

SEROPREVALENCE AND RISK FACTORS OF SYPHILIS AMONG HIV/AIDS PATIENTS IN ISTANBUL, TURKEY

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SUMMARY

Objective: Data on syphilis seroprevalence among human immunodeficiency virus (HIV)/Acquired immunodeficiency syndrome (AIDS) patients are unavailable in Turkey although they have common transmission routes. Our study is oriented towards the assessment of the seroprevalence of syphilis and the related risk factors in the HIV/AIDS patients followed in our outpatient clinic.

Materials: Newly diagnosed HIV/AIDS cases (n = 308) who attended our outpatient clinic between January 2006 and April 2013 were included in the study. Patient characteristics, medical history, physical examination findings, CD4⁺ T lymphocyte count, HIV RNA level, rapid plasma reagent (RPR) and *Treponema pallidum* hemagglutination (TPHA) test results were analyzed retrospectively. TPHA positivity was considered indicative of syphilis-causing *T. pallidum* exposure.

Results: HIV infection was transmitted through heterosexual (n = 176) or homosexual (n = 131) contact (266 male, 86.3%; age 38.3 ± 11.7 years; CD4⁺ T lymphocyte count, 330.6 ± 15.17/mm³). 50.7% of the patients attained only primary education. Out of the 245 cases, who were asked about the number of their sexual partners, 40 patients (26 women) lived in a monogamous relationship. Condom usage was not practiced (57.2%) or was only occasional (34.4% – particularly with their legal spouses and for contraception). Physical exam revealed no signs of syphilis or other STIs. TPHA (+/- RPR) positivity was determined in 40 patients (12.9%), indicating *T. pallidum* exposure. All patients with positive syphilis serology were male (p = 0.0026). *T. pallidum* exposure was determined in 21.3% of homosexual and 6.8% of heterosexual cases (p = 0.0003).

Conclusion: Since sexual contact is the most common route of transmission for both infections, syphilis seroprevalence was relatively high in our HIV/AIDS patients. Male and homosexual HIV/AIDS patients constituted a group at the highest risk for syphilis.

Key words: syphilis, HIV, epidemiology, Turkey, seroprevalence

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INTRODUCTION

Sexually transmitted infections (STI) cause serious public health problems in many parts of the world. Syphilis is an STI caused by *Treponema pallidum*. Unprotected sexual contact, blood transfusion, vertical transmission from mother to baby are the main transmission routes for syphilis and human immunodeficiency virus (HIV) infections (1). The relationship between HIV and syphilis has not been clearly identified despite 30 years of clinical experience (2). HIV/AIDS patients with early-stage syphilis have greater HIV transmission risk due to the presence of genital/oral ulcers, decreased CD4⁺ T lymphocyte count and increased viral load. On the other hand, impaired cellular and humoral immunity in HIV infection lowers host defense against *T. pallidum*, leading to changes in the natural course and clinic progression of syphilis, shortened incubation time, and increased number and infectiousness of syphilis lesions (3, 4). Therefore, international guidelines recommend periodic serological testing of syphilis in all HIV-infected patients (5, 6). The first case of HIV/AIDS in Turkey was reported in 1985. The current number of HIV-infected cases in Turkey is 6,188 according to the surveillance conducted by the Turkish Ministry of Health from October 1985 to December 2012 (7). In a recent study of antiretroviral

naive HIV-1 infected patients, sexual contact was predominantly reported as an infection transmission route – heterosexual contact in 64% and homosexual contact in 32% of cases (8). An increase in the number of HIV/AIDS patients as a sexually active group has been observed in Turkey, which might have led to an increase in the number of syphilis cases. In Turkey, various investigations on potential risk groups revealed syphilis seroprevalence as 0.11% among blood donors, 4.4–9.1% among sex workers, and 14% among homosexual men (9–12). Even though they share transmission routes, there are no data on syphilis seroprevalence of HIV/AIDS cases in Turkey. This study intends to determine the seroprevalence of syphilis and investigate the related risk factors among HIV/AIDS patients followed in our outpatient clinic.

MATERIALS AND METHODS

All HIV/AIDS patients newly-diagnosed by Western Blot verification test (HIV BLOT 2.2, MP Biomedicals Asia Pacific, Singapore) who visited our clinic (n = 308) during the period from January 2006 to April 2013 were included in the study. Patients' files containing records on age, gender, education level, marital status, probable transmission route of HIV infection, number of

sexual partners, condom usage, history of STIs and STI treatments, physical exam, CD4⁺ T lymphocyte count, HIV RNA levels, rapid plasma reagent (RPR), and *Treponema pallidum* hemagglutination test (TPHA) results were analyzed.

As a part of the physical examination, routine evaluation for STIs was performed by infectious disease and clinical microbiology specialists and consultation with dermatology, gynecology, and urology specialists, when necessary. CD4⁺ T lymphocyte count was determined using standard flow cytometry (FACScalibur, Becton Dickinson, New Jersey, USA). HIV RNA level was measured by PCR (COBAS Ampliprep/COBAS TaqMan HIV-1 Test, Roche Molecular Systems, USA). Serum RPR (Spinreact, Spain) and TPHA (Spinreact, Spain) tests were used together for the syphilis screening. TPHA positivity (with positive or negative RPR) was considered indicative of exposure to the syphilis-causing agent *T. pallidum*.

Graphpad Prism 5.01 (GraphPad Software, Inc, CA, USA) was used for the statistical analysis and graphical drawings of the study. Plasma CD4 and HIV RNA levels were shown as mean \pm SEM. Plasma CD4 and HIV RNA levels were compared between groups using unpaired t test. Fisher's exact Chi-square test was used for the comparison of the groups by gender, Yates-corrected Chi-square for the comparison of the transmission route of HIV infection, and Chi-square for the comparison of all other non-parametric variables (condom usage, number of partners, marital status, education level and age). The level of significance was set at $p < 0.01$ for Fisher's exact Chi-square test and $p < 0.001$ for Yates-corrected Chi-square test.

RESULTS

All cases ($n = 308$) included in the analysis were infected with HIV-1. Mean age was 38.3 ± 11.7 and 266 (86.3%) were male. Mean CD4⁺ T lymphocyte count was $330.6 \pm 15.1/\text{mm}^3$ during the first visit. Probable transmission route of HIV infection was heterosexual contact in 176 patients (57.1%) and homosexual contact in 131 patients (42.5%). Only one female patient was thought to have contracted HIV infection through intravenous substance use. None of the cases showed any signs of syphilis or other STIs during the physical examination. Six patients had a history of syphilis infection, while 4 patients had a history of gonorrhea, and all 10 patients were treated for their infections. Five of the patients with a history of syphilis were treated with benzathine penicillin G, and the other patient was administered doxycycline due to known allergy to penicillin. The statistical relationship between syphilis seropositivity and age, gender, education level, marital status, transmission of HIV infection, number of sexual partners, condom usage, CD4⁺ T lymphocyte count, and HIV RNA levels was investigated and presented in Table 1.

Forty patients (12.9%) in total were considered to have been exposed to *T. pallidum*, 26 of whom were RPR and TPHA positive, and 14 were RPR negative but TPHA positive. RPR positivity was found in 1:2 titer in seven patients, 1:4 titer in 16 patients, and 1:8 titer in three patients. Of 14 patients with negative RPR and positive TPHA, 6 were previously treated for syphilis.

All patients with positive syphilis serology were male ($p = 0.0026$). Just 21 (8.4%) out of 250 patients were using condom routinely. Twenty eight of 131 homosexual patients (21.4%)

and 12 of 176 heterosexual patients (6.8%) were exposed to *T. pallidum* ($p = 0.0003$).

DISCUSSION

RPR and TPHA are complementary tests used together to screen such risk groups as sex workers, and yield the most accurate result in defining all the stages of syphilis (13–15). Results from our study indicate that 12.9% of HIV/AIDS patients have been exposed to *T. pallidum*. Syphilis seroprevalence in newly diagnosed HIV infected individuals was reported as 19.6% in China, 5.3% in Iran, 4.6–6.2% in Holland, 7% in men and 13% in women in USA (16–19). Although our results are in accordance with the foregoing studies, social, cultural and economic differences between countries may affect the frequency of STIs. In terms of education, half of our HIV infected patients (50.7%) were primary school graduates, although no significant relationship was found between education and syphilis seroprevalence. In terms of marital status, more than half of our patients were married. Eleven of the widowed patients had lost their spouse because of HIV infection. Ten of these patients were monogamous women infected by their spouses. This is the result of multiple partnerships of husbands of monogamous Turkish women. Eighty seven percent of our cases had multiple sexual partners. Although syphilis seroprevalence was increasing with increasing number of sexual partners, the relationship was not statistically significant.

Sexually transmitted disease report from the Centers for Disease Control and Prevention (USA) for the year 2011 indicates that syphilis prevalence is increasing among homosexual and bisexual men (20). The reasons for increase in syphilis prevalence among HIV infected homosexual men are stated as multiple sexual partners, poor condom usage, finding HIV infected sexual partners on the Internet and common use of psychostimulants and drugs that improve sexual performance (21, 22). In addition, prevalence of syphilis is increased among homosexual men due to a common belief that oral sex is "safer" regarding transmission of HIV infection, while syphilis may be transmitted through oral ulcer lesions (23, 24). Similar arguments are valid for statistically significantly higher syphilis seroprevalence among homosexual men compared to heterosexual men in our study. It is also noteworthy that in this study all syphilis seropositive patients were male. This male dominance is thought to be related to the high percentage of homosexual men ($n = 28$, 70%) among the 40 men detected as syphilis seropositive. Male patients having multiple partners (unregistered sex workers and foreign partners) further contributed to this gender bias.

Routine and correct use of latex condom is fairly effective for protection against HIV, syphilis and other STIs (25). However, the frequency of patients indicating routine condom use was low (8.4%) and routine condom use was adopted mostly after being infected with HIV. In fact, almost none of our patients practice routine condom use, and prefer condom use only with their legal spouse and for the purpose of contraception, which may account for not detecting a significant association between syphilis seroprevalence and condom usage. In studies of the syphilis effect on CD4⁺ T lymphocyte count and HIV RNA levels, syphilis was determined to cause a transient increase in viral load and decrease in CD4⁺ T lymphocyte count, which improved after treatment,

Table 1. Demographic characteristics and laboratory findings of the patients (n = 308) according to syphilis seropositivity

	TPHA (+) n (%)	TPHA (-) n(%)	p
Gender			
Female	0	42	0.0026*
Male	40	226	
Age			
20–40	23	168	0.74
41–60	16	91	
≥ 61	1	9	
Education			
Illiterate	2	4	0.37
Primary school	15	120	
Secondary or high school	9	78	
College	7	43	
Marital status			
Married	19	145	0.73
Single	16	94	
Widowed	5	29	
Transmission of HIV infection			
Heterosexual intercourse	12 (6.8%)	164 (93.2%)	0.0003**
Homosexual intercourse	28 (21.4%)	103 (78.6%)	
Number of sexual partners			
1	1	39	0.09
2–10	30	146	
11–20	2	18	
≥ 20	2	7	
Condom usage			
No	17	126	0.94
Yes	3	18	
Occasional	11	75	
CD4 ⁺ T lymphocyte count (/mm ³)	323.9 ± 31.7	335.5 ± 16.2	0.79
HIV RNA level (copy/ml)	909100 ± 378100	905700 ± 253200	0.99

*Fisher's exact test, $p < 0.01$; **Yates-corrected Chi-square test, $p < 0.001$.
Data are given as number of patients (n).

similar to the effects observed in other acute infections (26, 27). In our study, no difference was detected in terms of CD4⁺ T lymphocyte count and HIV RNA levels in syphilis seropositive and seronegative patients, which could be explained by the absence of early stage syphilis in our patient population.

In conclusion, transmission route of HIV infection was either heterosexual or homosexual contact, in accordance with the HIV/AIDS patient's profile in Turkey. Since the main mode of transmission was sexual, syphilis seroprevalence was high in our patient group. Male and homosexual HIV/AIDS patients were determined as a group at highest risk of syphilis. Following syphilis serology in all HIV infected cases is critically important for early stage recognition and treatment, and hence to lessen the likelihood of further transmission of either infection.

Conflict of Interests

None declared

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