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Co-Occurrence of *Trichomonas vaginalis* and Bacterial Vaginosis Among HIV-Positive Women

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Abstract

Trichomonas vaginalis (TV) and bacterial vaginosis (BV) were examined among human immunodeficiency virus+ women. The prevalence rates were 28.0% for TV, 51.4% for BV, and 17.5% for TV/BV co-infection. Among human immunodeficiency virus+/TV+ women, the rate of BV was 61.0%. Research is needed to examine how BV affects the clinical course and treatment of *T. vaginalis*.

Trichomonas vaginalis (TV) and bacterial vaginosis (BV) are both common infections found among human immunodeficiency virus (HIV)-positive women, with respective prevalence rates in this population ranging from 11% to 30%^{1–6} and 35% to 55%.^{1,6–9} Both conditions have been separately associated with HIV acquisition^{10–13} and increased genital shedding,^{14–18} which may enhance sexual and perinatal transmission of HIV. Also, both TV and BV have high recurrence rates that indicate the complexity of successfully treating each condition.^{19,20} Studies among mostly HIV-negative women have shown a strong association between TV and BV, which imply that the 2 frequently occur together,^{21–28} but this relationship has not been well studied among HIV-positive women.

The co-occurrence of TV and BV suggests that one of these conditions may alter a woman's susceptibility to the other. A prospective study found that abnormal vaginal flora was associated with an increased risk of acquiring TV, suggesting that BV may increase a woman's susceptibility to TV infection.²¹ Conversely, a cross-sectional study found a constant prevalence of TV in women with Nugent scores ≥ 4 and demonstrated a nonlinear association between TV and abnormal vaginal flora.²⁹ The nonlinear relationship suggests that infection with TV may create an environment that favors the development of BV. Otherwise, one would expect to see a gradual increase in the prevalence of TV as vaginal flora deviation from normal increased.

The purpose of this study was to examine the cross-sectional relationship between TV and abnormal vaginal flora among a group of HIV-positive women in the United States, and to examine factors associated with the presence of BV among HIV-positive women with TV infection.

HIV-positive women were recruited from the HIV Outpatient Program in New Orleans, LA, between June 2002 and January 2005 to participate in a cross-sectional screening study to investigate multiple issues surrounding sexually transmitted diseases. Women with the following criteria were eligible: age ≥ 18 years, scheduled to undergo a gynecological examination, and provide informed consent. Data and specimen collection methods have been previously published.¹⁴

In brief, clinical information collected for the study included the following laboratory diagnosis: TV by InPouch culture (Biomed Diagnostics; White City, OR), BV by Gram stain, *Neisseria gonorrhoea*, and *Chlamydia trachomatis* using the ProbeTec strand displacement DNA amplification method (Becton Dickinson, Sparks, MD), and vulvovaginal candidiasis by culture. Gram stains were scored using Nugent et al criteria³⁰ with scores of 0 to 3 considered normal, 4 to 6 intermediate, and ≥ 7 BV. We defined abnormal vaginal flora as Nugent scores ≥ 4 . Genital odor, vaginal discharge, vaginal petechiae, and erythema were observed by the clinical provider. The provider also performed wet mount microscopy.

Respondents were interviewed using computer-assisted self-administered interviews or computer-assisted personal interviews, depending on the woman's preference. Interviews were conducted either before or after the clinical examination, depending on the clinic flow, and captured sociodemographic and behavioral characteristics of the women.

The prevalence rates were calculated from participants in the screening study using those with complete testing data as the denominator for each diagnosis. TV-positive rates were examined across categories of Nugent scores, and odds ratios were calculated to measure the association. The analysis was then limited to HIV+/TV+ women, and the rate of BV was determined. Baseline associations between BV status and selected clinical and behavioral characteristics were examined using χ^2 or Fisher exact test as appropriate. All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC).

A total of 397 HIV-positive women were screened, with more than half of the women (57.9%, $n = 230$) on antiretroviral therapy. There was demographic data available for 377 women, with a mean age of 36.4 years (± 9.2). A majority were black (84.4%, $n = 318$) and not married/cohabitating (81.7%, $n = 308$). In the last 4 weeks, 66.3% of the women had at least 1 male sex partner ($n = 250$).

The prevalence rates were as follows: 28.0% for TV (106/378), 51.4% for BV (196/381), 64.8% for abnormal vaginal flora (247/381), 17.5% for TV/BV coinfection (64/365), and 23.0% for the combination of TV/abnormal vaginal flora (84/365). There was a significant association between TV and BV (61.0% of TV+ women had BV 64/105 vs. 47.3% of TV- women 123/260; $P = 0.02$) and a strong association between TV and abnormal vaginal flora (80.0% of TV+ women had abnormal vaginal flora 84/105 vs. 58.9% of TV- women 153/260; $P = 0.0001$). The prevalence rates for other infections were as follows: 3.4% for *C. trachomatis* (13/387), 0.8% for *N. gonorrhoea* (3/387), and 28.4% for candidiasis (110/387).

The distribution of TV infection by vaginal flora was examined (Table 1). There was a significant difference in the prevalence of TV among women with normal vaginal flora (16.4%) versus women with intermediate flora (40.0%, $P = 0.0008$). The prevalence of TV among women with intermediate flora and women with BV was similar (40.0% vs. 34.2%; $P = 0.45$).

The analysis was then limited to HIV-positive women with TV infection. Of the HIV+/TV+ women with complete Gram stain results ($n = 105$), demographic and behavioral information was available on 101 participants with a median age of 35 years (range, 18–54).

The majority of these women were black (93.1%, $n = 94$), not married or cohabitating (83.2%, $n = 84$), unemployed (82.2%, $n = 83$), and had a high school education or less (79.2%, $n = 80$). Most women reported douching (79.2%, $n = 80$), using a condom at last vaginal intercourse (67.3%, $n = 68$), and having at least one male sex partner in the last 4 weeks (74.3%, $n = 75$).

Approximately half of the HIV+/TV+ women were on antiretroviral therapy (51.4%, $n = 54$). Per the provider assessment, 16.2% of the women had unusual genital odor ($n = 17$), 13.3% had vaginal erythema ($n = 14$), 5.7% had vaginal petechiae ($n = 6$), and 57.1% had moderate to copious amounts of vaginal discharge ($n = 60$). Of 102 women with information from wet mount preparations, 31.4% had a positive whiff test ($n = 32$) defined as amine or fishy odor after KOH was added to the wet preparation, and 21.6% had clue cells present ($n = 22$). In total, 61.0% of the HIV+/TV+ women also had BV ($n = 64$).

Table 2 presents baseline characteristics of the HIV+/TV+ women by BV status. Women with BV were more likely to have one or more male sex partners in the last 4 weeks ($P = 0.001$) and to have one or more alcoholic drinks in an average week ($P = 0.005$) compared to the women without BV. From the provider assessment, HIV+/TV+ women with BV were more likely to have unusual genital odor ($P = 0.05$), abnormal consistency of vaginal discharge ($P = 0.03$), abnormal color of vaginal discharge ($P = 0.03$), positive whiff test (0.002), and clue cells present on wet preparation ($P = 0.02$). The women with BV were also more likely to douche ($P = 0.18$) and less likely to have used a condom at last vaginal sex ($P = 0.18$), but not at significant levels. There were no differences found by BV status about other infections, specifically chlamydia, gonorrhea, and candidiasis.

To our knowledge, this is the first prevalence study of TV/BV coinfection among HIV-positive women in the United States. The prevalence of TV/BV coinfection was high at 17.5%. A majority of HIV-positive women with TV also had BV (61.0%). If the presence of TV infection creates an environment that favors the development of BV, the expectation would be that BV is more frequent among women with TV infection.²⁶ In our group of HIV-positive women, a significantly higher prevalence of BV was found among women with TV infection compared with TV-negative women. We also examined the presence of abnormal vaginal flora and found a significantly higher prevalence of abnormal vaginal flora among women with TV infection compared with TV-negative women.

The association between TV and gradations of vaginal flora was not linear. TV prevalence increased sharply between HIV-positive women with normal flora and those with intermediate flora; however, the prevalence of TV remained the same for women with intermediate flora and BV. Our findings are consistent with the findings of Moodley et al that showed a nonlinear relationship between TV prevalence and vaginal flora among African HIV-positive and -negative women.²⁹ The similar prevalence of TV in women with abnormal vaginal flora (intermediate and BV Nugent scores) supports the notion that TV infection may create an environment that is conducive to a shift away from normal flora, and therefore, may be a factor in the development of BV. Our study design was cross-sectional, and future prospective, longitudinal studies are needed to examine the relationship between TV and BV using methods to establish temporality. The magnitude of this frequent combination has implications for worldwide HIV prevention and control strategies.

For health care providers of HIV-positive women, the high rate of BV that accompanies TV infection has implications for treatment decisions. The Centers for Disease Control and Prevention no longer recommends the metronidazole 2 g oral single dose for treatment of BV, yet this treatment regimen is still recommended for TV infection³¹ and may result in women being undertreated if they have both TV and BV. Also, if the combined presence of

TV and BV has a synergistic effect on genital shedding of HIV, adequate treatment for both conditions would be paramount.

In our study, the HIV-positive women with TV and BV had more clinical signs compared to the women with TV only, including higher rates of unusual genital odor, abnormal consistency and color of vaginal discharge, positive whiff tests, and presence of clue cells. However, these clinical signs alone would not have identified many of the cases of BV. The sensitivity of Amsel et al criteria³² compared to Nugent score for the diagnosis of BV among HIV-positive women is only 34% to 37%,^{1,33} and therefore, BV diagnosis will frequently be missed at the point of care.

One or more recent sex partners and weekly alcohol use were positively associated with BV among our group of HIV-positive women with TV infection. Alcohol use has been previously associated with BV^{6,34–36} in groups of HIV-positive and -negative women, and the association between BV and sexual contact has been well established.³⁷

In conclusion, health care providers for HIV-positive women should be aware of the high prevalence of TV/BV coinfection in this population, as well as the high rate of BV among HIV-positive women with TV infection. Given these results, research is needed to examine potential interactive effects of these 2 conditions on the clinical course and treatment of both in HIV-positive women.

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TABLE 1
 Distribution of *Trichomonas vaginalis* According to Nugent Score Categories and Association Between Vaginal Flora and *T. vaginalis* Infection Among HIV-Positive Women (n = 365)

Vaginal Flora (Nugent Score)	No. Women	Percentage Infected With <i>T. vaginalis</i>	Odds Ratio for <i>T. vaginalis</i> Infection	95% Confidence Interval	P
Normal (0–3)	128	16.4%	Ref.	—	—
Intermediate (4–6)	50	40.0%	3.40	1.63, 7.08	0.0008
Bacterial vaginosis (7–10)	187	34.2%	2.65	1.52, 4.63	0.0005
Abnormal (4–10)	237	35.4%	2.80	1.63, 4.79	0.0001

TABLE 2

Characteristics of HIV+/TV+ Women by BV Status (N = 105)

	Co-Infection TV/BV (n = 64) %	Single Infection TV (n = 42) %	P
Demographic *			
African American	95.1%	90.0%	0.43 †
Unemployed	83.6%	80.0%	0.64
Not married/cohabitating	82.0%	85.0%	0.69
High school education or less	84.7%	76.9%	0.33
Age, ≥ 35 yr	44.3%	50.0%	0.57
Behavioral *			
Douches	83.6%	72.5%	0.18
Condom used at last vaginal sex	62.3%	75.0%	0.18
1 male sex partner in last 4 wk	87.9%	60.0%	0.001
Drinks alcohol weekly, on average	47.5%	20.0%	0.005
HIV disease			
On ART	50.0%	53.7%	0.71
Other infections *			
Chlamydia	6.5%	5.1%	1.00 †
Gonorrhea	3.2%	2.6%	1.00 †
Candidiasis	31.8%	35.0%	0.73
Provider assessment			
Unusual genital odor	21.9%	7.3%	0.05
Vaginal erythema	12.5%	14.6%	0.75
Vaginal petechiae	6.3%	5.0%	1.00 †
Amount of vaginal discharge: moderate to copious (vs. scant to none)	59.4%	53.7%	0.56
Consistency of vaginal discharge‡: purulent, curdy, or milky/creamy (vs. normal)	80.7%	61.0%	0.03
Color of vaginal discharge‡: white/grey, yellow, green, bloody (vs. none or clear)	92.2%	76.9%	0.03
Positive whiff test§	46.4%	15.8%	0.002
Clue cells present§	29.5%	9.8%	0.02

* Total n = 101.

† Fisher exact test.

‡ Total n = 103.

§ Total n = 102.

ART indicates antiretroviral therapy; TV, *Trichomonas vaginalis*; BV, bacterial vaginosis.