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A Syndemic Approach to Explore Factors Associated with Bacterial Vaginosis

Ana S. Salazar¹, Nicholas F. Nogueira¹, Violeta J. Rodriguez^{2,3}, Alejandro Mantero⁴, Emily M. Cherenack⁴, Patricia Raccamarich¹, Marissa Maddalon¹, Theodora Brophy¹, Emily Montgomerie¹, Nichole R. Klatt⁵, Deborah L. Jones³, Maria L. Alcaide¹

¹ Division of Infectious Diseases, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida

² Department of Psychology, University of Georgia, Athens, Georgia.

³ Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, Florida.

⁴ Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, Florida.

⁵ Division of Surgical Outcomes and Precision Medicine Research, Department of Surgery, University of Minnesota, Minneapolis, Minnesota.

Abstract

Bacterial vaginosis (BV) is the most common genital infection in women and is associated with an increased risk of sexually transmitted infections and HIV. This study uses a syndemic approach to evaluate factors associated with BV. Non-pregnant, HIV-negative, sexually active cis-gender women aged 18–45 years living in Miami, Florida were recruited from Nov.2018- Jun.2021. Participants completed a sociodemographic and behavioral questionnaire along with gynecological examinations. BV was diagnosed by Amsel criteria and confirmed by a Nugent score ≥ 4 . A syndemic score was calculated as the sum of factors associated with BV. The association between syndemic score and BV was assessed using logistic regression. Of 166 women included, 60.2%

Corresponding Author: Maria L. Alcaide, MD, Professor of Clinical Medicine, Director, Infectious Diseases Research Unit and CFAR Clinical Core, Division of Infectious Diseases, Department of Medicine, University of Miami Miller School of Medicine, 1951 NW 7th Ave, Miami, FL 33136 Suite 2300, T: 305.243.8434 malcaide@med.miami.edu F: 305.243.2732.

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Conflicts of Interest

All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest beyond research funding related to the work presented in this manuscript.

Ethics approval: The questionnaire and methodology for this study was approved by the Institutional Review Boards of the University of Miami. This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Consent: Informed consent was obtained from all individuals participants included in the study.

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had BV. Race, ethnicity, education, vaginal sex, recent cannabis use, and reasons for intravaginal practices were included in the syndemic score. Higher odds of BV were found in women with a score of 3 compared to women with a score of 0/1. A higher syndemic score was associated with increased odds of having BV. Multilevel interventions to decrease BV are needed to decrease women's risk of acquiring HIV.

Resumen

La vaginosis bacteriana (VB) es la infección genital más común en mujeres y está asociada con un mayor riesgo de enfermedades de transmisión sexual (ETS) y de VIH. Este estudio utilizó un enfoque sindémico para evaluar factores asociados con VB. Entre noviembre del 2018 y junio del 2021, se reclutaron mujeres cisgénero de entre 18–45 años, que no estuvieran embarazadas, que fueran VIH negativas y sexualmente activas, y que vivieran en Miami, Florida. Las participantes completaron un cuestionario sociodemográfico y de comportamiento junto con un examen ginecológico. Se diagnosticó VB empleando los criterios de Amsel y se confirmó empleando el criterio de Nugent con una puntuación 4. La puntuación sindémica fue calculada como la suma de factores asociados con VB utilizando. La asociación entre la puntuación sindémica con VB se evaluó mediante una regresión logística. De 166 mujeres incluidas, 60.2% fueron diagnosticadas con VB. Los factores incluidos en la puntuación sindémica fueron la raza, etnia, educación, sexo vaginal, consumo reciente de cannabis, y el uso de prácticas intravaginales. Se encontraron mayores probabilidades de VB en mujeres con una puntuación 3 en comparación con aquellas con una puntuación de 0/1. Una puntuación sindémica alta se asoció con una mayor probabilidad de tener VB. Son necesarias intervenciones multinivel para disminuir la VB y disminuir el riesgo de que las mujeres contraigan ETS y VIH.

Keywords

Bacterial Vaginosis; Syndemic; HIV; Sexually Transmitted Infections

Introduction

BV is the most common genital infection among women (1, 2). It is characterized by a vaginal microbiome that has deviated from the normal flora, lacking *Lactobacillus* and having an abundance of *Gardnerella species* (3). If symptomatic, BV may present with abnormal discharge, itchiness, and malodor (4, 5). Further gynecological and obstetric complications from BV include preterm births, pelvic inflammatory diseases, and importantly, increased susceptibility to acquiring sexually transmitted infections (STI) (6) and HIV (3). However, the factors implicated on the etiology of BV are still unknown.

BV has been also associated with intravaginal practices (IVP) and the use of products that alter the vaginal compartment (7, 8). IVP refer to a variety of behaviors to maintain a vagina that women perceive as hygienic, healthy, or pleasing to sexual partners (9). IVP include cleansing, douching, or the insertion of products intravaginally. These practices are especially widespread among women from Sub-Saharan African cultures and ethnic minorities in the United States (1, 10–17). In addition to an increased risk for BV, IVP can also increase the risk for STI and HIV due to the disruption of intravaginal mucosal integrity.

Furthermore, having new or multiple sexual partners, identifying as Black or African-American, and having low income, have also been strongly associated with BV among women in the US (18–21). Therefore, investigating additive relationships between risk behaviors, sociocultural factors, and biological factors allows for a syndemic approach to assess multilevel predictors of BV (22, 23). A “syndemic” is defined as multiple interacting conditions that synergistically fuel each other resulting in increased risk for disease (24). The syndemic model is an analytic approach to understand how a combination of risk factors interact to exacerbate the burden of negative health outcomes in the context of disease clusters (24, 25). Understanding risk factors for BV, could guide interventions to better protect women from BV and future co-occurring incidence of HIV.

Florida is the epicenter of the HIV epidemic, and women living in Miami are among those at highest risk for HIV in the US (26, 27). Currently, limited information is known about how the combination of demographic and behavioral factors contributes to BV among women in the US. Consequently, this study aims at exploring the factors associated with BV in a diverse population of women using a syndemic approach.

Methods

Between November 2018 and June 2021, participants were recruited from the community using flyers, word of mouth, and through the Center for AIDS Research (CFAR) and the Center for HIV Research and Mental Health (CHARM) located in Miami, Florida. Cis-gender women, aged 18–45 years, who were HIV-negative and sexually active within the previous three months were invited to participate. Women who were pregnant; immunosuppressed; with an intrauterine device; had a history of cervical surgical treatment; antibiotic use; or diagnosed with STI within two months prior to being screened were excluded from the study. Participants were recruited as part of a longitudinal study evaluating factors associated with recurrent BV utilizing a multidisciplinary approach. Results reported in this study are findings from participants who completed the baseline visit. The study was approved by the University of Miami Institutional Review Board (IRB# 20180758) and informed consent was obtained before completion of study assessments. Human subjects research was conducted conforming to the University of Miami’s ethical standards and the Helsinki Declaration of 1975, revised in 2013.

Measures

Participants were screened and asked to complete an in-person/electronic/telephone questionnaire prior to an in-person visit at the Infectious Diseases Research Unit at the University of Miami. The questionnaire collected information on sociodemographics, sexual behavior, substance use, and IVP. These included age; race (Black or African-American, White, and Other); ethnic origin (Hispanic, Non-Hispanic, and Other); education (less than high school - 0 to 11 grade, high school, or more than high school - college, some college, or graduate school); average monthly income (<\$1,000, \$1,000-\$3,000, >\$3,000); number of sexual partners in the past month; number of sexual encounters; frequency of condom use; type of sex (vaginal sex only or vaginal and oral sex); cigarette smoking; alcohol intake; drug use (marijuana/cannabis, cocaine); frequency of alcohol and drug use (for cannabis

and cocaine use - in the past year, month, week, day or today; for alcohol use - less than a drink per month, less than 7 drinks a week, or daily); use of any IVP (e.g., intravaginal douches, soap, water, or other products) and reasons for IVP (hygiene “to clean myself”, partner preferences “to please my partner”, or health “to prevent infections such as STI”).

During the in-person visit, participants underwent HIV and pregnancy testing to confirm eligibility, and an ensuing gynecological examination was conducted to assess for BV. During the gynecological examination, a bivalve speculum previously moisturized with sterile normal saline was introduced in the vagina to retract the vaginal wall. Sterile swabs were used to assess Amsel criteria and Nugent scoring (28, 29). Identification of Amsel criteria required measuring the vaginal pH, performing a Whiff test, and placing a drop of vaginal fluid on a grease free glass slide for clue cells detection. For Nugent scoring, the vaginal discharge was also smeared on clean glass slides, air dried, and transported to a microbiology laboratory for Gram’s staining and review by trained laboratory technicians. An episode of BV was diagnosed if a participant met three out of four Amsel criteria (presence of discharge; pH >4.5; 20% of clue cells; positive whiff test) and confirmed by a Nugent score 4 (29, 30). Women diagnosed with symptomatic BV were provided with same-day standard of care treatment with metronidazole as per CDC guidelines (500 mg PO bid for 7 days) (31, 32).

Statistical Analysis

Descriptive analyses were conducted to examine the distribution of variables. Demographic and behavioral variables were operationalized as categorical factors; in multiple separate Chi-square and Fisher’s exact test analyses to test for significant differences, and the distribution of participants in each category was compared between those with and without BV. T-tests or Mann-Whitney tests were used for continuous comparison of groups.

Six factors were determined to be associated with BV via Fisher’s exact test and Chi-square analyses; and were evaluated for appropriateness to include in a syndemic conditions summary score: (1) Race, (2) Ethnicity, (3) Education, (4) Vaginal Sex, (5) Recent Cannabis Use, (6) Reasons for IVP. Levels associated with significant elevations in risk for BV were assigned a point in our final scoring. For example, one point each was assigned for identifying as Black, non-Hispanic, not completing high school, reporting vaginal sex in the previous month, reporting recent (less than one week) cannabis use, and use of IVP for hygiene purposes. The number of syndemic factors were calculated as a sum score (33–37). Cumulative syndemic scores were operationalized as ordinal variables. Due to small number of individuals reporting 0 or 6 syndemic factors, those with 0 or 1 syndemic factors and those with 5 or 6 syndemic factors were each collapsed into a single category, with final categories including 0/1, 2, 3, 4, or 5/6 syndemic factors.

A logistic regression model was conducted to assess for associations between syndemic scores and BV diagnosis. Syndemic levels were dummy coded and compared with the reference category of 0/1 syndemic factors. Odds ratios were estimated as effect sizes, and estimated effects are reported with 95% confidence intervals. A stacked barplot was generated in ggplot and presented the percent of positive BV for each syndemic factor score against the fitted probability positive for each syndemic factor from the logistic regression.

Statistical significance was determined by $\alpha = 0.05$ and analyses were conducted using R Version 4.0.4.

Results

Sociodemographic Characteristics, Risk factors, and Intravaginal Practices with Bacterial Vaginosis by Nugent Score

Table 1 compares sociodemographic characteristics, sexual behaviors, substance use, and IVP between women with and without BV diagnosis. A total of 166 women were enrolled in the study, of which more than half self-identified as non-Hispanic (72.9%) and Black or African American (61.4%). Many women reported a low household monthly income (<\$1,000 was reported by 53.6%) and had low education (only 46.4% completed high school or higher) and engaged in IVP (68.7%).

Overall, 60.2% of women were found to have BV. BV was more common among non-Hispanic women than Hispanic women (Table 1). It was also commonly found in Black women and women reporting race as other compared to White women. Women who did not complete high school (38) had also higher proportions of BV compared to women who completed high school or other higher education. Participants who reported vaginal sex in the previous month, and who reported recent cannabis use were more likely to be diagnosed with BV (Table 1). Lastly, there was a higher proportion of BV in women who engaged in hygiene reasons for IVP compared to pleasing their sexual partner or for health reasons (preventing or cure infections).

Syndemic Factors and Associations with Bacterial Vaginosis by Nugent Score

Race, ethnicity, education, vaginal sex, recent cannabis use, and reasons for IVP were included in the syndemic score. The total syndemic score had a range of 0–6. Syndemic scores by BV outcome are reported in Table 2 and Figure 1. There were a greater proportion of women with more syndemic factors in the BV group, compared to women without BV.

The odds of BV in women with a score of 3 (Odds Ratio [OR] 3.67; 95% Confidence Interval [CI] 1.13–12.97; $p=0.04$) was higher than the odds of BV in women with a syndemic score of 0/1 group. Compared to women with 0/1 syndemic conditions, women with a score of 4 (OR 8.00; 95% CI 1.77–46.40; $p=0.01$), and with a score of 5/6 (OR 21.99 95% CI 3.18–453.71; $p=0.01$) had higher odds of BV. No difference in the odds of being diagnosed with BV was found between women with 0/1 syndemic factors and 2 syndemic factors (OR 1.89 95% CI 0.59–6.49; $p=0.29$). Generally, in predicting BV using syndemic scores as seen in Table 3, we found increasingly higher odds of BV compared to reference group.

Discussion

This study used a syndemic approach to identify demographic and behavioral factors that correlate with BV among racially and ethnically diverse women of reproductive age living in Miami, Florida, a city with high prevalence of women with HIV. Race, ethnicity, education, vaginal sex, cannabis use, and reasons for IVP were independently associated with BV.

However, when analyzed together, women with three or more syndemic factors were at increased odds of having BV compared to women with 0/1. Our findings are in alignment with previous research supporting the use of a syndemic approach for understanding involvement of risky behaviors and poor health outcomes (39). This study is the first to incorporate demographic and behavioral factors in a syndemic score to predict BV among reproductive age women.

Previous studies focused on understanding the etiology of BV have also found multiple factors associated with BV, which is helpful in identifying potential risk factors in isolation. Previous research reveal that Black women have higher rates of BV than other racial groups. BV is more common in Black women of African ancestry, and biological differences have been observed in their vaginal microbial profiles when compared to women of European ancestry (40, 41). In addition, several biological and behavioral factors are correlated with differences in the vaginal microbiome and the relative abundance of BV-associated species (3, 5, 41). Examples include body mass index, diet, smoking, alcohol use, number of sexual partners, and socioeconomic status as potentially associated with BV. However, examining several syndemic factors provides a better understanding of how the combination of multiple interrelated risk factors increase women's vulnerability to BV.

The relationship between sociodemographic and behavioral factors with BV suggests interventions may be needed to reduce BV risk, especially those with high syndemic scores (e.g., women identifying as non-Hispanic Black with less education). African American women have been found to be more likely than Latina or Caucasian women to learn about IVP for cleansing purposes from their mothers (1), which suggests education, cultural norms, and motivations for IVP may intersect with race and ethnicity. As such, any behavioral interventions should be culturally sensible and consider sociocultural factors (e.g., educational attainment, cultural/family norms) that could contribute to BV risk or barriers to change in health behaviors. For example, implementing patient education on reducing cleansing behavior should use plain language, while aware of the patient's health literacy, and use the patient's primary language. Furthermore, it should also consider cultural beliefs to try to improve adherence. Discussion of the gynecological and obstetric implications, and HIV risk in the context of BV could be conducted during routine clinical visits. Of note, most women knowledge about vaginal cleansing comes from family members or friends (42, 43), which suggests that conducting outreach to mothers of young girls may be one avenue for the delivery of interventions. However, due to the link between low educational attainment and BV, delivering interventions in schools may not reach those most at risk

On the other hand, while symptomatic BV would compel gynecological evaluation, more than 50% cases of BV are asymptomatic, which still poses a risk for women's health (44). Our findings support further research to develop a screening tool that incorporates demographic and behavioral practices such as IVP and substance use to identify those at higher risk for BV (45).

Interestingly, our results show that engaging in IVP for cleansing purposes was associated with BV, but the overall use of IVP was not. Potential reasons could be related to the

frequency of IVP use. For instance, women who engage in IVP for cleansing purposes may be engaging in IVP more often than women who engage in IVP for different purposes (46). Furthermore, the use of specific products (e.g., soap) and techniques used for cleaning purposes could be more abrasive than products used by women engaging in IVP for other reasons (8, 43). Finally, there may be reverse directionality; women who have symptoms of BV may engage in IVP to manage symptoms associated with cleanliness, such as odor and discharge. Longitudinal research is needed to examine whether IVP occurs prior to BV or if BV symptoms prompt IVP.

On the other hand, not finding a link between IVP and BV is in accordance with recent literature. Despite several studies finding an association between IVPs and negative vaginal health outcomes, conclusive evidence is still conflicting, and results were not replicated in other studies. A recent systematic review showed that while 6 studies found an association between vaginal douching and BV, STIs, and HIV, results were mixed or found no association in several others (47). Relevant potential reasons listed as responsible for introducing bias were 1) study design (e.g., cross sectional and retrospective instead of prospective); 2) sampling conditions (e.g., populations that are known to have an increased risk for negative vaginal outcomes; and 3) not controlling for relevant confounders (definition, frequency, intensity, and reasons for IVP) (8, 47).

There are several limitations to the study that warrant mention. Cross-sectional data was presented from a longitudinal study evaluating factors associated with BV recurrence. Thus, the sample size for this analysis was not calculated a priori. Due to the small sample size, we were not able to evaluate interactions between syndemic factors, and collinearity might also contribute to the wide confidence intervals for the odds ratio. Data collected relied on self-report regarding behavior, and responses may have been affected by recall bias and social desirability. There may be a bi-directional relationship wherein women with BV may have been experiencing more vaginal discharge and malodor, leading to higher levels of IVP. In addition, there are multiple sociocultural mechanisms through which demographics such as race may be associated with BV (e.g., chronic stress due to racism); although the current study did not collect such information. Due to the high prevalence of racial and ethnic minorities and results may be not generalizable to other populations with different demographic characteristics.

Conclusions

Our study is the first to use a syndemic approach to better understand how the interaction of demographic and behavioral factors contribute to the development of BV among reproductive-aged women (43, 48). Results support the development of multilevel interventions to reduce the incidence of BV as a strategy to reduce HIV transmission (42, 48, 49). Such interventions would be particularly relevant for women at greater risk for HIV infection.

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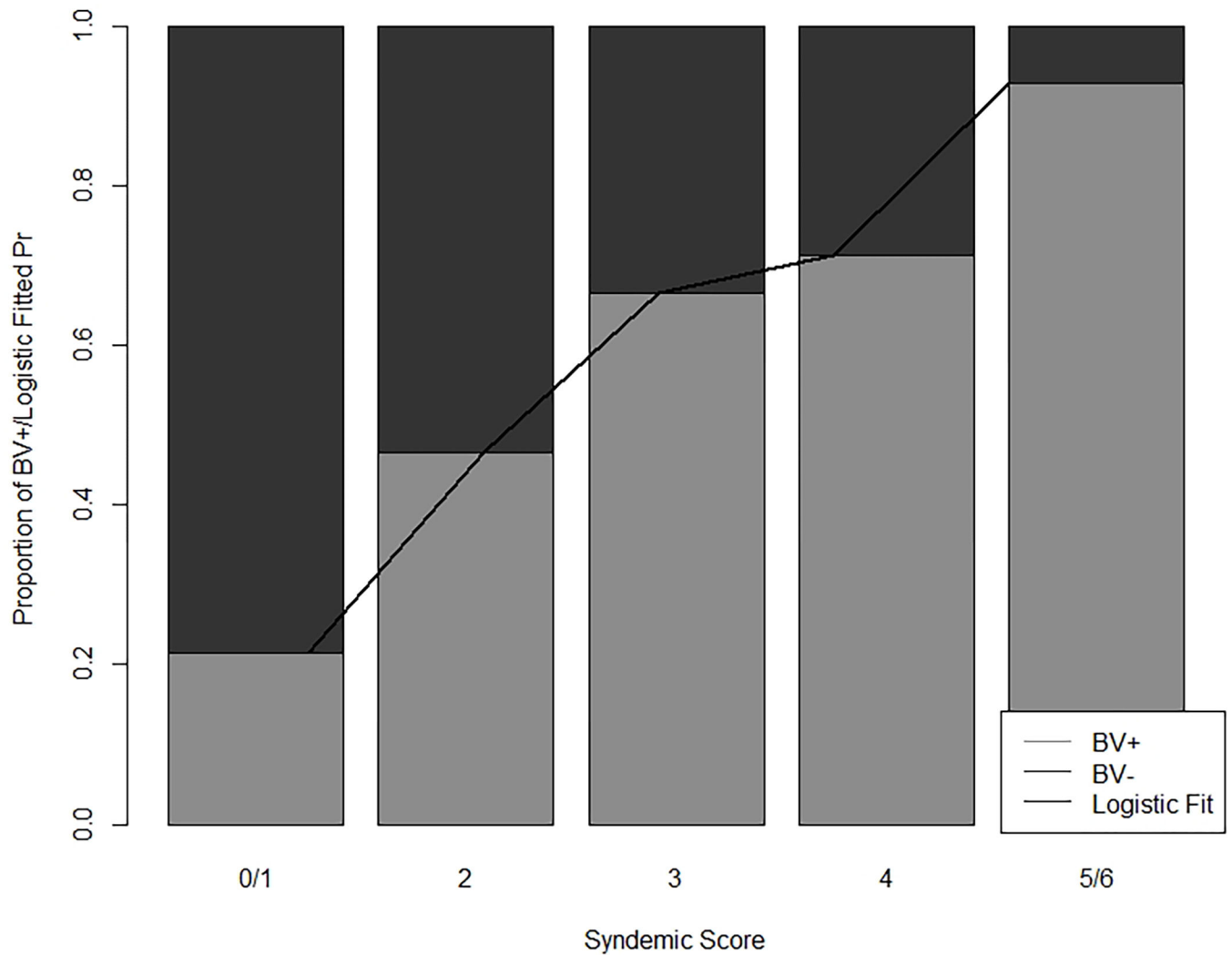


Figure 1. Probability of a Positive Diagnosis of Bacterial Vaginosis by Syndemic Score

A Stacked Barplot illustrating the percent BV positive for each syndemic level and the fitted probability positive for each syndemic score from the logistic regression. Syndemic factors included: Race, Ethnicity, Education, Vaginal Sex, Recent Cannabis Use, Reasons for Intravaginal Practices. A higher syndemic score was associated with increased odds of having BV among women of reproductive age

Table 1.

Sociodemographic, Sexual Behaviors, Substance use, and Intravaginal Practices by Diagnosis of Bacterial Vaginosis

	No Bacterial Vaginosis	Bacterial Vaginosis	Test Statistic	P
Total N=166^a	N=66 (39.8)	N=100 (60.2)		
Sociodemographic				
Age, mean ± SD	32.7 ± 8.1	32.4 ± 7.6	0.25	0.80
Ethnicity^b			4.00	0.04
Hispanic	24 (53.3)	21 (46.7)		
Non-Hispanic	42 (34.7)	79 (65.3)		
Race^b			21.69	<0.01
Black/African American	28 (27.5)	74 (72.5)		
White	34 (66.7)	17 (33.3)		
Other	4 (30.8)	9 (69.2)		
Education^b			2.63	0.01
Less High School	5 (17.2)	24 (82.8)		
High School	22 (36.7)	38 (63.3)		
Household Monthly Income			5.94	0.05
<\$1000	28 (31.5)	61 (68.5)		
1000 to \$3000	24 (45.3)	29 (54.7)		
>\$3000	13 (56.5)	10 (43.5)		
Sexual Behaviors^c				
Number of male partners, mean ± SD	1.35 ± 1.70	1.34 ± 1.3	0.03	0.98
Number of new sexual partners, mean ± SD	0.35 ± 1.09	0.28 ± 0.9	0.39	0.70
Use of male condoms^c			1.40	0.72
Always	15 (46.9)	17 (53.1)		
Sometimes	7 (33.3)	14 (66.7)		
Never	30 (38.0)	49 (62.0)		
Did not have vaginal sex	3 (50.0)	3 (50.0)		
History of Sex Work^d			NA	1.00
Yes	4 (36.4)	7 (63.6)		
No	62 (40.0)	93 (60.0)		
Type of Sex^{b c}			6.49	0.04
Vaginal and Oral	41 (48.2)	44 (51.8)		
Vaginal Only	14 (26.4)	39 (73.6)		
No Sex	11 (39.3)	17 (60.7)		
Substance use				

	No Bacterial Vaginosis	Bacterial Vaginosis	Test Statistic	P
Cannabis – Last Use^b			13.56	0.01
In the past year or later	14 (66.7)	7 (33.3)		
In the past month	10 (50.0)	10 (50.0)		
In the past week	1 (11.1)	8 (88.9)		
In the past day	4 (28.6)	10 (71.4)		
Today	2 (16.7)	10 (83.3)		
Cocaine – Last Use^d			NA	0.84
In the past year or later	6 (46.2)	7 (53.8)		
In the past month	1 (50.0)	1 (50.0)		
In the past week	0 (0.0)	2 (100.0)		
Today	0 (0.0)	1 (100.0)		
Alcohol Use – Frequency^d			NA	0.25
Less than one drink a month	7 (53.8)	6 (46.2)		
Less than 7 drinks a week	31 (44.9)	38 (55.1)		
Daily	2 (20.0)	8 (80.0)		
Intravaginal Practices				
History of IVP^c	46 (40.4)	68 (59.6)	<0.01	0.87
Reasons for IVP^{b d}			NA	<0.01
To clean myself	32 (34.8)	60 (65.2)		
To please my sex partner	13 (76.5)	4 (23.5)		
To prevent or cure infections	1 (20.0)	4 (80.0)		

Note: T-tests or Mann-Whitney tests were used for median/mean comparison of groups unless otherwise specified.

^aN (%) unless otherwise specified

^bVariables included in the Syndemic Score

^cTimeframe refers to the previous month

^dFisher's exact test

Table 2.

Syndemic Scores by Diagnosis of Bacterial Vaginosis

Score	No Bacterial Vaginosis N (%)	Bacterial Vaginosis N (%)
0	4 (80)	1 (20)
1	8 (61)	5 (38)
2	18 (51)	17 (49)
3	12 (35)	22 (65)
4	3 (20)	12 (80)
5	1 (9)	10 (91)
6	0 (0)	1 (100)

Note. A total of 166 were enrolled in the study. Syndemic factors included were race, ethnicity, education, vaginal sex, recent cannabis use, and reasons for IVP.

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Table 3.

Relationship of Syndemic Scores with Diagnosis of Bacterial Vaginosis

	Estimate	Standard Error	Z	p	Odds Ratio [95% Confidence Interval]
Intercept ^a	-0.69	0.50	-1.39	0.17	0.50 [0.17-1.29]
2 Syndemic Factors	0.64	0.60	1.05	0.29	1.89 [0.59-6.49]
3 Syndemic Factors	1.30	0.62	2.11	0.04	3.67 [1.13-12.97]
4 Syndemic Factors	2.08	0.82	2.55	0.01	8.00 [1.77-46.40]
5 to 6 Syndemic Factors	3.09	1.16	2.67	0.01	21.99 [3.18-453.71]

^aReference group is 0-1 Syndemic Factors

Syndemic factors included were race, ethnicity, education, vaginal sex, recent cannabis use, and reasons for IVP.

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