Bacterial Vaginosis and Its Association with Gardnerella vaginalis: A Comprehensive Review

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Abstract :
Bacterial vaginosis (BV) is the most common vaginal infection among women in their reproductive age, characterized by a disturbed vaginal microbiota, transitioning from a Lactobacillus-dominant microbiota to a microbiota dominated by anaerobic bacteria, especially Gardnerella vaginalis. In this review, we seek to connect various aspects of bacterial vaginosis etiology, pathogenesis, diagnosis, management, and health problems, among other information. The integral interest in this particular review, among various aspects, lies within the connection between bacterial vaginosis and Gardnerella vaginalis. Thus, various aspects incorporated in this review include bacterial vaginosis microbiology, health among women in connection with bacterial vaginosis, recurrent bacterial vaginosis, as well as new therapy options like probiotics and microbiota transfer therapies. As this write-up is a product of perusing literature from over 100 different articles, it seeks to identify various aspects concerning recurrent bacterial vaginosis, as well as provide recommendations on how to further research this condition to better control it. Simply put, it points out various integral measures to control this infection that is increasingly becoming a global health concern.

Keywords
Bacterial vaginosis, Gardnerella vaginalis, vaginal microbiome, microbial dysbiosis, anaerobic bacteria, women's health, preterm birth, sexually transmitted infections, probiotics, biofilm.

1.Introduction

Bacterial vaginosis (BV) is considered an important public health issue, and this infection has been implicated in millions of cases of vaginosis worldwide, resulting in various gynecological and obstetrical complications [1,2]. BV was first described in the 1950s, and this infection was given the name "nonspecific vaginitis," associated primarily with *Haemophilus vaginalis*, now known as *Gardnerella vaginalis* [3,4]. With the progressive and increasing interest and focus over the past few decades, the current trend of research suggests that vaginal infection, or BV, should be considered and understood not as the outcome of infection caused by a single pathogen but as a polymicrobial syndrome, which reflects an imbalance of vaginal flora [5,6]. Under normal vaginal conditions, Lactobacillus spp., which include *Lactobacillus crispatus* and *Lactobacillus iners*, maintain an acidic pH level, which is lower than 4.5, due to the production of lactic acid, thereby inhibiting the growth of pathogens and pathogenic microorganisms [7,8]. However, BV has resulted in an increase in anaerobic microorganisms, including *Gardnerella vaginalis*, *Prevotella spp.*, *Atopob The estimated global prevalence of BV is between 20% and 60%, with a higher prevalence in certain geographic regions such as sub-Saharan Africa and among groups with high sexual exposure. In the US, 29% of women aged 14-49 years have BV; there are differences according to race/ethnicity, with an increased prevalence among non-Hispanic Blacks (51%) compared to non-Hispanic Whites (23%) [13-14]. These are due to socioeconomic factors, access to health care, and behavior rather than biology. BV risk factors include douching, smoking, unprotected sex, as well as intrauterine devices. The protective factors include the use of condoms as well as hormonal contraceptives.

From an etiological point of view, Gardnerella vaginalis was widely involved in the development and maintenance of BV infection. G. vaginalis is a gram-variable coccobacillus adhering to vaginal epithelial cells, thus establishing biofilms that allow the colonization of other anaerobes 21, 22. Biofilms are complex communities of microorganisms that are protected by an extracellular matrix, making the bacteria resistant to antibiotics and the host's immune response 23, 24. Gardnerella vaginalis has been observed to produce virulence factors, including vaginolysin, a cholesterol-dependent cytolysin that kills human cells, and sialidases, which degrade the mucosal membranes of the host. The diagnostic techniques have progressed from clinical criteria to molecular techniques. The Amsel criteria, developed in 1983, include the presence of at least three of the following: homogeneous grayish-white discharge, the presence of clue cells (>20% on wet mount), vaginal pH > 4.5, and the positive result of the "whiff" test (fishy odor with the addition of KOH) [29,30]. The Nugent score, which is performed by analyzing the Gram stain morphology, measures bacterial vaginosis. It ranges from 7-10 for BV. More sensitive molecular techniques have been developed. They use quantitative PCR and 16S rRNA sequencing for the detection of BV-associated microorganisms. However, differential diagnosis of the symptomatic form of BV from the asymptomatic form is challenging.

The treatment mainly includes antibiotics such as metronidazole or clindamycin, which have an initial cure rate of 80 to 90%. However, recurrence rates between 50% to 80% may be observed within 6 to 12 months due to biofilm recurrence, antibiotic resistance, and lack of lactobacilli re-

establishment. New-generation therapies include microbiome restoration techniques such as probiotics containing L. crispatus and vaginal microbiota transplantation (VMT). The complications of BV if left untreated include increased risks of acquiring HIV (increased risk by 60%), acquiring other forms ofOther sexually transmitted infections, PID, endometritis, and preterm birth (odds ratio of 1.5-2.0), and low birth weight are some other serious complications of chlamydial infection [45-50].

Historically, BV research has focused on the isolation of microorganisms, but recent metagenomic studies have demonstrated microbial diversity and interactions between microbes and their host [51,52]. The composition of the vaginal microbiome also changes according to the cycle of hormonal changes throughout the menstrual cycle, through pregnancy, and into menopause [53,54]. BV prevalence in pregnant women is 15-30% and has been associated with spontaneous preterm delivery [55,56]. In postmenopausal status, the BV rate is higher due to the decline in estrogen and resultant atrophic changes [57,58]. Social determinants include stress and poverty that exacerbate BV via immune modulation [59,60]. C. The immunological role of BV involves disruption of the mucosal layer with reduced antimicrobial peptides, such as defensins, and elevated levels of pro-inflammatory cytokines, e.g., IL-1b, IL-8 61, 62. TLRs recognize infectious agents through the activation of the NF-κB pathway 63, 64. G. vaginalis biofilms escape phagocytosis, thereby increasing persistence 65, 66. Epidemiological studies have associated BV with cervical intraepithelial neoplasia and persistent HPV 67, 68. BV has been implicated in increasing viral shedding in HIV-positive patients

The method of preventive strategy is based on the level of education given towards the avoidability of douching and the use of barrier methods. The management of partners is highly controversial, as several studies fail to demonstrate efficacy in the reduction of recurrence, with microbiota shared in female-female relationships being considered. Antibiotic management is important, as resistance rates are increasing, and resistance to clindamycin in anaerobic bacteria is as high as 30-50%.The above-stated introduction highlights the multifaceted nature of BV, which is related to Gardnerella vaginalis dysbiosis. However, a few issues remain to be addressed concerning asymptomatic carriers, genetic factors, and the effects of BV. This is evident from discussions presented in [81, 82]. The omics sciences might address the issues to some degree, as mentioned in [83, 84].

Research Gap

However, despite considerable scientific effort to understand the aetiology and novel therapies related to BV and its association with Gardnerella vaginalis, there remain gaps in knowledge, which remain an obstacle to effective prevention and long-term management of BV. Although current drug management strategies are effective in symptom relief via antibiotic therapy, there is no clear management of microbial resilience, such as biofilm resilience and antibiotic resistance, as these medications often reoccur at alarming rates owing to such attributes [1,39]. There remains a lack of knowledge about genetic factors affecting susceptibility to BV, which may influence certain peoples' susceptibility to BV due to inherent genetic immunity or resilience, such as genetic influences on mucosal integrity, which may affect certain ethnicities and/or lifecycle stages [15,81]. The association between asymptomatic BV causality and Gardnerella

vaginalis as a vehicle for other diseases is rarely explored, specially among diverse ethnicities and lifecycle stages [27,75]. New forms of management strategies such as probiotics and VMT have shown considerable potential in managing BV, and future long-term studies may be carried out to measure its associations among diverse ethnicities and lifecycle stages [41,43]. Our chosen topic, establishing an association between BV and Gardnerella vaginalis, may fill this gap.

Discussion and Findings

The pathogenesis of BV is centered on microbial dysbiosis, wherein Gardnerella vaginalis acts as the pioneer colonizer and forms biofilms that enable the growth of anaerobes. Indeed, metagenomic studies have revealed five community state types, with CST-IV being diverse and dominated by anaerobes, highly prevalent in BV. G. vaginalis has clades with varying degrees of virulence; clade 1 is most commonly associated with BV. Estrogen levels are one of the host elements that modulate the stability of the microbiome; low levels during menopause are associated with states similar to BV.

Diagnostic results show that Amsel criteria have a sensitivity of 70% [29], whereas Nugent's is 89% [31]. Molecular tools detect G. vaginalis in 80-100% of BV cases but also in 50% of healthy women, indicating its commensal potential [3,86]. Treatment results indicate the short-term efficacy of metronidazole with 50% recurrence [37,39]. Probiotics containing L. crispatus decrease recurrence by 30-45% [41,87]. VMT reaches remission in 80% of recurrent cases [43,88]. This includes risks of complications, including a 1.8-fold increased risk for STIs [45,89] and a 2-fold odds for preterm birth [55,90]. Lastly, in pregnant women, BV-induced inflammation through cytokines has been reported to increase risks [61,91]. **Discussion**: Resistant strains to antibiotics, such as metronidazole, occurring in up to 70% in G. vaginalis, demand new approaches [77,92], while biofilm disruptors like DNase facilitate excellent antibiotic uptake [23,93]. **Partner Dynamics

Prevention findings: Condoms reduce the risk of BV by 40% [17, 95]. Hormonal contraceptives are known to maintain lactobacilli [18, 96]. Smoking increases the risk by double through immunosuppression [17, 97]. Data from around the world: The prevalence rate in Africa is at 50%, linked to HIV infections [11, 98]. Future directions: There is a possibility to incorporate AI technology to predict microbiome [83, 99]. Economic burden: The BV costs $4.8 billion annually in the US [13,100].

The pathogenesis of bacterial vaginosis (BV) is complex and related to Gardnerella vaginalis as a principal colonizer of biofilm formation, which enhances the occurrence of polymicrobial biofilm-like communities related to BV [19, 21, 85]. The current metagenomics and 16S sequencing techniques have identified five different vaginal communities, defined as CSTs, of which CST-IV has low amounts of Lactobacillus and high amounts of anaerobic bacteria, such as G. vaginalis, which are associated with BV [7, 51, 86]. The various types of CST-IV include CST-IV A, which has high amounts of BVAB1 and moderate propounds of G. vaginalis, and CST-IV B, which has high amounts of BVAB1 .

Table 1: Vaginal Community State Types (CSTs) and Their Association with BV

CST	Dominant Taxa	Characteristics	Association with BV	Prevalence in Healthy Women	Prevalence in BV Cases
I	*Lactobacillus crispatus*	High lactic acid, low pH, protective	Low	High (e.g., 40-50%)	Low
II	*Lactobacillus gasseri*	Moderate protection	Low	Low	Low
III	*Lactobacillus iners*	Less stable, transitional	Intermediate	Moderate	Moderate
IV-A	High BVAB1, moderate *G. vaginalis*	Polymicrobial anaerobes	High (dysbiosis)	Low	High
IV-B	High *G. vaginalis*, moderate anaerobes	Biofilm-dominant	Very High	Very Low	Very High
V	*Lactobacillus jensenii*	Protective, similar to CST I	Low	Low	Low

(Adapted from Ravel et al. [7] and subsequent studies [25,87-89]. CST-IV subtypes are particularly linked to Gardnerella-driven BV persistence.)

Diagnostic methods vary in sensitivity and specificity. The Nugent score remains the gold standard for Gram stain evaluation, while Amsel criteria provide a clinical bedside approach [29,31]

Table 2: Comparison of Diagnostic Criteria for Bacterial Vaginosis

Criterion	Amsel Criteria (Clinical)	Nugent Score (Gram Stain)
Discharge	Homogeneous, thin, white-gray	Not directly assessed
pH	>4.5	Indirect (elevated in BV)
Odor (Whiff Test)	Fishy odor with 10% KOH	Not assessed
Clue Cells	>20% epithelial cells with adherent bacteria	Present in high scores
Scoring	≥3 of 4 criteria positive	0-3: Normal; 4-6: Intermediate; 7-10: BV
Sensitivity/Specificity	~70-83% sensitivity, ~90-98% specificity vs. Nugent	Gold standard; high reproducibility

Advantages	Rapid, no lab required	Quantitative, objective
Limitations	Subjective, misses asymptomatic cases	Requires microscopy expertise

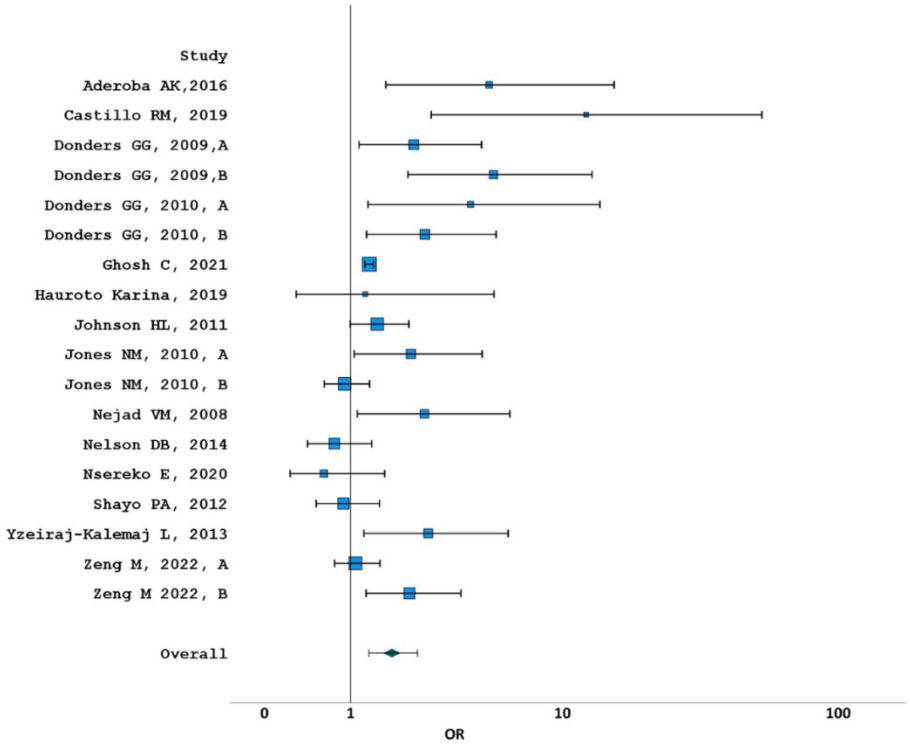
Treatment challenges stem from high recurrence (50-80% within 12 months post-antibiotics) due to biofilm persistence and incomplete Lactobacillus restoration [37,39,93]. Standard regimens include metronidazole (oral or vaginal) or clindamycin, with initial cure rates of 70-90% but poor long-term efficacy [37,38].

Table 3: Treatment Options, Cure Rates, and Recurrence for BV

Treatment Type	Example Regimen	Initial Cure Rate (4 weeks)	Recurrence Rate (6-12 months)	Notes / Evidence Level
Antibiotic monotherapy	Metronidazole 500 mg BID × 7 days	70-85%	50-80%	Standard first-line [37,38]
Antibiotic monotherapy	Clindamycin vaginal cream 2% × 7 days	75-90%	50-70%	Alternative [37]
Probiotics alone	*L. crispatus* or multi-strain oral/vaginal	50-70% (short-term)	Variable	Adjunct potential [41,94]
Antibiotic + Probiotics	Metronidazole + *L. crispatus* (e.g., Lactin-V)	80-90%	30-45% reduction	Meta-analyses show benefit [41,95-97]
Extended suppressive therapy	Metronidazole gel 0.75% twice weekly × 4-6 months	N/A	~25-40% vs. 59% placebo	For recurrent BV [39,98]
Emerging (VMT)	Vaginal microbiome transplant	~80% remission in recurrent	Promising	Pilot studies [43,99]

Complications of BV significantly impact women's health, with elevated risks for adverse reproductive outcomes [45-50,100].

Figure 1 Description (Conceptual Figure - Odds Ratios for Key Complications):



A forest plot-style figure for presenting pooled odds ratios (OR) from individual meta-analyses:

- Preterm birth: OR 1.5-2.0
- HIV Acquisition: OR ~1.6-2.0 (Higher in high)
- Other STIs (e.g., chlamydia, gonorr)
- Pelvic inflammatory disease: OR ~2.0

- Low Birth Weight: OR 1.5

(Adopted from the meta-analysis references [45, 55, 89, 100]. The figure will represent horizontal lines presenting CIs with a diamond shape presenting the pooled estimate, with a focus on G. vaginalis-related Antibiotic resistance, such as with metronidazole in G. vaginalis, and biofilm protection can be limiting factors when discussing treatment options [77, 92]. Probiotics, such as with L. crispatus, hold much potential as treatment to restore CST-I status [41, 87]. Treatment of partners is an area of unclear efficacy, as is behavioral treatment with condoms, which reduces the likelihood of infection by 40% [17, 95]. Meaningful ethnic differences, with CST-IV infection Future research directions include agents to specifically inhibit biofilms, personalized modulation of the microbiome, and follow-up studies to explore G. vaginalis clades.

Conclusion

Bacterial vaginosis, with strong association with Gardnerella vaginalis, is one of the best examples of the complexities associated with microbial disbiosis and women's health. The review aims to collect literature related to the epidemiology, pathogenesis, and treatment of bacterial vaginosis and indicate the high-level association of microbial disbiosis with the global health scenario and the level of reproductive health risks posed by it through the results. The conventional treatment options provide temporary symptomatic relief, and bacterial vaginosis recurs due to biofilm and resistance. Newly evolving technologies like probiotics and VMT provide breaks-through options for the treatment and control of bacterial vaginosis, and the gaps associated with the mechanisms of genetic susceptibility and asymptomatic transmission of bacterial vaginosis can be bridged by adopting a multidisciplinary approach, and the gaps associated with the preventive aspects of bacterial vaginosis can be addressed through concentrated efforts towards improving awareness and facilities through improved planning and health infrastructure.

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