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Do Sexually Transmitted Infections Coexist? Evidence from Human Immunodeficiency Virus and Syphilis Coinfection in a Tertiary Care Center

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ABSTRACT

Objective: Syphilis and human immunodeficiency virus (HIV) are sexually transmitted infections that share common risk factors and may facilitate each other's transmission. This study aimed to evaluate the frequency of syphilis coinfection among individuals living with HIV over a five-year period.

Materials and Methods: In this retrospective study, anti-HIV, rapid plasma reagin (RPR), *Treponema pallidum* hemagglutination assay (TPHA), *Treponema pallidum* total immunoglobulin, and HIV confirmatory test results of individuals aged ≥18 years were evaluated between 2020 and 2024. Patients who had both HIV- and syphilis-related tests during the period of HIV positivity were included. Syphilis seropositivity was defined according to the institutional diagnostic algorithm based on the combination of treponemal and non-treponemal tests. Active infection was defined as concurrent positivity of treponemal and RPR tests, whereas isolated treponemal positivity was considered a past infection.

Results: Among 200 individuals living with HIV, 162 underwent syphilis testing. Of these, 85.5% were male. Syphilis seropositivity was detected in 41 patients (25.3%), including 24 (14.8%) with active infection and 17 (10.5%) with past infection. No significant differences were observed based on age, sex, or year ($p>0.05$). During the same period, syphilis seropositivity among HIV-negative individuals was 0.96%. HIV positivity was strongly associated with syphilis seropositivity (OR: 34.8; 95% CI: 23.1–52.6; $p<0.001$).

Conclusion: The high rate of syphilis seropositivity among HIV-positive individuals underscores the importance of routine screening at diagnosis and during follow-up.

Keywords: Coinfection, human immunodeficiency virus, rapid plasma reagin, seropositivity, syphilis.

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INTRODUCTION

Syphilis is a sexually transmitted disease caused by *Treponema pallidum* that can lead to multisystem involvement and serious health problems.[1] Human immunodeficiency virus (HIV) infection is also a sexually transmitted disease and results in a chronic condition characterized by acquired immunodeficiency syndrome (AIDS), which is associated with immunosuppression and the development of opportunistic infections.[2]

Sexually transmitted infections (STIs) are highly prevalent among sexually active individuals and may progress silently, facilitating their spread within the community.[3]

Syphilis and HIV are two systemic sexually transmitted infections that share common risk factors. The World Health Organization (WHO) estimates that there were 7.1 million new syphilis cases worldwide in 2020.[4] According to UNAIDS 2024 data, an estimated 40.8 million people worldwide were living with HIV in 2024, with 1.3 million new infections and approximately 630,000 AIDS-related deaths reported during the same period.[5]

There is a bidirectional epidemiological and biological interaction between these two infections. First, HIV infection may increase the risk of syphilis transmission by weakening the immune system. Conversely, syphilis causes mucosal damage, and syphilitic ulcers provide a portal of entry for HIV, potentially increasing the risk of HIV transmission by approximately twofold. Syphilitic lesions lead to the recruitment of activated immune cells, including macrophages and $CD4^+$ T lymphocytes, to the site of infection, thereby increasing the number of HIV target cells and facilitating HIV acquisition and transmission.[6] All of these interactions make HIV and syphilis coinfection a significant public health concern.[1,7,8]

The aim of this study was to evaluate the frequency of syphilis coinfection among HIV-positive individuals followed at a tertiary care hospital over a five-year period.

KEY MESSAGES

- Syphilis seropositivity was significantly higher among individuals living with HIV compared to HIV-negative individuals, indicating a strong epidemiological association between the two infections.
- Routine and systematic syphilis screening for individuals living with HIV is essential, as coinfection may remain undetected without regular testing at the time of diagnosis and during follow-up.
- Observed differences in HIV/syphilis coinfection rates are influenced by screening practices and population characteristics, emphasizing the need for standardized screening strategies and multicenter data to guide clinical and public health interventions.

MATERIALS AND METHODS

Study Design and Setting

This retrospective, observational, single-center study was conducted in the microbiology laboratory of Sivas Cumhuriyet University Hospital between January 1, 2020, and December 31, 2024. This date range was selected to ensure more complete access to patient data from the hospital system. The study protocol was designed to evaluate syphilis coinfection among HIV-positive individuals aged 18 years and older.

Participants and Data Collection

The study included unique HIV-positive patients who had both HIV-related and syphilis-related serological test results during the period of confirmed HIV positivity. Anti-HIV, rapid plasma reagin (RPR), *Treponema pallidum* hemagglutination assay (TPHA), *Treponema pallidum* total immunoglobulin, and HIV confirmatory test results were retrospectively collected from laboratory records. Cases without documented syphilis testing were excluded from the primary analyses.

Diagnostic Criteria

HIV positivity was defined based on confirmatory testing according to the standard protocols of the General Directorate of Public Health. Syphilis seropositivity was determined by serological testing, including RPR, TPHA, and *T. pallidum* total immunoglobulin results. A TPHA titer of ≥1/80 was considered positive. Syphilis seropositivity was defined as reactivity in at least one treponemal test, and infection status was classified based on the combination of treponemal and non-treponemal results. Cases with reactive treponemal tests (TPHA and/or *T. pallidum* total immunoglobulin) and non-reactive RPR were interpreted as consistent with past or previously treated infection. Concurrent positivity of treponemal and RPR tests was classified as active infection. The term "syphilis seropositivity" encompassed both active and past infections based on the combined interpretation of treponemal and non-treponemal test results.

Inclusion and Exclusion Criteria

Inclusion criteria encompassed all individuals aged ≥18 years with confirmed HIV infection and available syphilis serological test results during the study period. Patients with only a single visit and no subsequent syphilis testing were excluded from the comparative analysis.

Laboratory Methods

Anti-HIV and *T. pallidum* total immunoglobulin tests were performed using enzyme-linked immunosorbent assay (ELISA). The tests were conducted on the Roche cobas 6000 device (Roche Diagnostics, Switzerland) between 2020 and 2022, and on the Architect i2000 device (Abbott Diagnostics, Illinois, USA) between 2023 and 2024. RPR testing was performed using agglutination-based flocculation methods, and TPHA testing was carried out using hemagglutination techniques. The RPR test was performed with Plasmatec test kits from the UK between 2020 and 2022, and with Carbogen and Tulip Diagnostic test kits from India between 2023 and

2024. Omega Diagnostics (UK) and Dialab (Austria) branded kits were used for the TPHA test during the study years. All assays were interpreted according to the manufacturers' instructions.

Syphilis Testing Algorithms

Syphilis serological results were evaluated using both the conventional algorithm (non-treponemal testing followed by treponemal confirmation) and the reverse algorithm (treponemal testing followed by non-treponemal confirmation), depending on the laboratory's available testing strategy. RPR was considered a non-treponemal test, whereas TPHA and *T. pallidum* total immunoglobulin were considered treponemal tests. The use of both algorithms reflected temporal changes in testing strategy and kit availability during the five-year study period. Regardless of the initial screening method, final interpretation was based on the combined assessment of treponemal and non-treponemal test results.

Individuals living with HIV were screened for syphilis as recommended in the HIV-AIDS diagnosis and treatment guidelines of the Ministry of Health of the Republic of Türkiye.[9] When HIV positivity was detected, initial screening for syphilis was performed. If the individual remained at risk, periodic screening (generally once a year) was conducted thereafter. In individuals with multiple partners, a history of unprotected sexual intercourse, those who engage in sex while using drugs, or those with a partner exhibiting these behaviors, screening was performed more frequently (every 3-6 months).

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. Variables that did not follow a normal distribution were presented as medians with interquartile ranges (IQR), while categorical variables were expressed as counts (n) and percentages (%). Associations between categorical variables were evaluated using the chi-square test or Fisher's Exact Test, as appropriate. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess the association between HIV status and syphilis seropositivity. A p-value<0.05 was considered statistically significant.

Ethical Approval

Ethics approval for this study was obtained from the Sivas Cumhuriyet University Health Sciences Research Ethics Committee (Approval Number: 2025-11/41, Date: 20.11.2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design of the study, the requirement for informed consent was waived.

Table 1. Distribution of syphilis seropositivity by age group and sex among individuals living with HIV (n=162)

Variable	Syphilis positive n (%)	Syphilis negative n (%)	Total	p
Age group				0.766*
18–24	4 (26.7)	11 (73.3)	15	
25–44	21 (23.1)	70 (76.9)	91	
≥45	16 (28.6)	40 (71.4)	56	
Sex				0.176**
Male	38 (27.1)	102 (72.9)	140	
Female	3 (13.6)	19 (86.4)	22	
Total	41 (25.3)	121 (74.7)	162	

*: Fisher's Exact test; **: Pearson Chi-square test.

RESULTS

During the study period, a total of 226,228 anti-HIV tests were performed in the laboratory, and HIV positivity was confirmed by confirmatory tests in 200 distinct individuals (0.09%). Of these individuals, 171 were male (85.5%) and 29 were female (14.5%). The median age of the study population was 38 years (IQR: 29–48.8).

Of the 200 individuals identified as HIV-positive, 162 (81%) underwent syphilis screening during follow-up in accordance with the HIV-AIDS diagnosis and treatment guidelines after their HIV-positive status was confirmed. The remaining 38 individuals, who were not screened for syphilis, had only a single visit to our hospital during which HIV positivity was detected and did not return thereafter.

Among the 162 individuals who underwent syphilis screening, syphilis seropositivity was detected in 41 patients (25.3%). There was no statistically significant difference in syphilis positivity based on sex (p=0.176) or age group (18–24, 25–44, and ≥45 years) (p=0.766). Among HIV-positive individuals who underwent syphilis serological testing (n=162), no significant difference in syphilis seropositivity was observed across the study years (Fisher's Exact Test, p=0.740). The analysis of a linear trend across years did not demonstrate a significant increase or decrease in syphilis seropositivity (Chi-square test for trend, p=0.764). The relevant data are presented in Tables 1 and 2. The distribution of disease activity status according to the serological results of individuals screened for syphilis is shown in Table 3.

During the same study period, a total of 9,393 non-duplicated patients who underwent both HIV and syphilis testing were

Table 2. Syphilis seropositivity by year (n=162)

Year	Positive, n (%)	Negative, n (%)	Positivity rate (%)
2020	16 (26.2)	45 (73.8)	26.2
2021	8 (25.8)	23 (74.2)	25.8
2022	9 (19.6)	37 (80.4)	19.6
2023	3 (30.0)	7 (70.0)	30.0
2024	5 (35.7)	9 (64.3)	35.7
Total	41 (25.3)	121 (74.7)	25.3

This table includes HIV-positive individuals who underwent serological testing for syphilis (n=162). No statistically significant difference in syphilis seropositivity was detected across years (p>0.05). The p-value was calculated using Fisher's Exact Test. A chi-square test for trend (linear-by-linear association) was performed to evaluate temporal trends.

Table 3. Disease activity according to serological results in individuals living with HIV who underwent syphilis screening

Serological status (n=162)	n (%)
Syphilis positive	41
Active infection	24 (14.8)
Previous infection	17 (10.5)
Syphilis negative	121 (74.7)

HIV: Human immunodeficiency virus.

Table 4. Results of patients tested simultaneously for HIV and syphilis

Group	Syphilis positive n (%)	Syphilis negative n (%)
HIV positive	41 (25.3)	121 (74.7)
HIV negative	89 (0.96)	9,142 (99.04)

Chi-square test: p<0.001; Odds ratio (OR)=34.8 (95% CI: 23.1–52.6); HIV: Human immunodeficiency virus.

evaluated. Of these patients, 162 were HIV-positive, and syphilis seropositivity was detected in 41 of them (25.3%). Among the 9,231 HIV-negative patients, syphilis seropositivity was identified in 89 individuals (0.96%). Syphilis seropositivity was significantly higher in individuals living with HIV compared to HIV-negative individuals (Chi-square test, p<0.001). An approximately 35-fold increased association was observed between HIV positivity and syphilis seropositivity (OR: 34.8; 95% CI: 23.1–52.6). The relevant data are shown in Table 4.

A binary logistic regression analysis was performed to evaluate potential independent predictors of syphilis seropositivity. Age and sex were included as independent variables in the model. Neither age (OR: 0.99; 95% CI: 0.96–1.02; p=0.390) nor sex (OR: 2.48; 95% CI: 0.69–8.91; p=0.165) was independently associated with syphilis seropositivity. The results of the logistic regression analysis are presented in Table 5.

Table 5. Binary logistic regression analysis of factors associated with syphilis seropositivity

Variable	OR	95% CI	p
Age (per year increase)	0.99	0.96–1.02	0.390
Male (vs female)	2.48	0.69–8.91	0.165

OR: Odds ratio; CI: Confidence interval.

Table 6. Studies investigating HIV/syphilis coinfection in Türkiye

Study	Study period	HIV-positive individuals (n)	Syphilis coinfected individuals n (%)
Yağcı Çağlayık et al.[23]	1985–2024	1,042	259 (24.9)
Korkusuz et al. [17]	2015–2019	1,057	194 (18.3)
Sarıgül et al.[21]	2015–2018	384	97 (25)
Arıcı et al.[16]	2015–2023	284	103 (36.2)
Öztürk[18]	2016–2020	201	47 (23.3)
Alıravcı et al.[24]	2018–2024	142	26 (18.3)
Şahin et al.[25]	2019–2022	44	11 (25)
Present study	2020–2024	162	41 (25.3)

HIV: Human immunodeficiency virus.

An evaluation of the syphilis diagnostic algorithms used during the study period revealed that 65 results (40.1%) were assessed using the conventional algorithm, while 97 results (59.9%) were evaluated using the reverse algorithm.

DISCUSSION

In this study, the rate of syphilis seropositivity was significantly higher in individuals living with HIV compared to HIV-negative individuals. Syphilis seropositivity was detected in more than one-quarter (25.3%) of individuals living with HIV who underwent syphilis screening, which is considerably higher than the prevalence observed among HIV-negative individuals (0.96%). The strong association between HIV positivity and syphilis seropositivity appears to be consistent with the shared routes of transmission and common risk factors for both infections. Additionally, recent surveillance reports indicate that syphilis remains a growing public health concern in many regions, particularly among key populations, further underscoring the importance of integrated HIV–syphilis screening strategies.[10,11]

Treponema pallidum and HIV can coexist in the same host, as both are sexually transmitted pathogens. The Ministry of Health's HIV/AIDS diagnosis and treatment guidelines recommend periodic screening for sexually transmitted infections at the initial visit and during follow-up for individuals infected with HIV.[9] HIV and syphilis coinfection rates vary depending on the prevalence of infections in the community and individual risk factors. In a multicenter study reported from Türkiye,[12] the HIV/syphilis coinfection rate was 8%, and rates reported from different centers are summarized in Table 6.

Variable rates have also been reported in international studies. In a study from Spain, in which individuals living with HIV were followed for 38 months, the baseline syphilis seroprevalence was reported as 13%, and new syphilis cases were detected at a rate of 4% during follow-up.[13] In an eight-year study conducted in Japan, syphilis seropositivity among individuals living with HIV was reported to be 2%.[14] The coinfection rate of 25.3% observed in the present study is comparable to some of the rates reported in the literature but higher than those reported in other studies. These differences may be related to variations in screening strategies across centers and the characteristics of the study populations.

Furthermore, it should not be overlooked that individuals who do not maintain continuity in healthcare access after diagnosis may be at increased risk, both due to delays in syphilis screening and the potential for ongoing transmission. These findings support the importance of regular syphilis screening in individuals living with HIV, both for individual patient management and public health.

Mutagoma et al.[15] reported a sixfold increased association of syphilis seropositivity in individuals living with HIV compared to HIV-negative individuals. Similarly, in the present study, syphilis seropositivity was found to be significantly higher among individuals living with HIV than among HIV-negative individuals, with an approximately 35-fold increased association for syphilis positivity. Several factors may explain this difference. First, individuals living with HIV are routinely screened for syphilis, whereas HIV-negative individuals may be tested primarily when clinically indicated, potentially leading to detection bias. Second, the tertiary care setting may represent a population with higher baseline risk behaviors or referral bias. Third, regional differences in sexual network structures and transmission dynamics may contribute to higher local coinfection rates. Therefore, the observed odds ratio should be interpreted cautiously in light of differential screening practices and study setting characteristics. Consistent with this interpretation, binary logistic regression analysis in our cohort did not identify age or sex as independent predictors of syphilis seropositivity, suggesting that the observed coexistence may be driven primarily by unmeasured behavioral factors rather than demographic characteristics alone.

In a multicenter study conducted by Sarıgül et al.,[12] 96% of coinfected cases were reported to be male. Arıcı et al.[16] reported that all cases in their study were male, while Korkusuz et al.[17] reported a rate of 97.9% and Öztürk[18] reported a rate of 95.8% among males. According to the Ministry of Health's HIV/AIDS statistics in Türkiye, a total of 54,472 individuals living with HIV were reported between 1985 and November 2025, of whom 82.1% were male.[19] In the present study, 92.7% of coinfected cases were male, which is consistent with the literature. Although a lower proportion was observed compared to some similar studies, differences in the number of patients included and the sexual contact patterns of the studied populations may explain this variation. The predominance of HIV positivity among males further supports this finding. The literature reports that unprotected sexual intercourse among men who have sex with men (MSM) has contributed to an increase in syphilis cases.[8] In the United States, one-third of MSM reported having sexual intercourse with women, while this proportion has been reported as 28% in China, 47% in Peru, and 79% in Russia.[20] This suggests that the MSM population may potentially act as a bridge for transmission between high-risk men and lower-risk women. Although data on MSM status could not be obtained in the present study, the current findings are valuable in terms of guiding screening strategies. We believe that assessing sexual behaviors in individuals diagnosed with HIV, performing relevant investigations, and providing counseling on behavior-related transmission prevention methods may help interrupt the transmission cycle.

Sarıgül et al.[21] reported that 55% of coinfected individuals were in the 25–44 age group, while Köksal et al.[22] reported a rate of 53.2%. In the present study, a similar proportion (51.2%) was observed. This distribution may be related to the fact that the 25–44 age group represents a sexually active period with potentially higher exposure to sexually transmitted infections, as well as more pronounced shared risk behaviors among individuals living with HIV, such as unprotected intercourse, multiple partners, and MSM relationships.

From a clinical perspective, undiagnosed syphilis in individuals living with HIV may lead to delayed treatment, ongoing transmission, and potential complications. Regular and repeated screening facilitates early diagnosis and timely management. From a public health standpoint, strengthening integrated HIV–syphilis surveillance systems, routine screening policies, and behavioral risk assessment strategies is essential to control coinfection at the population level.

This study has several limitations due to its retrospective and single-center design. The lack of data on behavioral risk factors and routes of transmission limited a more detailed analysis of coinfection dynamics. The results are limited in their generalizability because the study only includes data from a single center. Additionally, the relatively limited number of HIV-positive individuals may have reduced the statistical power to detect small differences between subgroups (e.g., age strata and sex). Therefore, nonsignificant findings in subgroup analyses should be interpreted cautiously. Nevertheless, data obtained from a center that follows individuals living with HIV provide important information regarding the frequency and demographic characteristics of coinfection.

CONCLUSION

In conclusion, syphilis seropositivity was found to be 25.3% in a tertiary care center where individuals living with HIV were followed. It is important not to overlook syphilis coinfection in individuals living with HIV, and regular syphilis screening should be maintained at the time of diagnosis and throughout follow-up. Data obtained from different centers will better elucidate the epidemiology of HIV and syphilis coinfection and contribute to the development of screening strategies. Multicenter studies with larger populations are needed to better clarify the epidemiology of HIV and syphilis coinfection and optimize screening strategies.

Ethics Committee Approval: Ethics committee approval was obtained from Sivas Cumhuriyet University Health Sciences Research Ethics Committee (Approval Number: 2025-11/41, Date: 20.11.2025).

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