies suggest that individuals with HIV are significantly more susceptible to syphilis reinfection and hepatitis complications due to immunosuppression and potential behavioral risk factors (7,8). For instance, the immunosuppressive nature of HIV can alter the clinical course of syphilis, resulting in

***Corresponding Author:** Hacer Özlem Kalaycı, Department of Medical Microbiology, Faculty of Medicine, Ordu University, Ordu, Türkiye
E-mail: kalayciozlem55@gmail.com, Phone: +90506 284 19 59
ORCID ID: Hacer Özlem Kalaycı: 0000-0003-2358-6764, **Huseyin Erdal:** 0000-0003-0786-5077, **Ahmet Burak Gürpınar:** 0000-0003-3227-4682, **Mustafa Kerem Calgin:** 0000-0003-4236-6177
Received: 18.07.2024, **Accepted:** 06.11.2024

atypical presentations and making diagnosis and treatment more challenging. Additionally, the coexistence of HIV and hepatitis viruses can accelerate liver damage, impede the response to ART, and increase the risk of ART-related liver toxicity (9). Understanding the frequency and impact of syphilis and hepatitis in HIV patients is crucial for optimizing clinical management strategies (10). Early diagnosis and treatment of these co-infections are vital to mitigate their detrimental effects on HIV progression and overall patient health. Moreover, integrated care approaches that address the prevention, diagnosis, and treatment of these co-infections are essential for improving health outcomes in HIV-infected populations.

This study aims to elucidate the frequency of syphilis and hepatitis co-infections in individuals with HIV. By examining epidemiological trends, risk factors, and clinical outcomes, the research seeks to contribute to the development of targeted interventions and inform public health strategies to reduce the burden of these co-infections in HIV patients.

Materials and Methods

Our research involved HIV-positive individuals who were tested for HIV at the Medical Microbiology Laboratory of our hospital from May 2021 to 2024 and subsequently confirmed. Anti-HIV test results of 2443 patients were retrospectively analyzed. The outcomes of serological tests for syphilis, HBsAg, anti-HBs, HBV-DNA, and anti-HCV, which were conducted simultaneously with or after the anti-HIV test, along with the patients' demographic data, were retrospectively reviewed and assessed.

HIV was detected in serum samples utilizing the fourth-generation anti-HIV ELISA test (Roche Diagnostics, Mannheim, Germany). The kit used is a fourth generation kit that detects both HIV p24 antigen and HIV type 1 (HIV-1 group M and group O) and HIV type 2 antibodies with a signal/cut off value in the range of 0-0.89. Information on patient age and gender was obtained from the hospital's automation system. Repeatedly reactive samples were sent to the National HIV-AIDS Confirmation and Viral Hepatitis Reference Laboratory, General Directorate of Public Health, Ministry of Health of the Republic of Turkey, Microbiology Reference Laboratories and Biological Products Department, for confirmatory tests.

Serological indicators of HBsAg, anti-HBs, anti-HCV, Treponema pallidum total antibody were studied by chemiluminescence method (Roche Diagnostics, Mannheim, Germany). TPHA (Treponema Palladium Hemagglutination) test was performed on patients with syphilis reactivity. HBV-DNA PCR (Roche Diagnostics, Mannheim, Germany) test was performed on patients with HBsAg reactivity.

Ethical approval: Ethics Committee permission was obtained from an Ordu university Medical Faculty Clinical Research Ethics Committee with the decision number 2023/11/24-303.

Statistical Analysis: Statistical analyses were performed using the MedCalc (version 20.009; Ostend, Belgium) statistical package program. In the statistical description of the data, numerical data were expressed as number, mean and standard deviation. Categorical data were expressed as number, frequency and percentage. Chi-square test was used to evaluate categorical data. Logistic regression analysis was performed for modeling of the study and was shown in a table. In the logistic regression table, the group relative to the reference group is shown in quotation marks. Categorical data were shown as a stacked percentage column. The results were evaluated according to the significance level as $p<0.05$.

Results

Anti-HIV test results of 2443 patients were retrospectively analyzed in Ordu University, Faculty of Medicine, Medical Microbiology Laboratory between May 2021-2024 and 72 patients were found to be reactive. 64 of 72 patients were tested for Treponema pallidium total antibody and 12 (18.8%) were found to be reactive. TPHA test results of 8 of 12 patients with HIV/Syphilis coinfection were 1/2560 and 2 were 1/160. Of the 72 patients with reactive HIV confirmation results, 60 (83.3%) were male and all 12 patients with reactive syphilis results (100%) were male. No syphilis was detected in any of the 12 female patients with reactive HIV confirmation results. When patients with HIV reactive and HIV/Syphilis co-infection were analyzed in terms of gender, a statistically significant relationship was found between them ($p<0.0001$). Forty (55.6%) of the patients with HIV were between the ages of 18-45 and 28 (38.9%) were between the ages of 45-65. Among our patients with HIV/Syphilis co-infection, 9 (75%) were between

Table 1: Logistic regression analysis of the relationship between age, gender, syphilis and hepatitis in patients with HIV

Variables	β	SE	Wald X2	P	OR	OR (%95 GA)	
Age	-0,0051024	0,0074894	0,4641	0,4957	0,9949	0,9804	1,0096
Gender="Female"	-2,66117	0,37528	50,2856	<0,0001*	0,0699	0,0335	0,1458
Syphilis="Reactive"	3,69803	0,58265	40,2833	<0,0001*	40,3679	12,8847	126,4732
HBsAg=" Reactive"	0,78156	0,71996	1,1785	0,2777	2,1849	0,5328	8,9592
Anti HBs="Reactive"	0,29724	0,28577	1,0819	0,2983	1,3461	0,7688	2,3569
AntiHCV="Reactive"	-21,03346	8865,06565	0,000005629	0,9981	7,333E-10		
Model X2=145.38, (DF=6; p<0.0001)							
Nagelkerke R2= 0.268							
Hosmer & Lemeshow test X2=14.38 (DF=8; P=0.072)							
N=2435							

* Significance at <0.05 level

the ages of 18-45 and 2 (16.7%) were between the ages of 45-65. HBsAg was reactive in 4 (5.6%) HIV-infected patients, all of whom also had reactive HBV-DNA tests. According to the chi-square test, we found a statistically significant association between HIV and HBsAg positivity (p<0.0017). HIV/Syphilis/HBV coinfection was observed in only 1 patient. HIV/HCV coinfection was not observed in any patient in our study.

In logistic regression analysis, individuals with syphilis were 40 times (p<0.0001) more likely to have HIV, while individuals with HBV were 2.18 times more likely to have HIV. HIV reactivity was 14.3 times less common in women than in men. A significant relationship was found between genders in terms of HIV reactivity (p<0.0001) (Table 1).

Discussion

HIV is still a public health problem that is increasing in Central Asia and Eastern Europe, where our country is located, and it is frequently seen together with syphilis and viral hepatitis HBV and HCV because of their similar transmission routes (11).

In the present study, we aimed to investigate the frequency of syphilis, HBV and HCV coinfection in HIV-infected individuals in our region. Our findings indicate that among co-infections with syphilis and viral hepatitis in HIV-positive cases, HIV/syphilis is the most prevalent, followed by HIV/HBV co-infection. We found that 83.3% of HIV-positive patients and every case of HIV and syphilis co-infection were male. An individual with syphilis was 40 times more likely to be HIV reactive, and an individual with HBV was 2.18 times more likely to be HIV reactive. However, no connection was found between HIV and HCV. Only one patient (1.4%) exhibited a combination of HIV, syphilis, and HBV.

Several studies conducted in our country, HIV/syphilis co-infection is between 8-25% (12–14). The frequency of syphilis co-infection in HIV patients admitted to our hospital in the last three years was determined as 18.8%. The TPHA seropositivity rate in these patients was found to be 13.9% (10/72) and our results are consistent with the study of Çabalak and Bal (15). Syphilis and HIV are sexually transmitted disease agents and since they can infect the same host together, it is recommended to be screened together when first diagnosed (14).

All of our patients with HIV/syphilis co-infection were male. In the study conducted by Aydın et al., the prevalence of syphilis in HIV-infected individuals was determined as 12.9%, and all cases were male (12). It is noteworthy that HIV/syphilis coinfection is more common in male patients both in our study and in other studies conducted in our country (13,14,16–18).

In our study, 55.6% of HIV-infected patients and 75% of patients with HIV/Syphilis coinfection were between the ages of 18-45. In a similar study conducted in our country, HIV/Syphilis coinfection was found to be 64% between the

ages of 18-44 (13). In Öztürk's study, this rate was found to be 57.3% in patients coinfected with syphilis (19).

It is accepted that 6-14% of HIV positive cases worldwide are infected with chronic HBV. In our study, the prevalence of HIV/HBV coinfection was found to be 5.5%, which is lower than the world average. According to the results of meta-analysis studies conducted in recent years, the HIV/HBV coinfection rate was reported as 7.4% (20). In studies conducted in Türkiye, the HIV/HBV coinfection rate ranged from 3.2% to 5.9%, and similar rates were found with our study (15,21–23). In our study, we found anti-HBs positivity to be 50%. Tozun et al found this rate to be 31.9%, similar to the general population (24). Thanks to national vaccination programs, there has been a decrease in HBV seroprevalence in HIV-infected individuals. It is recommended that newly diagnosed HIV patients be screened for HBV and either treated or immunized accordingly.

The frequency of HIV/HCV coinfection varies by race and route of HIV transmission (25). In studies conducted in our country, this rate varies between 0.9% and 4.4% (22,23,26). Since anti-HCV formation may be delayed in HIV-infected individuals, HCV RNA should be checked or the anti-HCV test should be repeated (27). However, this was not possible in our study and may have caused us to encounter HCV seropositivity. Çabalak and Bal also did not encounter anti-HCV positivity in their study (15).

In conclusion, since the main transmission route of syphilis, as in HIV infection, is known to be sexual contact, we found a very high rate of syphilis in HIV-infected individuals in our study. More comprehensive and multi-center studies can be conducted on HIV-infected patients in our region, contributing to epidemiological data and providing guiding data to clinicians on the management of coinfections. Early diagnosis by performing serological tests for both syphilis and viral hepatitis in all HIV-infected patients will be beneficial in reducing transmission.

References

1. Peeling RW, Mabey D, Chen XS, Garcia PJ. The Syphilis. Lancet. 2023;402(10398):336-346.
2. Ghanem KG, Ram S, Rice PA. The Modern Epidemic of Syphilis. Campion EW, ed. N Engl J Med. 2020;382(9):845-854.
3. Siripurapu R, Ota Y. Human immunodeficiency virus: Opportunistic infections and beyond. Neuroimaging Clin. 2023;33(1):147-165.
4. Bailey H, Turkova A, Thorne C. Syphilis, hepatitis C and HIV in Eastern Europe. Curr Opin Infect Dis. 2017;30(1):93-100.
5. Organization WH. Integrating the Prevention and Control of Noncommunicable Diseases in HIV/AIDS, Tuberculosis, and Sexual and Reproductive Health Programmes: Implementation Guidance. World Health Organization; 2023.
6. Hook EW. Syphilis. Lancet Lond Engl. 2017;389(10078):1550-1557.
7. Ren M, Dashwood T, Walmsley S. The Intersection of HIV and Syphilis: Update on the Key Considerations in Testing and Management. Curr HIV/AIDS Rep. 2021;18(4):280-288.
8. Karp G, Schlaeffer F, Jotkowitz A, Riesenberg K. Syphilis and HIV co-infection. Eur J Intern Med. 2009;20(1):9-13.
9. Navarro J. HIV and liver disease. AIDS Rev. 2022;24(2).
10. Bruno R, Sacchi P, Puoti M, et al. Pathogenesis of liver damage in HCV-HIV patients. AIDS Rev. 2008;10(1):15-24.
11. Gökengin D, Doroudi F, Tohme J, Collins B, Madani N. HIV/AIDS: trends in the Middle East and North Africa region. Int J Infect Dis. 2016;44:66-73.
12. Aydın ÖA, Karaosmanoğlu HK, Sayan M, İnce ER, Nazlıcan Ö. Seroprevalence and risk factors of syphilis among HIV/AIDS patients in Istanbul, Turkey. Cent Eur J Public Health. 2015;23(1):65-68.
13. Sarıgül F, Üser Ü, Öztoprak N. HIV/AIDS hastalarında sifilis koinfeksiyonu seroprevalansı ve risk faktörleri. Klimik Derg. 2019;32(2):161-164.
14. Dinc HO, Alkan S, Ozbey D, et al. Evaluation of Syphilis Coinfection in HIV-Infected Individuals/HIV'le Infekte Bireylerde Sifilis Koinfeksiyonunun Degerlendirilmesi. KLIMIK J. 2020;33(3):292-297.
15. Çabalak M, Bal T. Hıv pozitif olgularda viral hepatit ve sifiliz koinfeksiyonu seroprevalansının irdelenmesi. Flora İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Dergisi. 2020;25(3), 354 - 360.
16. Korkusuz R, Şenoğlu S. Syphilis Seroprevalence and Associated Risk Factors in HIV-infected Individuals. Mediterr J Infect Microb Antimicrob. 2020;9:13.
17. Lin KY, Yang CJ, Sun HY, et al. Comparisons of Serologic Responses of Early Syphilis to Treatment with a Single-Dose Benzathine Penicillin G Between HIV-Positive and HIV-Negative Patients. Infect Dis Ther. 2021;10(3):1287-1298.

18. Arıcı N, Ankaralı H, Kansak N, Adaleti R, Aksaray S. Evaluation of syphilis co-infection and monitoring of rapid plasma reagin (RRP) titer according to syphilis-stage in human immunodeficiency virus-infected patients. Anatol Clin J Med Sci. 2023;28(3):404-410.
19. Öztürk S. HIV ile Yaşayan Bireylerde Sifilis Koinfeksiyonu: Üçüncü Basamak Hastane Verileri. Klimik Journal Klimik Derg. 2023;36(1).
20. Platt L, French CE, McGowan CR, et al. Prevalence and burden of HBV co-infection among people living with HIV: A global systematic review and meta-analysis. J Viral Hepat. 2020;27(3):294-315.
21. Özel AS, Altunal LN, Çağlar Özer M, Özen Aksakal Ş. Evaluation of Hepatitis B and Hepatitis C Seroprevalence in People Living with HIV. Compr Med. 2023;15(2):107-111.
22. Inci A. Investigation of hepatitis B and hepatitis C seroprevalence in HIV-infected patients. Klimik Derg. 2018;31(1):34-36.
23. Şahin M, Aydın ÖA, Karaosmanoğlu HK, Yıldırım M. Seroprevalence of HBsAg and Anti-HCV among HIV Positive Patients. Viral Hepat Journal Viral Hepatit Derg. 2021;27(1).
24. Tozun N, Ozdogan O, Cakaloglu Y, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect. 2015;21(11):1020-1026.
25. Yang T, Chen Q, Li D, et al. High prevalence of syphilis, HBV, and HCV co-infection, and low rate of effective vaccination against hepatitis B in HIV-infected patients in West China hospital. J Med Virol. 2018;90(1):101-108.
26. Ergen P, Çaşkurlu H. Hepatitis C Coinfection Among People Living with HIV in a University Hospital in İstanbul. Viral Hepat Journal Viral Hepatit Derg. 2021;27(2).
27. Thomson EC, Nastouli E, Main J, et al. Delayed anti-HCV antibody response in HIV-positive men acutely infected with HCV. Aids. 2009;23(1):89-93.