

Lower genital tract infections in HIV-seropositive women in India

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Abstract

Objectives: The presence of STD facilitates shedding of HIV and increases HIV-1 disease progression, possibly by increasing plasma viremia. Our aim was to study the presence of various associated Sexually transmitted disease/ Reproductive tract infections in HIV-seropositive women in India. **Materials and Methods:** The study included 40 HIV-seropositive women attending the antiretroviral therapy (ART) clinic at Lok Nayak Hospital. An informed consent was taken from all subjects. All cases were subjected to detailed gynecological examination and two types of swabs, i.e., a vaginal swab and a cervical swab were taken for STD/RTIs evaluation. The vaginal swabs were used for preparation of wet mount and KOH mount for diagnosis of trichomoniasis and candidiasis; to make a vaginal smear for Gram staining to diagnose bacterial vaginosis (BV) as per Nugent's criteria; for culture of aerobic bacteria and *Candida* spp. The cervical swab was used for isolation of *Neisseria gonorrhoeae* by culture and for detection of *Chlamydia trachomatis* antigen by Chlamydia microplate enzyme immunoassay kit (BIORAD). All data were analyzed using appropriate statistical tests. **Results:** All 40 cases were evaluated for the presence of STD/RTIs associated with HIV infection. The women belonged to the reproductive age group (15–45 years) and majority (40%) of them were para 2. Most of the women (14, 35%) were in World Health Organization (WHO) stage I and maximum number (28, 70%) had their CD4 cell count more than 200 cells/ μ l. There was no significant correlation between WHO stage of HIV-seropositive women and their CD4 cell count ($P=0.092$). Out of 40 cases, 15 (37.5%) were on ART with maximum cases (53.3%) in WHO stage III. The duration of ART was more than 6 months in 9 (60%) cases. The most common presenting complaint was vaginal discharge in women with WHO stage II and III and 27.5% women showed vaginitis on per speculum examination. Laboratory tests showed high prevalence of BV (30%), mixed infection (30%), and candidiasis (10%) among HIV-seropositive women ($P<0.001$ in both). Women with BV were mostly in WHO stage I (38.4%) and stage II (36.3%), while those with mixed infection were mainly in WHO stage III (36.3%) and stage IV (40%). Women with candidiasis were mainly in WHO stage III. *C. trachomatis* antigen was found only in one subject (prevalence 2.5%). Both WHO stage and CD4 cell count had no significant correlation with presence of BV ($P=0.056$ and 0.063 , respectively) and candidiasis ($P=0.492$ and 0.530 , respectively). Maximum number of patients on ART had mixed infection (53.3%), while most of the patients (36%) not on ART had BV. There was no significant association between duration of ART and the presence of vaginal infections. **Conclusions:** The prevalence of gynecological symptoms and RTIs in HIV-seropositive women is high enough to warrant routine gynecologic evaluation and RTI screening in these patients. However, larger studies and trials are needed to evaluate the effects of ART on these abnormalities as well as to choose the best screening tool in HIV-seropositive women.

Key words: HIV, lower genital tract infections, women

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INTRODUCTION

Abnormal vaginal discharge in women may be differentiated into cervicourethral and vaginal discharge syndromes, on the basis of the site of preference of the causative microorganism. Discharge caused by *Trichomonas vaginalis* and yeasts, as well as that associated with bacterial vaginosis

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(BV), originates from the vagina. Historically, the three causes of vaginal discharge have been a lesser public health priority than are cervical infections and have been viewed largely as merely a nuisance and not a serious threat to the health of women.^[1] Vaginal infections, including BV, *T. vaginalis*, and yeast vaginitis (YV), are common among HIV-infected women.^[2] Symptomatic vaginal yeast infections are increased among HIV-infected women with low CD4 cell count in the absence of antifungal prophylaxis.^[3,4] BV and *T. vaginalis* have been shown to increase the risk of HIV acquisition among women, underscoring their importance from a public health perspective.^[5-8] Thus, these vaginal infections directly cause significant morbidity, especially among HIV-infected women, and may contribute to increased risk of sexual and perinatal HIV transmission.

The effect of antiretroviral therapy (ART) on vaginal infections among HIV-infected women has been evaluated only to a limited extent.^[9-11] Changes in vaginal milieu, such as immunologic cell populations, cellular activation, and cytokine production, would alter susceptibility or response to infections, influencing their incidence and prevalence. The changes in rates of these common vaginal infections over time are important to evaluate in the context of increasing utilization of ART.^[2] The objectives of this study were to study the presence of lower genital tract infections among HIV-infected women in India and to evaluate the effect of ART on these infections.

MATERIALS AND METHODS

The study included 40 HIV-seropositive women attending the ART clinic at Lok Nayak Hospital. After informed consent was obtained, each woman was interviewed regarding her medical, social, and treatment history as well as current symptoms. All women underwent a physical examination, including pelvic examination. Swabs were used to collect vaginal secretions from the posterior vaginal fornix for preparation of saline wet mounts and smears for subsequent Gram staining. BV was identified by means of Gram stain of air-dried smear of vaginal secretions and examined at 1000× magnification for bacterial morphotypes, pus cells, and hyphal forms. Smears were scored using the Nugent's criteria as normal (scores of 0–3 indicate predominant lactobacilli morphotypes), intermediate (scores of 4–6 indicate decreased lactobacilli and increased other morphotypes), or BV (scores of 7–10 indicate markedly decreased or absent lactobacilli morphotypes and increased Gram variable and Gram-negative rods).^[12,13]

Yeast or trichomonal vaginitis was identified by means of 10% potassium hydroxide (KOH) and saline wet mount examinations of vaginal secretions. The presence of pseudohyphae or budding yeast cells was considered diagnostic of candidal infection. The presence of trichomonads with characteristic motility was considered diagnostic of trichomonal infection.^[14] CD4 lymphocyte subsets were quantified using standard flow cytometric methods.

RESULTS

A total of 40 HIV-seropositive women were enrolled in the study. The median age was 30 years (range 21–43 years) with most of them (14, 35%) being in the age group 26–29 years followed by 13 (32%) between 30 and 35 years, and 6 (15%) less than 26 years. Most of the women were para 2 (40%), followed by para 1 (30%) and para 3 (22.5%). The most common infection among the asymptomatic cases [Figure 1] was mixed infection, i.e., both BV and candidiasis (29%), while among the symptomatic cases candidiasis was most common (29%). The characteristics of HIV-infected women included in the study are shown in Table 1. Out of 40, 14 women (35%) presented clinically with abnormal vaginal discharge. The prevalence of BV by Gram stain was 50% and yeast vaginitis 45%. Mixed infection was present in 22.5% of the women. At the time of the study, 15 (37.5%) of the women were on ART.

Table 2 shows the correlation of lower genital tract infections with World Health Organization (WHO) stage and CD4 cell count. Most of the women with BV (50%) were in WHO stage I and their CD4 cell count was more than 200 cells/μl. While majority of the women with YV were in WHO stage I and III

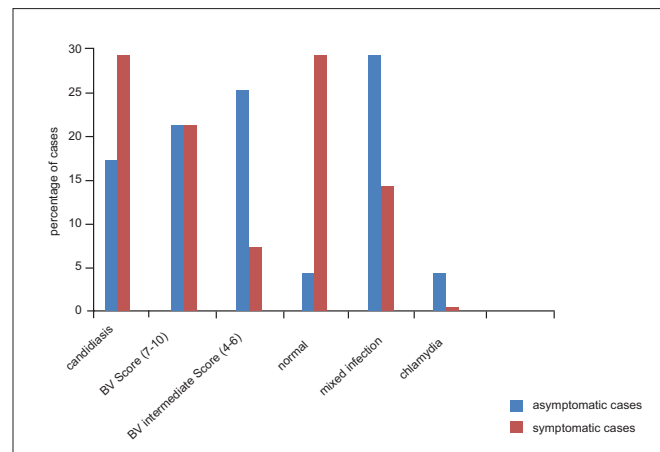


Figure 1: Comparison of LGTIs among symptomatic cases with asymptomatic cases

(33.3% and 27.75%, respectively) with most of them also having CD4 cell count more than 200 cells/ μ l. Only one woman had chlamydial infection and she was in WHO stage I with CD4 cell count less than 200 cells/ μ l. There was no significant correlation of WHO stages and CD4 cell counts with BV ($P<0.5$) and YV ($P<0.5$).

When Nugent's Gram stain score [Table 3] was applied to the smear of the vaginal discharge of the 40 HIV-seropositive women, 11 (27.5%) women scored 0–3, 8 (20%) scored from 4 to 6, and 20 (50%) women scored from 7 to 10. There was little difference between the percentage of women with low and intermediate scores, but there was a significantly higher prevalence of women with a

high score. Detection of yeast on Gram stain was associated with an increasing BV score.

The association of presence of lower genital tract infection in HIV-infected women with ART and its duration has been shown in Table 4. Out of 20 women with BV, 7 were on ART with 4 women being on ART for more than 6 months. Among women with YV, 11 were on ART with 6 being on ART for more than 6 months duration. The woman who had chlamydial infection was not on ART. The presence of vaginal discharge was more common in women who were not on ART (64.2%). In addition, clue cells and pus cells on Gram stain of vaginal smear were mostly present in women not on ART (66.6%). There was no significant correlation between vaginal infections and duration of ART. However, the prevalence of BV was low in women who were on ART (35%) vs. (65%) in those not on ART, but YV was more in women taking ART (61%) vs. (38.8%) in women not on ART.

Table 1: Characteristics of HIV-infected women included in the study

Characteristic	No. of HIV-infected women (n=40)	%
Vaginal discharge		
Yes	14	35
No	26	65
ART		
Yes	15	37.5
No	25	62.5
CD4 cell count		
<200	12	30
200-500	23	57.5
>500	5	12.5
WHO stage		
I	14	35
II	11	27.5
III	12	30
IV	3	7.5
Vaginal Gram stain result		
Normal	5	12.5
Intermediate	4	10
BV	20	50
YV	18	45
Mixed infection	9	22.5
Trichomoniasis on wet mount	0	0
Cervical <i>Chlamydia trachomatis</i>	1	2.5

DISCUSSION

This study was undertaken to assess the prevalence of lower genital tract infections among HIV-seropositive women at their baseline visit to the ART clinic at Lok Nayak Hospital, New Delhi. The effect of ART on these infections was also studied.

BV was common (50%) followed by YV (45%), mixed infection, i.e., both BV and YV (22.5%) and *Chlamydia trachomatis* (2.5%) among the 40 HIV-seropositive women studied. Most of the other studies have also reported similar findings. Watts *et al.*^[2] reported that at baseline visit, BV was present in 42.8% of HIV-infected women and YV in 10% followed by *T. vaginalis* in 6.1%. Another study^[15] in the United States found that the prevalence of BV among HIV-positive women was 35% followed by trichomoniasis (12%), *C. trachomatis* (4%), and YV (3%).

BV is recognized as a syndrome in which there is

Table 2: Correlation of Lower genital tract infections with WHO stage and CD4 cell count

	BV n=20 (%)	YV n=18 (%)	Mixed infection n=9 (%)	Chlamydial infection, n=1
WHO stage				
I	10 (50)	5 (27.7)	3 (33.3)	1
II	4 (20)	4 (22.2)	1 (11.1)	0
III	3 (15)	6 (33.3)	2 (22.2)	0
IV	3 (15)	3 (16.6)	3 (33.3)	0
CD 4 cell count				
<200 cells/ μ l	8 (40)	8 (44.4)	5 (55.5)	1
>200 cells/ μ l	12 (60)	10 (55.5)	4 (44.4)	0

Table 3: Distribution of HIV-infected women and yeast colonization in them according to Gram staining categories of BV

Nugent's score	No. of HIV-infected women (%)	Colonized by yeast (%)
0-3	11 (27.5)	4 (36.3)
4-6	8 (20)	4 (50)
7-10	20 (50)	9 (45)

Table 4: Association of lower genital tract infections with ART and its duration

LGTI	Women on ART		Women not on ART (%)
	<6 months (%)	>6 months (%)	
BV (20)	3 (15)	4 (20)	13 (65)
YV(18)	5 (27.7)	6 (33.3)	7 (38.8)
Mixed infection (9)	2 (22.2)	3 (33.3)	4 (44.4)
Chlamydial infection (1)	0	0	1
Clue cells			
Present (15)	3 (20)	2 (13.3)	10 (66.6)
Absent (25)	2 (8)	7 (28)	16 (64)
Pus cells			
Present (14)	2 (14.2)	3 (21.4)	9 (64.2)
Absent (26)	4 (14.3)	6 (23.1)	16 (61.5)
Vaginal discharge			
Present (14)	3 (21.4)	2 (14.2)	9 (64.2)
Absent (26)	3 (11.5)	7 (26.9)	16 (61.4)

an imbalance of the vaginal ecosystem.^[16] Hydrogen peroxide producing lactobacilli have been identified as key components in maintaining a normal vaginal milieu.^[17] The pathogenic mechanism for BV is unknown, but it may vary from the use of topically applied substances with antimicrobial effect to a localized immunologic defect or it may result from infection with an organism that competes or interferes with the lactobacilli. Such an infection may be sexually transmissible or of endogenous origin.^[1]

Whether HIV-induced vaginal immune impairment plays a role in the development of BV could not be concluded from our data. However, other researchers^[5,6,18,19] have found a strong association between the prevalence of HIV infection and the level of abnormal vaginal ecology. In our study, there was no statistically significant correlation between BV and WHO stage and CD4 cell count of HIV-positive women suggesting that the risk of BV was not associated with immunological status. Similar results were obtained for YV. Other studies^[20,21] have reported that in HIV-seropositive women, vulvovaginal candidiasis is very common and is correlated with the immunological status of the host.

We showed a positive association between HIV

infection and increasing BV score of Gram stain. Yeast colonization on Gram stain was also associated with increasing BV score. However, one study^[1] has reported that yeast colonization and vulvovaginal candidiasis were inversely related to Nugent's score.

Gram stain diagnosis remains the "gold standard" for study of BV, but detection of *T. vaginalis* by wet mount is less sensitive than culture, PCR testing, or antigen detection and likely detects only approximately half of infections.^[22] Wet mounts were used in our study to detect trichomonas infection. Out of 40 cases, none of the women had trichomoniasis according to the wet mount examination. If HIV infection led to higher levels of *T. vaginalis* in the genital tract, wet mounts would be expected to be positive more frequently in HIV infected women, but we did not find this. Requiring a combination of symptoms and microscopic detection of budding yeast cells and pseudohyphae should increase the specificity of diagnosis of YV. However, again sensitivity is likely to be less than with consistent culture testing.

Among the HIV-infected women, those who were on ART showed lower prevalence of BV but higher prevalence of YV. Symptomatic vaginal discharge was more common in women who were not on ART. On Gram stain, the presence of pus cells and clue cells was also less in women on ART; however, this finding did not reach statistical significance. Duration of ART had no effect on the presence of vaginal infections. Watts *et al.*^[2] has also reported a decrease risk of vaginal infections among HIV-positive women, and use of ART was associated with this decrease. Women who are on ART have more medical visits for monitoring of therapy, and therefore this provides them with additional opportunities for diagnosis and treatment of lower genital tract infections, hence decreasing the risk of infection in them.

Vaginal infections are a common problem for the HIV-infected women, even in the ART era, underscoring the need for regular gynecologic assessment. These infections may increase the HIV levels in the genital tract and facilitate HIV transmission to sexual partners and infants. Further research is needed to identify improved strategies for treatment of these infections and recolonization of the genital tract with lactobacilli will ensure a healthy vaginal milieu. Men mostly are the asymptomatic transmitters and therefore the inclusion of metronidazole in the treatment of those who seek medical attention for any sexually transmitted disease has the potential to decrease the prevalence of this infection in women.

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