

## Sexually Transmitted Diseases among Patients with Human Immunodeficiency Virus in Northern Israel

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### Abstract

**Background:** The co-morbidity of human immunodeficiency virus and other sexually transmitted diseases in Israel has not been established.

**Objectives:** To compare the prevalence of STDs among HIV-positive patients to HIV-negative patients visiting an STD clinic in northern Israel.

**Methods:** Between December 2000 and December 2001, 176 HIV-positive individuals (53% males) were screened and compared to 200 HIV-seronegative individuals (76% males). Demographics, symptomatology and risk factors were obtained via questionnaire. First-void urine samples were tested for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Serum was tested for type-specific herpes simplex virus-2, hepatitis B and syphilis.

**Results:** Relative to the seronegative STD patients, HIV-positive patients exhibited significantly greater risk-reducing sexual behaviors such as consistent condom use [29/86 (33.7%) vs. 16/187 (8.6%),  $P < 0.001$ ], and abstinence in the previous 6 months [43/125 (34%) vs. 7/185 (3.8%),  $P < 0.001$ ]. Nevertheless, STD prevalence was higher among HIV-positive than HIV-negative patients (79.5% vs. 37.5%,  $P < 0.001$ ). HSV-2, syphilis and HBV were more common among HIV-positive than HIV-negative patients [120/175 (68.8%) vs. 18/200 (9%),  $P < 0.001$ ], [43/161 (26.7%) vs. 0%,  $P < 0.001$ ], [13/171 (7.6%) vs. 3/200 (1.5%),  $P < 0.01$ ], respectively. In contrast, Chlamydia and gonorrhea were more common in HIV-negative patients than HIV-positive patients [3/176 (1.7%) vs. 13/200 (6.5%),  $P < 0.05$ ] vs. [0% vs. 5/200 (2.5%),  $P < 0.05$ ], respectively.

**Conclusion:** Despite the low risk sexual behavior of Israeli HIV patients, they had a high prevalence of chronic STDs (e.g., HSV-2, HBV and syphilis). The lower prevalence of Chlamydia and gonorrhea among HIV-immunosuppressed patients may be attributed to routine antibiotic prophylaxis against opportunistic infections. Nevertheless, as advocated by international health organizations, it appears prudent to recommend the routine screening of these asymptomatic HIV-positive patients for STD pathogens.

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Sexually transmitted diseases and human immunodeficiency virus facilitate the sexual transmission of one another and this inter-relationship is commonly referred to as epidemiologic synergy [1-3]. STDs appear to increase the risk for both acquisition and transmission of HIV, and acute HIV infection is more frequent in individuals with an active STD [3]. Herpes simplex virus-2, for example, is regarded as a significant risk factor for the acquisition of HIV and is emerging as a cornerstone for HIV prevention programs [1-4]. The impact of HIV infection on other STDs is not as well established, although there is some evidence that concurrent HIV infection may adversely affect the natural history, clinical manifestations and response to treatment [2,4]. For example, Musher et al. [5] found that among HIV patients, neurosyphilis was more common than among HIV-seronegative patients. Moreover, skin lesions and VDRL antibody in HIV-infected patients with secondary syphilis appeared to respond more slowly to penicillin treatment [5]. HIV infection also impacts on HSV-2 [1-5]. HSV-2 infection in HIV-infected patients is frequently more severe, prolonged and less responsive to first-line antiviral treatments than in HIV-seronegative individuals [2,5]. While the findings noted above relate to epidemiologic synergy among individuals with ulcerative lesions, there is also substantial scientific evidence that such synergy is also prevalent among individuals with non-ulcerative lesions [2].

Several mechanisms may be involved, including increased susceptibility with the disruption of mucosal integrity in the former, increased inflammation and higher level of HIV cellular targets in the latter, as well as increased levels of HIV virus present in the genital tract in the presence of other STDs [2,3]. Understandably, in the case of the HIV-infected patient, the level of immunosuppression will impact on the acquisition and persistence of other STDs and degree of HIV shedding [2].

Although researchers have referred to such epidemiologic synergy as "lethal" [3], little is known about the co-morbidity of HIV and other STDs in Israel. As of June 2004 there are an estimated 4300 HIV-infected carriers residing in Israel [6], yet no data exist regarding the prevalence of STDs among HIV-positive patients, and no study has examined whether STDs are any more prevalent among HIV-positive patients than those seronegative patients with genitourinary symptoms. Although one might anticipate a higher rate of STD infection among HIV-seropositive patients

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STD = sexually transmitted diseases

HIV = human immunodeficiency virus

HSV = herpes simplex virus

HBV = hepatitis B virus

than among members of the general, seronegative population, a higher rate of infection among HIV-positive patients is not as certain when compared to seronegative patients complaining of genitourinary symptoms. Although the public health benefits of screening HIV-positive patients for STDs are widely recognized [2,3,7], a significantly higher rate of STD infection among HIV-seropositive relative to seronegative but symptomatic patients would suggest the increased urgency of such screening. Consequently, in the present study, we sought to provide some initial estimates regarding the rate of co-morbidity between HIV and other STDs in Israel, as well as to examine whether STD prevalence rates are any higher for HIV-seropositive patients than for seronegative patients with genitourinary symptoms.

## Patients and Methods

### Study setting

The Bnai Zion Medical Center STD Clinic provides care to approximately 350 patients per year from the metropolitan Haifa area and northern Israel. From December 2000 through December 2001, 176 seropositive HIV individuals (53% males and 47% females) were screened and compared with 200 HIV-seronegative individuals (76% males and 24% females). The HIV-seropositive patients were recruited from Rambam Medical Center's Allergy and AIDS Institute in Haifa, Israel.

The average age of the HIV-positive patients was 36.11 years ( $\pm 12.21$ ) and 34.59 years ( $\pm 11.18$ ) for the HIV-negative group. The HIV-positive sample population consisted of Ethiopian Jews [79% (138/176)], non-Ethiopian Jews [18.2% (32/176)] and Arabs [3.4% (6/176)]. The HIV-seronegative patients included non-Ethiopian Jews [73.1% (144/197)], Arabs [19.4% (39/197)] and foreigners [7.1% (14/197)].

### Questionnaires

All study participants were informed by a physician-interviewer that their participation in the study was completely voluntary and that all data would be kept strictly confidential. Study participants completed a self-administered questionnaire that included items relating to demographic background. They were then interviewed by the physician regarding the presence and duration of genitourinary signs and symptoms, other potential risk factors for the acquisition of STDs, and antibiotic use. Specifically, among the immunosuppressed individuals, the prophylactic treatments against opportunistic infections were recorded. Data were collected from those participants deemed to have potential language difficulties, based entirely on a physician interview conducted with the help of a translator.

### Laboratory investigation

HIV and HBV were tested using Axysym (Abbott, USA). First-void morning urine samples were tested for the detection of *C. trachomatis* and *N. gonorrhoeae* using AmpliCor polymerase chain reaction (Roche, USA). Serum was tested for type-specific HSV-2 antibodies using HerpeSelect R 2, enzyme-linked immunosorbent assay immunoglobulin G. Syphilis was tested with RPR (Becton Dickenson, USA) and TPHA (Biokit, Gamidor, Israel).

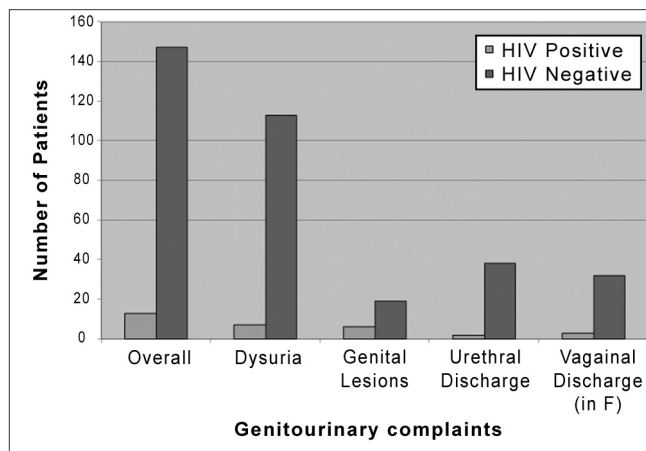


Figure 1. Genitourinary symptoms among symptomatic HIV-positive and HIV-negative patients

### Statistical analysis

Analysis for testing the associations between the categorical groups was performed using Fisher's exact test, when appropriate.

## Results

### Genital complaints and sexual behavior

Overall, genital complaints such as dysuria, genital lesions, and urethral/vaginal discharge were more common in the HIV-negative group than in the HIV-positive group [147/171 (85.9%) vs. (13/176 (7.3%) respectively,  $P < 0.001$ ] [Figure 1].

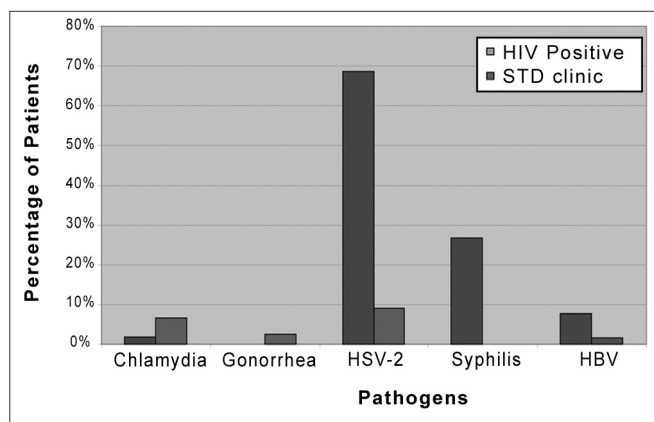
HIV-negative patients exhibited more high risk sexual behavior when compared with the HIV-positive patients. There was less consistent condom use [16/187 (8.6%) vs. 29/86 (33.7%),  $P < 0.001$ ] and less abstinence in the previous 6 months [7/185 (3.8%) vs. 43/125 (34%),  $P < 0.001$ ], respectively. There was no significant difference in sexual orientation (i.e., homosexuality) between the two groups [3/167 (1.8%) vs. 1/189,  $P = 0.5$ ].

### Pathogens

Overall, STD prevalence was higher among asymptomatic HIV-positive than symptomatic HIV-negative patients (79.5% vs. 37.5%,  $P < 0.001$ ). Moreover, HIV-seropositive patients were found to have multiple pathogens more commonly than the HIV-negative patients. Specifically, HSV-2, syphilis, and HBV were more common in the HIV-positive patients than in the HIV-negative patients [18/200 (9%) vs. 120/175 (68.8%),  $P < 0.001$ ], [43/161 (26.7%) vs. 0%,  $P < 0.001$ ] and [13/171 (7.6%) vs. 3/200 (1.5%),  $P < 0.01$ ], respectively. In contrast, Chlamydia and gonorrhea were more common in the HIV-negative than HIV-positive patients [13/200 (6.5%) vs. 3/176 (1.7%),  $P < 0.05$ ], [5/200 (2.5%) vs. 0%,  $P < 0.05$ ] respectively [Figure 2].

## Discussion

The results of our study demonstrate that the prevalence and clinical course of STDs are influenced by co-infection with HIV. Despite low risk sexual behavior (i.e., greater condom use and abstinence), Israeli HIV-seropositive patients had a greater preva-



**Figure 2.** Prevalence of STD pathogens among HIV-positive and HIV-negative patients

lence of STDs than high risk seronegative patients. Moreover, although 79.5% of seropositive patients were found to be infected with an STD, only 7.3% had genitourinary complaints. In this sense, our findings reinforce the importance of routinely screening HIV patients for STDs, regardless of the presence or absence of urogenital symptoms [8].

With regard to the clinical course of STD infection, our findings indicate that while symptomatic seronegative patients tested positive for more acute pathogens (i.e., *Neisseria gonorrhoeae* and *Chlamydia trachomatis*), HIV-infected individuals were found to be infected with more chronic STDs such as syphilis, herpes simplex virus-2 and hepatitis B. The relatively low rate of gonorrhoea and Chlamydia infection among HIV-positive individuals may stem from the fact that routine prophylaxis administration of antibiotics like respirim, aimed at preventing opportunistic infection, also guards such individuals against such acute STD infections. Still, it should be noted that the interpretation of syphilis serologic testing harbors some inherent pitfalls in our HIV-positive Ethiopian population: in early HIV infection, one may obtain a false-positive non-treponemal test. In addition, other spirochetal illnesses such as yaws, which occurs among rural populations in Africa, may yield positive non-treponemal and treponemal syphilis tests [9]. Moreover, one cannot ascertain the time of infection when interpreting positive serology for HSV-2. Consequently, we were unable to determine whether a particular HSV infection preceded HIV acquisition, whether HIV infection preceded HSV infection, or whether the two were acquired contemporaneously. In the future, researchers may wish to adopt a longitudinal, cohort design in order to more accurately determine the causal nature of such epidemiologic synergy between HIV and HSV.

#### Study limitations

Other limitations of this study should also be noted. First, the two groups examined in this study were different from one another in terms of sociodemographic characteristics with no Ethiopians in the seronegative sub-sample (thus making it impossible to control for ethnicity). Consequently, it is possible that some of the differences identified between these groups with regard to STD prevalence may stem from cultural and demo-

graphic factors rather than from differences relating to HIV status. In the future, researchers should attempt to either collect data from more demographically matched sub-samples or control for such demographic differences in their analyses. Second, although participants were informed that their participation was voluntary and that all data would be kept strictly confidential, it is possible that, given the highly personal nature of the questions, respondents may have under-reported promiscuity and other typically stigmatized sexual behaviors. Such under-reporting may have been particularly pronounced among Ethiopian subjects due to unique cultural norms and values. In the future, researchers may want to assess and then control for social desirability in their analyses of such matters [10].

#### Study implications

Although our study was not designed to compare STD prevalence between patients with different subtypes of the HIV virus or between African immigrants and native Israelis, our findings nevertheless suggest the need for research examining the possible role of HIV clade as a moderator of such epidemiologic synergy. Specifically, while our findings found a high rate of STD prevalence among HIV-positive individuals, most of the HIV+ individuals in our sample were Ethiopian. Given the fact that HIV-positive Ethiopians tend to be infected with HIV subtype C, whereas most Palestinian Arabs and non-Ethiopian Jews are infected with subtype B [11], it is possible that our findings are applicable only to the former, with STD prevalence rates for non-Ethiopian HIV-positive individuals being more similar to those of seronegative individuals. Although studies indicate that subtype C is a more infectious strain of HIV than subtype B [3], we are unaware of any research examining the degree to which strain type is associated with increased susceptibility to other STDs. While the size and ethnic composition of our current sample preclude such an analysis, we believe this to be an important issue to be addressed in future research.

Finally, the epidemiologic synergy between HIV infection and other STDs has significant public health implications. Treatment of STDs among HIV-infected individuals, for example, has been shown to reduce genital tract HIV levels, a variable so central in the infectiousness of HIV [2,3]. In a STD clinic in Malawi, a single injection of ceftriaxone for presumptive gonorrhoea in 86 men with urethritis resulted in a median seminal HIV RNA concentration decrease from approximately 120,000 to 40,000 copies/ml over a period of 3 weeks [12]. Importantly, no change occurred in plasma viral load. In Mwanza, Tanzania, a trial of improved clinic-based treatment of symptomatic STDs to reduce HIV incidence was conducted in six healthcare clinics in rural communities. Multiple interventions were implemented, including staff training, the provision of a regular supply of medications, a reference laboratory and more. After 24 months, there was a 38% reduction in HIV incidence in the intervention communities compared with the control communities [13]. Taken in concert with our research findings, these examples clearly illustrate how STD detection and treatment can and should become an essential component of the treatment for HIV.

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