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ORIGINAL ARTICLE

Lower Genital Tract Infections in HIV-Infected Women: Can We Afford to Miss?

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About the Author

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Abstract

Objectives To study prevalence of lower genital tract infections (LGTI) (bacterial vaginosis, trichomoniasis, and candidiasis) in HIV-seropositive women and correlation with CD4 counts and antiretroviral therapy (ART).

Methods Cross-sectional study conducted in 200 HIV-1-seropositive women (18 to 45 years) attending ART clinic of PGIMS, Rohtak. Vaginal samples sent for laboratory diagnosis of bacterial vaginosis, trichomoniasis, and candidiasis, CD4 count determined and data analyzed using Chi-square method.

Results Prevalence of bacterial vaginosis, candidiasis, and trichomoniasis was 47.7, 43.2, and 8.8 % respectively, 30 % women with CD4 counts <200 cells/μl had LGTI, and 17.4 % women with CD4 >200 Cell/μl had LGTI. Of 70 women not on ART, 18.6 % had LGTI and 30 of 130 on ART had LGTI.

Conclusions HIV-seropositive women had higher prevalence of LGTI especially at lower CD4 counts and women on ART did not have a lower prevalence of LGTI and should be screened for LGTI to decrease HIV transmission.

Keywords HIV · Bacterial vaginosis · Trichomoniasis · Candidiasis · CD4 · Antiretroviral therapy

Introduction

It is estimated that out of the 35.3 million adults living worldwide with HIV and AIDS, 39 % are women and 98 % of these women live in developing countries. India is the third largest country in terms of people living with HIV and AIDS and out of the total people infected with HIV in

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India, 39 % are women of reproductive age group. It has been proved by various studies that ulcerative lesions like syphilis, herpes, and chancroid cause increased HIV viral particle shedding and are associated with higher rates of HIV transmission and acquisition. Now it is being increasingly recognized that the non-ulcerative lower genitourinary infections (LGTI) like bacterial vaginosis, trichomoniasis, and candidiasis, which are prevalent all over the world, have a bidirectional interaction with HIV infection and are found more frequently in HIV-seropositive women. Being more prevalent in HIV-infected women, these LGTI lead to increased transmission of HIV infection (both heterosexual and vertical) and recurrence, reinfection, and persistence of LGTI. These effects are even more pronounced at lower CD4 cell counts. The effects of antiretroviral therapy (ART) on LGTI have been evaluated but to a limited extent. The present study was undertaken to assess the prevalence of LGTI (bacterial vaginosis, trichomoniasis, and candidiasis) among HIV-seropositive women of reproductive age group and their association with CD4 cell counts and ART.

Materials and Methods

The present study was a cross-sectional observational study conducted in 200 HIV-1-seropositive women in the age group of 18 to 45 years attending the ART clinic of Pt. BDS University of Health Sciences, Rohtak. Ethical approval was taken from the institutional ethical committee. Serologic reactivity to HIV-1 was determined by enzyme immunoassay (EIA) tests and positive results were confirmed by Western blot tests, using the standard techniques. Exclusion criteria were pregnancy, acute and chronic illness, lower genital tract malignancy, women on second line of ART, and women reporting use of antibiotics, steroids, and antifungals within the past 30 days.

After an informed consent, all women were interviewed regarding their disease history, treatment history, gynecologic history (vaginal discharge), and sexual history. Pelvic speculum examination was performed in all the women, and type of vaginal discharge if present was noted and vaginal sample was sent for laboratory diagnosis of LGTI. Trichomoniasis was diagnosed by the presence of trichomonads with characteristic motility on wet saline mount. The clinical diagnosis of bacterial vaginosis was made using Amsel criteria, if more than or three of the following objective criteria were present: abnormal vaginal discharge, vaginal pH > 4.5, presence of clue cells, and/or positive amine test with release of fishy odor on addition of 10 % KOH to vaginal secretions. Candidiasis was defined by curdy discharge on per speculum examination and culture positive for candida species when samples were aseptically cultivated on sabouraud's medium. Syndromic treatment was given to the patients with signs and symptoms of LGTI according to National AIDS Control Organization (NACO) guidelines. Blood samples were taken to determine the CD4 cell count using standard flow cytometric technique. At the end of the study, the data were collected and analyzed statistically using Chi-square method.

Results

The mean age of the HIV-seropositive women in the study was 31.0 ± 6.8 years. Ninety-two percent of HIV-seropositive women reported heterosexual mode of transmission, 6 % gave history of transmission by transfusion, and 2 % were ignorant of mode of transmission. Nearly 53 % of the women in the study belonged to WHO stage I, 29 % belonged to WHO stage II, 34 % to WHO stage III, and only 1 % were in stage IV disease. Out of 65 % women on ART, 25 % were taking ART for 3 years, followed by 23 % taking ART for less than 1 year while only 1 % were taking ART for more than 5 years. Sixty-six percent HIV-positive women (132 out of 200) had CD4 cell count more than 200 cells/μl while 34 % (68 out of 200) were more immunocompromised with CD4 cell count of less than 200 cells/μl.

Out of total 200 HIV-seropositive women, 44 had LGTI (22 %). The prevalence of bacterial vaginosis in the present study was 47.7 % (21/44), candidiasis was present in 43.2 % (19/44) of the HIV-seropositive women, and trichomoniasis accounted for 8.8 % (4/44) of the total LGTI (Table 1).

Thirty percent of women with CD4 count less than 200 cells/μl had LGTI, while only 17.4 % of HIV-seropositive women with CD4 count more than 200 cells/μl had LGTI ($p = 0.0348$). Thus CD4 count less than 200 cells/μl was significantly associated with LGTI (Table 2). In the present study, out of 70 seropositive women, not on ART, 13 (18.6 %) had LGTI. While out of the rest 130, who were on ART, 30 had LGTI. Out of these 30 HIV-seropositive women who were on ART and had LGTI, 21.3 % were on ART for less than a year, 19.15 were on ART for one to 2 years, 29.4 % were on ART for 2–3 years, and 29.2 % were on ART for more than 3 years ($p = 0.740$). Thus the present study did not find decrease in prevalence of LGTI in seropositive women who were on ART for any duration (Table 3).

Discussion

The non-ulcerative LGTI, including bacterial vaginosis, trichomoniasis, and candidiasis, are common among reproductive age women all over the world and can be

often asymptomatic. The prevalence of bacterial vaginosis, trichomoniasis, and candidiasis is estimated 8–23, 3.2, and 18 % respectively [1–3]. There is a complex interaction between HIV infection and LGTI. Many studies have shown increased prevalence, incidence, and severity of LGTI in HIV-seropositive women [4–7],while a few studies reported no differences in prevalence of LGTI in the HIV-infected and non-HIV-infected women of reproductive age group.

Bacterial Vaginosis and HIV

In the present study, the prevalence of bacterial vaginosis was 47.7 % in the HIV-seropositive women which is quite higher than the prevalence rate in the HIV-uninfected women of reproductive age group (8–23 %) [1]. Bacterial vaginosis rate was higher at lower CD4 cell counts and HIV-seropositive women on ART for any duration did not show a decrease in bacterial vaginosis.

The lower genital tract has a dynamic bacterial community that is influenced by multiple factors like age, sexual activity, hormone status, infection, immune system, and individual hygiene practices. The vaginal microbiota is composed predominantly of various lactobacilli which produce lactic acid and also hydrogen peroxide to outcompete pathogenic organisms and maintain vaginal health. When the type and relative proportion of bacteria are altered in lower genital tract, bacterial vaginosis results, where the chief microbiota shifts from lactobacilli to Gardnerella, Clostridiales, Mycoplasma, and Prevotella [8].

As mentioned above, various studies show an increased prevalence of bacterial vaginosis in HIV infection [4–7]. A 2008 meta-analysis of 23 studies found out that bacterial vaginosis increased the risk of HIV infection by 60 % [9]. Studies have also reported increased shedding of HIV viral particles in the vaginal secretions of HIV-seropositive women with bacterial vaginosis which is critical to female to male transmission and vertical transmission of HIV [10, 11].

The possible mechanism by which bacterial vaginosis might affect HIV acquisition and transmission is by inducing a pro- inflammatory environment, consisting of cytokines and toll-like receptor (TLR) ligands, which is conducive to HIV propagation [8].

Trichomoniasis and HIV

In the present study, the prevalence of trichomoniasis was 8.8 % which is higher than the estimated prevalence of trichomoniasis, which is 3.2 %, in the HIV naïve reproductive age women [2]. Many studies have shown an increase in HIV seroconversion associated with trichomonas infection [5–7]. Also among HIV-seropositive women, infection with *Trichomonas vaginalis* is associated with higher genital levels of HIV-1 and increased shedding of *T. vaginalis* in vaginal secretions, which decreased after treatment of trichomoniasis and with institution of ART [12–14].

Trichomonas vaginalis increases susceptibility to HIV infection by causing epithelial barrier disruption and by changes in innate and adaptive immunity in the female genital tract [8].

Table 1 Prevalence of LGTI in the study

Type of LGTI	Percentage of HIV seropositive women
Bacterial vaginosis	47.7
Trichomoniasis	43.2
Candidiasis	8.8

Table 3 Frequency distribution of LGTI according to the duration of ART

ART (years)	LGTI present	LGTI absent (%)
Not on ART (n = 70)	13 (18.6 %)	57 (51.4)
0.1–1 (n = 47)	10 (21.3 %)	37 (78.7)
>1–2 (n = 42)	8 (19.1 %)	34 (80.9)
2–3 (n = 17)	5 (29.4 %)	12 (70.6)
>3 (n = 24)	7 (29.2 %)	17 (70.8)
Statistical significance[a]	$\chi 2 = 1.97$, df = 4, $p = 0.740$ not significant ($p > 0.05$)	

[a] By Chi-square method

Table 2 LGTI with respect to CD4 cell counts in HIV-seropositive women

CD4 count (cells/μl)	LGTI present	LGTI absent (%)
<200 (n = 62)	19 (30.6 %)	43 (69.4)
>200 (n = 138)	24 (17.4 %)	114 (82.6)
Total	43 (21.5 %)	157 (78.5)
Statistical significance[a]	$\chi 2 = 4.45$, df = 1, $p = 0.0348$ significant ($p < 0.05$)	

[a] By Chi-square method

Candidiasis and HIV

The present study also reported increase in prevalence of candidiasis in HIV-seropositive women, which was 43.2 % as compared to 18 % in the HIV-uninfected women of reproductive age group, and like other LGTI, risk of candidial vaginal colonization increases with lower CD4 cell counts [3, 7]. Likewise in the study conducted by McClelland et al., the risk of vaginal candidiasis in HIV-positive women with decreasing CD4 cell counts showed stepwise increase as compared with the risk in seronegative women [7]. There are various studies reporting chronic, recurrent candidial vaginitis to be more frequent among HIV-seropositive women. Studies have even reported that in HIV-seropositive women, vulvovaginal candidiasis is associated with an increased number of copies of cell—associated and cell-free HIV-1 RNA in cervicovaginal secretions, which can facilitate female to male transmission of HIV infection [15].

The present study reported increased prevalence of LGTI (bacterial vaginosis, trichomoniasis, and candidiasis) in HIV-seropositive women, especially at lower CD4 cell counts but no significant effect of ART on LGTI in these women. Higher prevalence of LGTI in the HIV-seropositive women can be because presence of LGTI is a risk factor for acquisition of HIV. Also higher prevalence of LGTI at lower CD4 cell counts can be attributed to advanced HIV-mediated immunosuppression which fails to clear these infections, affects the clinical course, and fails to prevent reinfection and recurrence. Also at lower CD4 cell counts, the LGTI are more severe and less susceptible to treatment [7]. Similar results were obtained in the study by Warren et al. with the prevalence of bacterial vaginosis to be 47 % in the HIV-positive women compared with 44 % in the HIV-negative women, and among HIV-positive women, they concluded that the use of antiretroviral drugs was associated with a lower prevalence of bacterial vaginosis [4]. Goel et al. found the prevalence of bacterial vaginosis to be 30 %, mixed infection 30 %, and candidiasis 10 % among HIV-seropositive women. They also found that there is no significant correlation between decreasing CD4 counts with bacterial vaginosis (40 vs. 60 % with CD4 counts less than 200 and more than 200 cells/μl) and candidiasis (44.4 vs. 55.5 % with CD4 counts less than 200 and more than 200 cells/μl). They found that those HIV-seropositive women who were on ART showed lower prevalence of bacterial vaginosis (15 % and 20 % in women on ART less than 6 and more than 6 months respectively) but higher prevalence of yeast infection [5].

Taking into account that the heterosexual mode of transmission is the most common mode of transmission of HIV in our population and the fact that these LGTI can lead to increased transmission and shedding of HIV, these LGTI are a serious health concern especially in the high-risk populations which have a higher prevalence of these LGTI. Prompt screening to identify LGTI and treatment (curative or prophylactic) can prove a cost-effective approach in the fight against HIV pandemic.

Limitations of the study was that it could not conclude whether the HIV-induced vaginal immune impairment played a role in the development of LGTI. Also high-risk behavior groups and sex partners of the women were not included in the study.

The non-ulcerative LGTI which are often undiagnosed and underdiagnosed are at many times asymptomatic and as mentioned above increase the sexual transmission of HIV. Even if the risk of transmission of HIV infection due to these non-ulcerative LGTI is lower than the ulcerative lesions like syphilis and herpes, it becomes magnified and significant due to higher prevalence of these LGTI in the population than ulcerative lesions. A vicious cycle circle can set up, where the LGTI promote transmission (heterosexual and vertical) and HIV infection causes persistence and recurrence of LGTI and so on.

Conclusion

From the present study, we can infer that HIV-infected reproductive age women have a higher prevalence of LGTI (bacterial vaginosis, trichomoniasis, and candidiasis) and should be screened to diagnose and treat the often asymptomatic LGTI to decrease HIV transmission (both heterosexual and vertical), especially HIV-seropositive women with lower CD4 cell counts in whom the prevalence of LGTI is still higher. More research is required to establish the ideal frequency of screening and to evaluate the effect of ART on LGTI and HIV viral shedding and the effect of HIV-mediated immunosuppression on frequency and severity of LGTI.

Acknowledgement Capsule cross-sectional study finding increased prevalence of bacterial vaginosis, trichomoniasis, and candidiasis in HIV-seropositive women especially at lower CD4 counts and no correlation with ART.The study was conducted in PGIMS, Rohtak.

Compliance with ethical requirements Ethical clearance was taken from the hospital ethical committee.

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