Original Article

DOI: 10.4274/haseki.galenos.2021.7217
Med Bull Haseki 2021;59:313-8

Risk Factors and Seroprevalence of Syphilis Among Naive HIV Patients: A Cross-Sectional Study From a Tertiary Center

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Abstract

Aim: Syphilis coinfection is common among human immune deficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) diagnosed patients. We aimed to investigate the rates of syphilis coinfection, social-demographical features, viral and immunological properties among naive HIV/AIDS patients.

Methods: Socio-demographical data, CD4+ T lymphocyte counts, HIV viral load, syphilis antibody results and physical examinations at the time of diagnosis of naive HIV infected patients who were admitted to our center between January 2017 and January 2021, were evaluated retrospectively from the medical records.

Results: Three hundred-two naive HIV patients were enrolled in the study. Positive syphilis antibody rate was detected as 21.5% and 86.2% of those patients were male and also found 31.4% ($p<0.01$) in patients in which route of transmission was men sex with men (MSM). Positive syphilis antibody rate was found to be statistically higher in patients with substance abuse ($p<0.01$), CD4+ T lymphocyte counts were under 200 cell/mm^3 ($p=0.018$) and viral load above 100.000 copies/mL ($p<0.01$).

Conclusion: Among HIV-infected patients, those with MSM and substance abuse constitute the group at highest risk of syphilis. Therefore, syphilis must be screened and treated, especially at HIV diagnosis and high-risk behaviors.

Keywords: AIDS, coinfection, HIV infections, syphilis

Introduction

Syphilis is a systemic infectious disease caused by the spirochete bacterium *Treponema pallidum* (1). Human immune deficiency virus (HIV) and syphilis are sexually transmitted infections with similar transmission routes, such as unprotected sexual contact, blood transfusion, and vertical transmission from mother to baby (2). For early-stage HIV-positive individuals, the already existing high risk of transmission might be further increased with the incidence of syphilis due to genital/oral ulcers, decreased CD4+ T lymphocyte count and an increase of viral load. Besides, the disease course of syphilis progresses differently in HIV patients with diminished host defense due to impaired immune response and results in shortening of incubation time and increasing in number and infectiousness of syphilis lesions (3,4).

Since the first reported HIV case in 1985, the total number of HIV cases in Turkey has reached 25,809, according to the Turkish Ministry of Health surveillance between 1985 and 2020 (5). On the other hand, in studies regarding the seroprevalence of syphilis in potential risk groups in Turkey, rates between 0.11% and 19.3% were revealed. The highest rates were detected among men sex with men (MSM), followed by sex workers and

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Received: 24.03.2021 **Accepted:** 22.05.2021

blood donors (6-8). Syphilis coinfection is common in HIV-infected individuals due to sharing similar transmission routes (9). Although there are several studies and reports on the seroprevalence of HIV and syphilis separately, there is a lack of data regarding the seroprevalence of syphilis in HIV patients. Because of these close relationships, current guidelines recommend routine serological testing for syphilis during HIV infection screening and/or in patients diagnosed with HIV infection (10,11).

In order to prevent the spread of HIV and syphilis, determining the seroprevalence and associated risk factors of syphilis among HIV-infected patients will provide important information. The present study which contributes to the literature intended to investigate the rates of syphilis coinfection, social-demographical features, viral and immunological properties among naive HIV/AIDS patients.

Methods

Study Design

The study was approved by the University of Health Sciences Turkey, Izmir Bozyaka Training and Research Hospital's Local Ethics Committee with the approval number (2020-172). Informed consent was obtained from all participants included in the study. This study was conducted at the University of Health Sciences Turkey, Izmir Bozyaka Training and Research Hospital, Clinical Microbiology and Infectious Diseases outpatient clinic, between January 2017 and January 2021. Syphilis test results at the time of diagnosis of naive HIV patients those admitted to our outpatient clinic were investigated retrospectively and evaluated. Besides, social-demographical data regarding age, gender, marital status, sexual orientation, education, smoking, alcohol usage, substance abuse, HIV transmission route and physical examination findings were obtained from medical records. CD4+ T lymphocyte count, HIV viral load and syphilis antibody status at the time of diagnosis were evaluated.

Laboratory Assessment

CD4+ T lymphocyte counts were determined by using flow cytometry BD FACSCanto II (BD Diagnostic Systems, Sparks, MD, USA). According to the Centers for Disease Control and Prevention (CDC) staging system for classification of HIV-infected persons, CD4+ T lymphocyte counts <200 cell/mm³ were defined as stage-3; CD4+ T lymphocyte counts 200-499 cell/mm³ were defined as stage-2 and CD4+ T lymphocyte counts >499 cell/mm³ were defined as stage-1 (12). HIV-RNA levels were measured by polymerase chain reaction method (Artus HI Virus-1 QS-RGQ Kit, QIAGEN, Germany). According to the viral load, HIV-RNA >100.000 copy/mL was defined as high viral load whereas, HIV-RNA <100.000 copy/mL was defined as low viral load. Since January 2017, a reverse algorithm has been used in terms of serological diagnosis of syphilis (13). A chemiluminescent microparticle immune assay (CMIA) based test (Architect Syphilis TP, Abbott, USA) was used in terms of the initial screening test. According to the algorithm, an additional test was not performed for patients with CMIA negative, whereas patients with positive CMIA were tested with rapid plasma reagin (Omega Diagnostics, England). Positive results in both tests were considered to be syphilis-positive. In case of incompatible results, positive results with CMIA were verified with Treponema pallidum hemagglutination (Omega Diagnostics, England) test.

Statistical Analysis

All statistical analyses were performed using SPSS 18.0 (Chicago, IL USA). A p-value less than 0.05 was considered statistically significant. Comparisons between the two groups were assessed by chi-square and Fisher's exact test analysis. Comparison of numerical variables between two groups was made using Student's t-test when the normal distribution condition was met. On the other hand, when the normal distribution condition was not met, numerical variables were made between groups using the Mann-Whitney U test. All of the numerical variables with normal distribution were expressed as the means ± SD. All of the numerical variables without normal distribution were expressed as median interquartile range values. Pearson analysis was used for univariate correlations between variables.

Results

A sum of 302 naive HIV patients were enrolled in the study. Sixty-five patients (22%) were syphilis-positive, and 237 patients (78%) were syphilis-negative. Male gender dominancy existed in both syphilis-positive and negative patients, but there was no significant difference between groups (p=0.11). There was no statistically significant difference between syphilis-positive and syphilis-negative patients in terms of age (p=0.20).

In terms of sexual orientation, 159 patients (53%) were homosexual, 128 patients (42%) were heterosexual, and 15 patients (5%) were transsexual. Syphilis-positivity rates were most common among homosexual patients (31%) p<0.01.

There was no significant difference between syphilis-positive and syphilis-negative patients in terms of smoking and alcohol usage. On the other hand, a considerable difference between syphilis-positive and syphilis-negative patients was found in substance abuse (p<0.01).

Patients with high viral load, defined as HIV-RNA levels above 100.000 copies/mL, were detected in 69% of syphilis-

positive patients, whereas it was 50% in Syphilis- negative patients. There was a significant difference between groups in terms of high viral load existence (p<0.01).

According to the CDC staging system of HIV-infected patients, the rate of patients in stage-3 was higher in syphilis-positive patients (28%) compared to syphilis-negative patients (15%). In terms of classifying patients according to CD4 counts (stage-1, stage-2 and stage-3), there was a statistically significant difference between syphilis-positive and syphilis-negative patients (p=0.01), respectively.

According to the physical examination findings and symptoms of 65 syphilis-positive patients, 9 patients (13.8%) were considered primary syphilis, and 25 patients (38.5%) were considered secondary syphilis. Two of the patients with secondary syphilis were with syphilitic uveitis. The remaining 31 patients (47.7%) without either symptom or physical examination findings were considered latent Syphilis.

The demographical features and laboratory results of patients with positive and negative syphilis are presented in Table 1.

Table 1. Demographical features and laboratory results of syphilis (-) and syphilis (+) patients

Total n=302	Syphilis (-) (n=237) n (%)	Syphilis (+) (n=65) n (%)	p
Gender Female Male Transgender Total (302)	29 (12.2) 196 (82.7) 12 (5.1) 237 (78.5)	3 (4.6) 56 (86.2) 6 (9.2) 65 (21.5)	0.11*
Age years	35±11	37±11	0.20**
Sexual orientation Heterosexual Homosexual Transsexual	 116 (48.9) 109 (46.0) 12 (5.1)	 12 (18.5) 50 (76.9) 3 (4.6)	**<0.01***
Marital status Single Married	 169 (71.3) 68 (28.7)	 54 (83.1) 11 (16.9)	0.05*
Education illiterate Primary school Secondary High school Universite	7(3) 49 (20.7) 35 (14.8) 73 (30.8) 73 (30.8)	1 (1.5) 14 (21.5) 9 (13.8) 18 (27.7) 23 (35.4)	0.73*
Reason for HIV testing another illness screening	89 (37.6) 148 (62.4)	32 (49.5) 33 (50.8)	0.08*
Smoking No Yes	 95 (40.1) 142 (59.9)	 23 (35.4) 42 (64.6)	0.49*
Alcohol No Yes	 107 (45.1) 130 (54.9)	 23 (35.4) 42 (64.9)	0.15*
Substance abuse No Yes Used to	 178 (75.1) 33 (13.9) 26 (11.0)	 40 (18.3) 20 (37.7) 5 (7.7)	**<0.01***
CD4 + T lymphocyte count (/mm³) ≥500 (stage-1) 200-499 (stage-2) <200 (stage-3)	 87 (36.9) 114 (47.9) 36 (15.3)	 27 (41.5) 20 (30.8) 18 (27.7)	**0.01***
HIV-RNA level(copymL) ≤100.000 >100.000	 119 (50.2) 118 (49.8)	 20 (30.8) 45 (69.2)	**<0.01***

*Chi-square test p<0.05 **Student's t-test

Discussion

Syphilis and HIV have mutual adverse effects on disease courses. Syphilis results in diminishing CD4 T lymphocyte levels and increasing HIV viral load during the HIV disease course. On the other hand, HIV results in increasing neurological complications and decreasing response to therapy during the syphilis disease course (14). Therefore, screening of HIV-infected patients in terms of other sexually transmitted diseases, including syphilis, is recommended at the time of diagnosis (15). Considering the high prevalence of syphilis and the increasing prevalence of HIV in many countries, early diagnosis of syphilis and HIV coinfection is very important. Although the relationship between HIV and syphilis has not been clarified yet, it was shown in the studies that syphilis enhances the contamination risk of HIV (16). The seroprevalence of syphilis among newly diagnosed HIV patients was reported as 25% in Mexico, 21% in Spain, 19.8% in China and 15.7% in the USA (17-20). The differences between countries regarding social, cultural, and economic differences seem to affect the incidence of sexually transmitted diseases. In Turkey, the seroprevalence of syphilis among HIV patients was reported between the range of 7.6% and 25%, and it was presented in Table 2 (21-26). In our study, the seroprevalence of syphilis among HIV patients was found to be 22%. This might be due to the differences between regions in terms of social, cultural, and economic reasons, which was shown in the studies in the literature (24).

Table 2. The studies about HIV-syphilis coinfection in Turkey

Researcher	Publication year	HIV (+) patients (n)	Syphilis patients n (%)
Kaptan et al. (21)	2009	92	9 (9.8)
Sayan et al. (22)	2012	117	9 (7.6)
Aydin et al. (23)	2013	308	40 (12.9)
Sarigül et al. (24)	2018	3641	291 (8)
Sarigül et al. (25)	2018	384	97 (25)
Korkusuz et al. (26)	2020	1057	194 (18.3)

HIV: Human immunodeficiency viruses

The dominancy of male gender among patients with HIV-syphilis coinfection, which was found in our study and

similar studies in the literature, is a remarkable finding. In the report of CDC, which was published in 2018, the rise of the incidence of HIV-syphilis coinfection was attributed to the rapid increase in the number of HIV-infected patients who were MSM and also, it was reported that, syphilis prevalence is increased among bisexual and homosexual men (27). In Turkey, while the contamination rate of HIV/AIDS among heterosexual patients was declined to 35.4% from 50%, the contamination rate among patients who were MSM, increased from 8% to 13.4% (24). In a recently published study, the contamination rate of HIV-syphilis coinfection among patients who were MSM was found to be increased from 23% to 43% between 2012 and 2015 (28). This rate was found as 52.6% in our study. In a meta-analysis in West Europe, the seroprevalence of syphilis was found between the range of 14% and 59% among HIV-infected patients who were MSM (29). In a study conducted in China this rate was found as 22% (30). In two recently published studies in Turkey, the rate of syphilis among HIV-infected patients who were MSM was between 22% and 55.9% (25,26). In our cohort, syphilis seroprevalence was found 31.4%, 9.4%, and 20% among MSM, heterosexual, and transexual patients, respectively. In addition, the syphilis-positivity rate was found statistically significant ($p<0.01$) among patients who were MSM, which was following the other studies.

The higher incidence among these patient groups was mostly attributed to various reasons such as multiple sexual partners among patients who were MSM, inappropriate condom usage, the increase in the tendency of easy partner finding at web/smartphone applications, commonly usage of psychostimulant agents and sexual performance-enhancing drugs, the common belief about the idea that oral sex is a safer way for sexual contact (31). In a study conducted in Turkey, the syphilis-positivity rate was found 16.8% among newly diagnosed HIV patients and the incidence was found to be increased at 18.3% during the follow-up period. The rise in the incidence rate was attributed to sexual contact with multiple partners and the low rates of condom usage (26).

In terms of marital status, 73.8% of our patients were single and the rate of single patients among syphilis-positive patients was 83%. Although it was not found to be statistically higher ($p=0.056$), the high rates were remarkable. Studies revealed that single patients have tendency in multiple sex partners compared to the patients who are married. As a consequence, the seroprevalence of syphilis and HIV was found to be increased in parallel to multiple sexual partners. On the other hand, men display more risky behavior in terms of sexual contact (30).

In a recent study conducted in Istanbul, 50.7% of HIV patients were found to be primary school graduates and syphilis seropositivity rates were found to be associated with low education levels (23). However, in our study, 31.8% of HIV patients were college degree educated and was seen no association between education level and syphilis seroprevalence. This might be due to the regional differences in terms of education since Istanbul is the biggest and most cosmopolitan city in Turkey. The education level in the general population is relatively better in Izmir compared to Istanbul.

The most common reason for HIV testing was found to be due to application for another illness (40.1%) and 26.4% of these patients were found to be syphilis-positive. The second common reason for HIV testing was own request for sexual transmitted disease testing (25.5%). The syphilis seropositivity rate was found 23.4% in these patients who were recorded to declare risky sexual contact.

Coinfection of HIV-syphilis was shown to affect disease course of HIV via increase in viral load and/or decrease in CD4+ T lymphocyte count (32,33). The coexistence of these two highly contagious diseases was investigated in several studies in public health literature (34). In our study, 17.9% of our patients were stage-3 patients (CD4+ T lymphocyte counts ≤200) and the syphilis-positivity rate was 33.3% which was statistically significant compared to patients at stage-1 and stage-2 ($p=0.018$). Classification of patients in terms of viral load revealed that 54% of patients had a high viral load (HIV-RNA >100,000 copy/mL). The syphilis-positivity rate was found 27.6% in this situation, in which contamination risk is highest, and is found statistically significant ($p<0.01$).

The existence of uveitis in patients with secondary syphilis and the dominancy of patients in latent period were in accordance with the findings in the literature which might be due to the variable clinical features in HIV-syphilis coinfection.

Study Limitations

The only limitations of this study are that it is a single-centre study. Not all patients were evaluated in terms of other sexually transmitted diseases at the time of diagnosis. Despite the limitations, the study will contribute to the literature by demonstrating the rise of syphilis seroprevalence in newly diagnosed HIV-positive patients in recent years.

Conclusion

According to the HIV/AIDS patient profile in Turkey, sexual contact seems to be the main transmission route. The possibility of HIV-syphilis coinfection should be kept in mind because of sharing the same transmission route. Therefore, screening tests for syphilis should be considered in the routine follow-up procedures of patients with suspicious clinical findings and risky behavior and the evaluation of newly diagnosed naive HIV patients.

Authorship Contributions

Concept: H.O.O., Design: H.O.O., I.B., S.T., Data Collection or Processing: I.B., Analysis or Interpretation: H.O.O., I.B., Literature Search: H.O.O., S.T., I.B., Writing: H.O.O., I.B.,

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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