ORIGINAL RESEARCH ARTICLE

Assessing sexually transmitted infections in a cohort of women living with HIV/AIDS, in Rio de Janeiro, Brazil

Beatriz Grinsztejn MD PhD1, Francisco Inácio Bastos MD PhD2, Valdílea G Veloso MD MSc1, Ruth Khalili Friedman MD1, José Henrique Pilotto MD1, Mauro Schechter MD PhD3, Monica Derrico BSc1, Angela Andrade MD1, Maria Cristina Lourenço MSc1, Ronaldo Ismério Moreira BSc MSc1, Fabio Russomano MD PhD4, Mariza Morgado PhD5 and Judith S Currier MD MSc6

1Evandro Chagas Clinical Research Institute/FIOCRUZ; 2Center of Scientific and Tecnological Information/FIOCRUZ; 3Federal University of Rio de Janeiro; 4Fernandes Figueira Institute/FIOCRUZ; 5Oswaldo Cruz Institute/FIOCRUZ, Rio de Janeiro, Brazil; 6Center for Clinical AIDS Research and Education/UCLA, Los Angeles, California, USA

Summary: A cohort of 458 HIV-positive women under antiretroviral therapy has been followed at a reference hospital in Rio de Janeiro, Brazil. Most of them belong to impoverished social strata. Patients were screened for sexually transmitted infections (STIs) and gynaecologic conditions. Some STIs were found to be uncommon (e.g. chlamydial and gonococcal infections), while some conditions (bacterial vaginosis) and STIs, e.g. hepatitis B and human papilloma virus (HPV) infection, were found to be quite prevalent. The latter is of special concern, due to the high prevalence of HIV/HPV co-infection (~51%) and its association with severe immunodeficiency, in a context of unacceptable high levels of uterine cancer and uneven gynaecological care. HIV-positive women are in need of comprehensive health services, including high-quality, regular, gynaecologic care in order to diagnose and treat lower genital tract infections and prevent the evolution of HPV-related lesions. Reproductive counselling should be a part of this approach.

Keywords: HIV/AIDS, sexually transmitted infections (STIs), human papilloma virus (HPV), co-infection, Brazil

Introduction

Globally, almost 50% of the adults living with HIV/AIDS are women, and this proportion is on the rise. The impact of HIV/AIDS is growing among the poorest, disenfranchized and youngest, with women over-represented in these population groups.

By June 2004, 113,314 female AIDS cases had been reported to the Brazilian Ministry of Health (BMoH). Between 1994 and 1998, the number of female AIDS cases increased by 75.3% compared with a 10.2% increase among men.

HIV infection is mostly acquired through sexual transmission, and HIV-infected women are also at risk of other sexually transmitted infections (STIs). HIV and other STIs (particularly ulcerative STIs) demonstrate clinical and epidemiological synergy, facilitating transmission/acquisition and changing the clinical course of infection and disease. Among HIV-infected women, gynaecological manifestations may appear early in the course of infection, and prevalence and incidence of these may be higher in this population.

A cohort was established at the Evandro Chagas Clinical Research Institute (IPEC), Fiocruz, Rio de Janeiro, aiming to characterize the natural history of HIV infection among women. We describe the sociodemographic characteristics of this cohort and the main findings regarding STIs are diagnosed at baseline.

Methods

Study population and procedures

The IPEC-Fiocruz HIV-infected female cohort is an open cohort established in 1996. Eligibility criteria include documented HIV-status and provision of
written informed consent. The study was reviewed and approved by the institution ethics review board. All diagnosed STIs were treated according to BMoH guidelines.

Clinical assessment and specimen collection

Study visits occurred every six months. Interviews using structured questionnaires collect information on medical and psychosocial history, antiretroviral therapy and chemoprophylaxis use, sexual and reproductive history, and use of alcohol and illicit drugs.

Clinical and laboratory assessment included collection of urine samples and a pelvic examination with specimen collection. Chart review was also performed.

Laboratory and data analysis

Trichomonal infection was defined by the presence of trichomonads on wet mount and vulvovaginal candidiasis by a positive culture for candida species plus at least one symptom suggestive of vaginitis (pruritus, vaginal discharge). Microscopy for hyphae was also performed.

Herpes simplex genital ulcers were presumptively diagnosed by their clinical presentation. Bacterial vaginosis was diagnosed using Nugent’s scoring system.

Human papilloma virus (HPV) deoxyribonucleic acid (DNA) detection was performed using the Hybrid Capture II (Digene Inc.) with probes for high- and low-risk types.

Diagnoses of Neisseria gonorrhoeae and Chlamydia trachomatis were performed using urine testing with ligase chain reaction (LCR-ABBOTT).

Venerale Diseases Research Laboratory (VDRL) serologies were performed on sera; if positive, results were confirmed by the fluorescent treponema antibody absorption test (FTA-ABS) or micro-haemagglutination TP (MHA-TP).

Serum samples were also tested for HBSag, anti-HBc and anti-HBs. Past hepatitis B virus (HBV) infection was defined by the presence of anti-HBc or anti-HBs, and current infection by the presence of HBSag.

CD4 lymphocyte (Becton Dickinson FACScan) counts were taken from medical charts.

Statistical analyses used χ² or Fisher’s exact tests for dichotomous variables: Mantel-Haenszel χ²-test for trend for categorical variables with more than two categories and Kruskal-Wallis test for means (χ² approximation) for continuous variables.

Results

A total of 458 women were enrolled in the cohort from May 1996 to March 2004; 52 (11.4%) deaths have occurred. Demographics are presented in Table 1.

HIV infection was acquired through sexual transmission for 72.5% of the women; five (1.1%) reported injection drug use and 17 (3.7%) were infected through the receipt of blood.

Age at first sexual intercourse was under the age of 16 years among 39%; the number of lifetime partners was less than three for 41% of the women. Among 261 (57.0%) women who were sexually active in the last year, the median number of partners was one for 84%. Condom use during the last sexual intercourse was reported by 58.2% (152/261). A contraceptive method other than condom or tubal ligation was reported by 25 (9.6%) women; among 43 (16.5%) who underwent tubal ligation, 13 (30.2%) reported no condom use in the last sexual intercourse (Table 2).

The majority (87%) of women had had at least one full-term pregnancy and 62 (13.5%) have had one HIV-infected child. Roughly half of the women reported having had an HIV-infected partner, and 96 (41%) of these had died from AIDS.

Only 50.8% of the women reported support from family or friends. A history of recreational drug use was reported by 37.6%; snorted cocaine and marijuana were reported by 36.6% and 33.7%, respectively.

Domestic violence was reported by 40.7% and a history of sexual abuse by 30.2%.

The median time elapsed from the last pelvic exam to the baseline interview was 16 months (SD 30.1); this was 24 months among those with advanced immunosupression (CD4 <200 cells/mm³); while 23 women (5.0%) reported having had a hysterectomy (Table 3).
A history of STI was reported by 220 women (48.0%), with 128 patients (27.9%) reporting a history of herpes, 86 (18.8%) a history of HPV lesions, 58 (12.7%) a history of syphilis, and 19 (4.1%) a history of gonorrhoea.

Vaginal discharge, vulvovaginal itching, and malodorous smell were reported by 55.5, 37.0, and 18.9% of the patients, respectively.

Among the 235 women who reported of never having had an STI, 23% were actually diagnosed as having at least one of the following: trichomoniasis, genital warts, N. gonorrhoeae or C. trachomatis infection, herpes, or syphilis. Vulvovaginal candidiasis was diagnosed in 108 women (23.5%).

Positive potassium hydroxide microscopy for hyphae was found in 27.7%. Severity of CD4 depletion was not associated with higher prevalence rates for fungal hyphae.

Trichomonal vaginitis was detected in 32 (7.0%) women. Bacterial vaginosis (Nugent score ≥ 7) was diagnosed in 85 women (18.6%). None of these conditions were found to be associated with CD4 counts.

Seroological reactivity to non-treponemal and treponemal syphilis tests was relatively common (13.5%). Prevalence of syphilis fell with declining CD4 cell counts, from 17.3% in >500 cells/mm³ strata to 7.5% among women with advanced immunodeficiency (CD4 <200 cells/mm³) (P = 0.02).
Antibodies to hepatitis B were found in 18.8% of the women, and 1.8% had current HBV infection. Genital warts were observed in 11.1% of the women (51/458). Prevalences for N. gonorrhoeae and C. trachomatis infections were low: 0.9% (4/458) and 2.2% (12/400), respectively. Overall prevalence of HPV DNA was 50.7% (229/452), being 94% (215/229) of them infected with a high-risk HPV and 30% (69/229) having both high- and low-risk HPV subtypes. A statistically significant association between HPV infection and severe immunodeficiency was found ($P = 0.016$) (Table 4).

**Discussion**

Women are biologically, socially and economically vulnerable to HIV/AIDS. Although Brazil has implemented a comprehensive set of preventive strategies targeting different populations, the rates of new infections among women are on the rise, especially among the poor. The present study assessed a population with very low levels of schooling and family income.

As in other studies carried out in different contexts, most of the women reported few lifetime

<table>
<thead>
<tr>
<th>Medical history and clinical data</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous pelvic exam (months)</td>
<td>447</td>
</tr>
<tr>
<td>More than 36 months</td>
<td>90 (19.7%)</td>
</tr>
<tr>
<td>More than 12 months</td>
<td>234 (51.1%)</td>
</tr>
<tr>
<td>Mean (DP)</td>
<td>28.17 (30.1)</td>
</tr>
<tr>
<td>Median</td>
<td>16.00</td>
</tr>
<tr>
<td>Current vaginal discharge</td>
<td>254 (55.5%)</td>
</tr>
<tr>
<td>Last CD4 count (cells/mm³)</td>
<td>451</td>
</tr>
<tr>
<td>&lt;200</td>
<td>139 (30.3%)</td>
</tr>
<tr>
<td>≥200</td>
<td>312 (68.1%)</td>
</tr>
<tr>
<td>Mean (DP)</td>
<td>367.55 (268.83)</td>
</tr>
<tr>
<td>Median</td>
<td>326</td>
</tr>
<tr>
<td>Self-reported history of STI</td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>220 (48.0%)</td>
</tr>
<tr>
<td>Herpes</td>
<td>128 (27.9%)</td>
</tr>
<tr>
<td>HPV</td>
<td>86 (18.8%)</td>
</tr>
<tr>
<td>Gonorrhoeae</td>
<td>19 (4.1%)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>58 (12.7%)</td>
</tr>
<tr>
<td>Use of antiretroviral therapy</td>
<td>309 (67.5%)</td>
</tr>
<tr>
<td>Type of antiretroviral combination</td>
<td></td>
</tr>
<tr>
<td>Dual nucleoside therapy</td>
<td>139 (45.0%)</td>
</tr>
<tr>
<td>HAART</td>
<td>170 (55.0%)</td>
</tr>
<tr>
<td>Use of PCP prophylaxis</td>
<td>259 (56.6%)</td>
</tr>
</tbody>
</table>

The cases not totaling 100% are due to non-response.

IPEC=Evandro Chagas Clinical Research Institute; FIOCRUZ=Fundação Oswaldo Cruz.
sexual partners. Physical and sexual abuse affect millions of girls and women worldwide, yet are known to be seriously under-reported. Domestic violence and sexual abuse represent a continuous risk that begins in childhood, contributing to a higher vulnerability to HIV infection during life.

About one-third of the women in our cohort reported a history of domestic violence and sexual abuse. Of note, these figures are similar to those reported among non-HIV-infected women worldwide.

We found a high proportion of women lacking social support. Lack of social support is associated with a high burden of suffering, anxiety and low quality of life among people suffering from chronic conditions. Almost half of the women reported having lost a partner with AIDS, and 62 reported having a child with AIDS, highlighting the burden faced by this population.

Illicit drug use was quite prevalent, indicating the pressing need to incorporate prevention strategies targeting drug- and alcohol-related risks and harms.

While the prevalence of lower genital tract signs and symptoms in our cohort were similar to the reported by Greenblatt et al., in the USA, we found an almost two-fold higher prevalence of women with vaginal discharge, compared with the women from that cohort. This may be related to the long interval between gynaecologic examinations reported by our study population. Regular consults may increase the opportunities for proper diagnosis and care. In our study population, patients showed a high level of acceptance of a comprehensive gynaecological evaluation. Therefore, the large interval between gynaecologic exams may be related to the paucity of services, combined with stigma and discrimination.

A history of STIs was common in our cohort, as reported in previous studies. Prevalence of STIs varies widely among studies conducted in different countries and populations, and using different methods of ascertainment. In our study, the prevalence of some genital tract infections was unexpectedly low. The fact that pelvic exam and STI screening tests were performed during scheduled appointments (rather than being symptom driven) may explain such findings. It may be also related to the age composition of our study population, since these infections are more common during adolescence and early adulthood. Data from the few Brazilian reports published show that chlamydial and gonococcal infections are relatively prevalent in Brazilian women attending either voluntary counselling and testing centres or family planning clinics.

Reduction of sexual risky behaviour, commonly observed among HIV-infected women, could also be related to the observed low STI prevalences, as well as advanced HIV infection, the use of antibiotics as prophylaxis or treatment for Pneumocystis carinii pneumonia and bacterial infections, coupled with loss of sexual partners.

Bacterial vaginosis and trichomoniasis prevalence in our cohort were comparable to the findings of international cohorts of HIV-infected women as well as to Brazilian women interviewed at family planning clinics. Such findings highlight the importance of comprehensive gynaecological care beyond classical assessment of STIs. Lower genital tract infections may facilitate HIV sexual acquisition and transmission. Proper management of reproductive tract infections may decrease HIV shedding and further HIV sexual transmission.

The prevalence of reactive syphilis serology was comparable to that observed by Cu-Uvin et al., in the USA and fell with declining CD4 cell counts, as previously reported. This trend may be related to a reduction in risky sexual behaviour, the effect of HIV disease progression and/or loss of sexual partners. In our study population, syphilis was significantly more prevalent than among HIV-negative Brazilian pregnant women (1.7%).

Ulcerative lesions suggestive of herpes were found in less than 3% of the women enrolled in our cohort, comparable to the prevalence (3.5%) observed by van Benthem et al., using the same diagnostic criteria. We found no ulcerative lesions among those women with CD4 cell counts higher than 500, and the occurrence of such lesions was found to be statistically associated with CD4 depletion.

HPV infection is relatively common among HIV-infected women, with prevalence rates reaching 95%, depending on the diagnostic technique and the study population. In this study, roughly half of the women had HPV infection, figures comparable to a former Brazilian study targeting HIV-infected women using the same diagnostic methodology and much higher than the 14% prevalence rates reported in studies of Brazilian women with unknown HIV serostatus. Incidence of cervical cancer remains unacceptably high in Brazil and diagnosis and treatment of HPV-associated lesions constitutes a top priority in the management and care of HIV-infected women.

A high prevalence of HBV infection was found in this cohort, as in other studies among HIV+ women conducted in the USA. Vaccination against hepatitis B is of utmost importance, since HBV co-infection has been associated with a poorer prognosis and a higher incidence of antiretroviral-related toxicities and liver disease is a leading cause of death among HIV+ individuals.

HIV-infected women are in need of comprehensive health services, including high-quality, regular, gynaecological care in order to adequately diagnose and treat lower genital tract infections and prevent progression of HPV-related lesions. Reproductive counselling should also be a part of this approach.

The IPEC cohort of women living with HIV/AIDS represents an invaluable resource to prospectively study HIV infection in impoverished Brazilian women, helping to reverse the current unfavourable picture.
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