Literature Review

National STD Curriculum Podcast

What's the Relationship Between Bacterial Vaginosis (BV) and STIs?

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Season 4, Episode 4

This episode discusses four articles focusing on the association between BV and chlamydia, gonorrhea, *Mycoplasma genitalium*, and human papillomavirus (HPV).

Topics:

- BV
- Chlamydia
- Gonorrhea
- Mgen
- STI

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Disclosures

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References

Paper #1 **Paper #2** **Paper #3** **Paper #4** **Paper #5**

Transcript

Read along with the audio or jump to a particular chapter.

In this episode:

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introduction**[00:00] Introduction**

Hello everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] literature review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

background**[00:21] Background**

A recent article was published on bacterial vaginosis, which is also called BV for short, and the relationship between BV and chlamydia infection that I wanted to review in this episode. BV is not an STI, but there is some data to indicate a relationship between a diagnosis of BV and common bacterial STIs, although the pathogenesis is not fully clear. So, what is BV? It's vaginal dysbiosis resulting from a change in the vaginal bacterial flora. There's a decrease in *Lactobacillus* species and an increase in anaerobic bacteria. The prevalence of BV is about 25%, although there is a range depending on the population that is a studied. While most persons with vaginal genitalia and BV are asymptomatic, BV can lead to vaginal discharge, burning, irritation, or a change in odor that can be quite uncomfortable. Here are a few articles we'll talk about in this episode in relation to BV and STIs.

paper-1**[01:21] Paper #1**

Brown SE, Tuddenham S, Shardell MD, Klebanoff MA, Ghanem KG, Brotman RM. Bacterial vaginosis and spontaneous clearance of *Chlamydia trachomatis* in the longitudinal study of vaginal flora. J Infect Dis. 2023 Sep 15;228(6):783-791. **[PubMed Abstract]**

This first article for review was published in the *Journal of Infectious Diseases* in September of 2023 by Dr. Brown and colleagues. It is titled “Bacterial vaginosis and spontaneous clearance of *Chlamydia trachomatis* in the longitudinal study of vaginal flora.” Between 1999 and 2003, the longitudinal study of vaginal flora group followed over 3,500 reproductive-age women quarterly for one year. The study examined whether bacterial vaginosis (or BV) assessed via Nugent score and Amsel criteria is associated with greater persistence or spontaneous clearance of untreated chlamydia infection within 12-week intervals. And this is without antibiotics to treat chlamydia infection.

So, let's take a moment here to discuss a bit more about the Nugent score and the Amsel criteria.

BV can be diagnosed by using either the Amsel criteria or determining the Nugent score. The Amsel criteria is more clinically focused, while the Nugent score is more microbiologically focused, and it looks at a vaginal Gram stain. The Amsel criteria requires at least three out of the four symptoms or signs of BV, which might include abnormal vaginal discharge, clue cells on a wet mount, a vaginal pH greater than 4.5, or amine odor when the vaginal fluid is exposed to potassium hydroxide. A Nugent score, on the other hand, gives a range depending on the vaginal microbiota. So, for example, 0-3 is consistent with normal vaginal microbiota, 4-6 with intermediate microbiota, and 7-10 with a diagnosis of BV.

Now, spontaneous clearance of urogenital chlamydia in the absence of antibiotic treatment can occur, but persistent and recurrent chlamydia infection does increase the risk for adverse reproductive sequelae. The mechanisms and factors associated with spontaneous clearance of a urogenital chlamydia infection remains unclear.

1. Doctors found that 23% percent of participants (or 823 women) had at least one chlamydia-positive visit. Of the chlamydia cases without antibiotic treatment, 48% spontaneously cleared by the next visit, and 52% persisted at the next visit.
2. The authors did not find an association between chlamydia persistence and either coinfection with trichomonas or gonorrhea.
3. Participants with untreated chlamydia and an intermediate or high BV Nugent score at the index visit had a 1.7-fold and 1.9-fold higher odds of chlamydia persistence at the next visit, and this was

compared to participants with a low Nugent score of 0-3. This was adjusted for age, hormonal contraceptive use, condom use between visits, and marital status.
4. Participants with untreated chlamydia and an Amsel diagnosis of BV had a 1.4-fold higher odds of chlamydia persistence at the next visit when compared to those without a diagnosis of BV, adjusting for these same factors.
5. The authors did not find that race, lifetime history of chlamydia, index visit coinfection with either gonorrhea or trichomonas, sexual activity, number of sex partners, new or concurrent sex partners, use of intravaginal products, and treatment for symptomatic BV as associated with chlamydia persistence in the adjusted models—so they did *not* find an association.
6. There was no effect modification by BV symptoms in the Nugent BV models and no difference between the estimates for symptomatic versus asymptomatic disease in the Amsel BV models.

This study evaluated the association between BV and spontaneous-clearance chlamydia in a large observational cohort of participants and found that a diagnosis of BV is associated with greater chlamydia persistence. They found a nearly 2-fold higher odds of persistence of untreated chlamydia infection when BV was present. It's interesting there was no difference in the association comparing those with asymptomatic versus symptomatic BV and those who were treated for BV with antibiotics. The current practice and standard of care is to treat BV only when it's symptomatic. The authors review some of the possible reasons how vaginal microbiota might play a role in spontaneous clearance of chlamydia infection in this article.

paper-2**[05:36] Paper #2**

Schwebke JR, Lee JY, Lensing S, Philip SS, et al. Home screening for bacterial vaginosis to prevent sexually transmitted diseases. Clin Infect Dis. 2016 Mar 1;62(5):531-6. **[PubMed Abstract]**

Balkus JE, Manhart LE, Lee J, et al. Periodic presumptive treatment for vaginal infections may reduce the incidence of sexually transmitted bacterial infections. J Infect Dis. 2016 Jun 15;213(12):1932-7. **[PubMed Abstract]**

The next article to discuss was published in *Clinical Infectious Diseases* in March 2016 by Dr. Schwebke and colleagues. This article was titled “Home screening for bacterial vaginosis to prevent sexually transmitted diseases.” So, in this trial, it determined whether regular screening and treatment for asymptomatic BV reduces the 1-year incidence of chlamydia and gonorrhea infection. An important point of this study is about treating asymptomatic BV. As I mentioned earlier, current guidelines and standard of care recommend only treating symptomatic BV.

1. Women ages 15-25 years were recruited from ten sites in six locations throughout the U.S. Participants were screened every two months for one year and then randomized to treatment with either oral metronidazole 500 mg twice a day for seven days or just observation alone.
2. There were over 1,300 participants enrolled in the study, and adherence with mailing specimens obtained at home was high in both groups—greater than 80%. I thought it was interesting that they did self-testing. The participants obtained a vaginal swab sample and then rolled the swab across a microscopic glass slide, which was then mailed to a study laboratory.
3. The authors point out that self-testing for BV with vaginal swabs has excellent reliability and validity compared with clinician-obtained swabs in the published literature. I can imagine that self-testing has higher patient satisfaction, as well.
4. The mean age was 21 years; 78% of participants were Black or African American, 47% had one sex partner, and 46% had two or more sex partners. Overall, 5% of the participants were positive for gonorrhea, and 14% were positive for chlamydia at baseline.
5. The authors found that incidence of gonorrhea and/or chlamydia infection was 19.1 per 100 person-years for the treatment group and 18.5 per 100 person-years for the observation arm, so not really different, and it was not statistically significant.

6. The 1-year incidence rate of gonorrhea or chlamydia was 18.3 per 100 person-years for the BV treatment arm and 19.2 per 100 person-years for the observation arm. This difference was also not statistically significant.

Although STIs were common in this study, with nearly 20 infections per 100 women-years, the authors found no difference in the incidence of chlamydia or gonorrhea infection during the one year of follow-up, and this was regardless of whether the asymptomatic BV was treated. It's possible that either asymptomatic BV is not associated with women's increased risk of STIs or that cure rates or duration of cure were insufficient to protect against future STIs in this study.

If you're interested in learning more, there was another article published by Dr. Balkus and colleagues in the *Journal of Infectious Diseases* in 2016, and it reported on the periodic presumptive treatment for BV in women in the U.S. and Kenya. In this article, they treated women with intravaginal metronidazole plus miconazole or matching placebo each month for 12 months, and they actually found that the incidence of any bacterial STI was lower in the intervention arm compared with the placebo arm. So it will be good to hear of future studies on this topic.

paper-3**[08:52] Paper #3**

Lokken EM, Balkus JE, Kiarie J, et al. Association of recent bacterial vaginosis with acquisition of *Mycoplasma genitalium*. Am J Epidemiol. 2017 Jul 15;186(2):194-201. **[PubMed Abstract]**

The third article to review was published in the *American Journal of Epidemiology* in June of 2017 by Dr. Lokken and colleagues. It is titled “Association of recent bacterial vaginosis with acquisition of *Mycoplasma genitalium*.” This was a prospective longitudinal study where vaginal fluid specimens were collected every other month to test for *Mycoplasma genitalium,* I'll say *M. genitalium* for short in this episode, and this was done in female sex workers in Mombasa, Kenya, from 2005-2006. Testing was done by NAAT (or nucleic acid amplification testing). They also assessed vaginal microbiota monthly and categorized the microbiota by Nugent score, with a score of 0-3 as normal microbiota, 4-6 intermediate microbiota disruption, and 7-10 as a BV diagnosis.

1. The authors found that among the 280 women who enrolled, at baseline, 16% had *M. genitalium* infection, and 40% had BV. Fifty-four percent were seropositive for HIV.
2. They did a discrete failure time analysis for multiple events using logistic regression. This helped them to evaluate the relationship between BV at the visit prior to the *M. genitalium* testing, and then estimate the odds of incident infection at follow-up visits.
3. There were 59 incident *M. genitalium* infections among 50 women for an incidence rate of around 35 cases per 100 person-years.
4. They found that BV at the preceding visit was associated with a 3.5-fold increase in the odds of incident *M. genitalium* infection.
5. Among women with BV, 55% had at least one recurrence of BV with a maximum of four recurrences. Only 8% of visits with BV were accompanied by symptoms, and metronidazole was prescribed in only 3% of visits with BV (or in 24 women).
6. The odds of incident *M. genitalium* infection increased by 16% for each incremental point increase in a continuous Nugent score.

This study evaluated whether BV enhances a woman's susceptibility to *M. genitalium* infection in a longitudinal study with monthly assessment of the vaginal microbiota using the Nugent score. Prevalence of *M. genitalium* and BV was high in this cohort of women. The authors found that women with BV had a 3.5 times the odds of acquiring *M. genitalium* by their next study visit compared with women with normal vaginal microbiota. The authors also found that the odds of incident *M. genitalium* increase with each point increase in the Nugent score, and that might indicate a correlation of the severity of BV with the risk of acquiring *M. genitalium*.

paper-4**[11:38] Paper #4**

Li W, Liu LL, Luo ZZ, et al. Associations of sexually transmitted infections and bacterial vaginosis with abnormal cervical cytology: A cross-sectional survey with 9090 community women in China. PLoS One. 2020 Mar 26;15(3):e0230712. **[PubMed Abstract]**

The next article to discuss was published in *PLoS One* in March of 2020 by Dr. Li and colleagues. It is titled "Associations of sexually transmitted infections and bacterial vaginosis with abnormal cervical cytology: A cross-sectional survey with 9,090 community women in China."

1. This study screened more than 9,000 women in Shenzhen City in China for HPV [human papillomavirus] serotype, cervical cytology, *Chlamydia trachomatis*, *Neisseria gonorrhoeae, Trichomonas vaginalis,* and BV.
2. A diagnosis of BV was made based on the Amsel criteria, which we discussed earlier in this episode. The prevalence of BV was around 2%, and 206 women had BV at the time of testing.
3. The authors found that overall, 4% of women (or 357) exhibited abnormal cytology. Of these, 192 women were positive for high-risk HPV type. High-risk HPV serotypes are associated with cell changes that can lead to cervical cancer.
4. The authors found that infection with high-risk HPV serotype, *Neisseria gonorrhea* infection, a diagnosis of bacterial vaginosis, and ages 40-46 years old (compared to 20-39 years of age) significantly increased the risk of abnormal cervical cytology.
5. BV was significantly associated with abnormal cytological findings with an adjusted odds ratio of 1.94 after adjusting for high-risk HPV status.

This study suggests that maybe BV and *Neisseria gonorrhea* infection may act as an independent risk factor for atypical squamous cell formation, but further studies are needed in this area. It would be interesting to see if a previous diagnosis of BV, prior to the cytology diagnosis, can predict atypical squamous cell formation and if treatment of BV (symptomatic or asymptomatic) would influence outcomes. I'd also be interested in seeing if the Nugent score, as opposed to Amsel's criteria for the diagnosis of BV, would be associated with abnormal cervical cytology. A longitudinal study where patients were followed over time would also be interesting.

summary **[13:49] Summary**

To conclude, I'd like to summarize some key points from this session:

1. There was nearly a 2-fold higher odds of persistence of untreated chlamydia infection when BV was present.
2. Treatment of asymptomatic BV with oral metronidazole did not affect the incidence of gonorrhea or chlamydia infection.
3. BV may enhance susceptibility to acquisition of *M. genitalium* infection.
4. BV may independently increase the risk for cervical cytology abnormalities, but further studies are needed in this area.

credits**[14:21] Credits**

This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by the Centers for Disease Control and Prevention.

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