Asian Jr. of Microbiol. Biotech. Env. Sc. Vol. 27, No. (3–4) : 2025 : 135-144

ISSN-0972-3005

DOI No.: http://doi.org/10.53550/AJMBES.2025.v27i03-04.002
Journal Home Page: www.envirobiotechjournals.com

BACTERIAL VAGINOSIS: UNDERSTANDING THE INFECTION, MECHANISMS, AND CHALLENGES OF RECURRENCE

N. PARVEEN[1], V. KHARE[2], F. HAIDER[3], S. KHAN[4], S.S. CHAUHAN[5], S. ALI[6] AND S.K. VISHWAKARMA*[7]

[1]Department of Microbiology, Era University, Lucknow 226 003, U.P., India
[4]Department of Pharmacology, PCPS College of Pharmacy, Mathura 281 004, U.P., India
[5]Yessthetics Face Clinic, Lucknow 226 031, U.P., India
[6]Department of Biotechnology, Amity University, Lucknow 226 028, U.P., India
[7]Department of Biotechnology, Kashi Institute of Technology, Varanasi 221 307, U.P., India

(Received 14 January, 2025; Accepted 3 March, 2025)

Keywords: *Bacterial vaginosis, Lactobacillus, Gardnerella, Biofilm, Vaginal infection, Preterm birth*

Abstract – One of the most common health issues affecting women is bacterial vaginosis (BV),that is result from alterations in the vaginal microbiome. It is frequently linked to vaginal inflammation, affects women's reproductive health and an increased chance of contracting sexually transmitted infections (STIs) such as HIV. Preterm premature rupture of the membranes and preterm birth are among the negative pregnancy outcomes that can result from BV in pregnant women, along with chorioamnionitis. Numerous risk variables, including age, sexual behavior, socioeconomic level, use of antibiotics, and ethnicity contributes to its pathophysiology. Due to the complicated polymicrobial nature of BV, diagnosis has proven difficult; nevertheless, there are numerous tests that may be used to determine the infection, including the gold standard now in use, which is the standardized evaluation of morphotypes on Gram stain analysis, as well as real-time clinical and microbiological testing. Conventional clinical and microscopic approaches have lower sensitivity and specificity, need more personnel and time, and are less accurate.Vaginal culture used improperly can be deceptive. Novel diagnostic techniques, such as point-of-care (POC) tests with high sensitivity and specificity. Inaccurate diagnosis of BV increases the risk of negative consequences for women's reproductive health and delayed treatment. Antigen-based diagnostics are expected to provide better insights into the disruption of vaginal flora caused by BV. Research highlights the global epidemiology of BV, risk factors, sexual transmission of BV-associated bacteria, and the potential of molecular diagnostic tests to improve detection and management.

INTRODUCTION

The human body is a holobiont consisting of the host and multispecies microbes, and the interdependency among them has been progressively enhanced in the approximately half a billion years of human–microbial coevolution. The vaginal microbiome is an intricate and dynamic microecosystem that constantly undergoes fluctuations during the female menstrual cycle and the woman's entire life.The common condition known as bacterial vaginosis (BV) is characterized by changes in the vaginal flora, where potential pathogens such as *Gardnerella vaginalis*, genital Mycoplasma, and fastidious anaerobic bacteria replace the normally prevalent *Lactobacillus* species. BV is a polymicrobial synergistic infection that produces complicated modifications in the normal vaginal flora by increasing the number of pathogenic organisms and decreasing the prevalence of lactobacilli (Abou Chacra *et al.,* 2022). Usually lactobacilli are the most common bacteria in the vaginal flora, while individual differences may exist. In the genital tract, bacteria linked to BV can cause viral replication and shedding, which could make women with BV more susceptible to HIV-1 infection

([1]Research Scholar, [2]Assistant Prof., [3]Associate Prof., [4]Pharmacist, [5]Dermatologist, [6]Research analyst, [7]Assistant Prof.)

in comparison to women with normal vaginal flora (Ziogou *et al.,* 2023). Bacterial vaginosis (BV) is the most common cause of vaginitis in women within the reproductive age range. It is the most common infection in the setting of outpatient gynecological care (Chee *et al.*, 2020). The flora of bacteria also include a variety of aerobic and anaerobic species. It is acceptable to refer to "disturbances of the normal vaginal flora," "vaginal infections," and "vaginal skin diseases" alike. Between 23% and 29% of women in the general population who are of reproductive age have BV worldwide. The prevalence of bacterial vaginosis in adults in India (Fig. 1) ranges from 17.8% to 63.7% (Farheen and Humera, 2017). According to the Centers for Disease Control and Prevention (CDC), it is the most prevalent vaginal infection among American women who are of reproductive age. Geographical and demographic factors determine the prevalence globally; studies indicate that up to 30% of women may be affected by BV at some point in their lives (Lachyan *et al.,* 2024). Vaginal health is defined as the absence of symptoms as well as the absence of risk factors for unfavorable outcomes like infection, infertility, miscarriage, or premature delivery. Certain *Lactobacillus* species dominate the vaginal microbiota of many women and have been linked to lower incidence of these reproductive health issues. The presence of lactobacilli at the mucosal surface of the gastrointestinal tract is linked to a downregulation of the immune response to inflammatory stimuli (Holdcroft *et al.,* 2023). This has led some to speculate that racial and genetic factors may affect the patterns of vaginal flora (Muzny and Schwebke, 2016).

Clinical features

The most common clinical manifestation of BV is increased, foul-smelling vaginal discharge. (Klebanoff *et al.*, 2004). The actual discharge is frequently thin and has a gray or milky hue (Xie *et al*., 2022). Pregnant women are more likely to give birth prematurely, and females who have been diagnosed with bacterial vaginosis are more likely to get other sexually transmitted infections (Kharsany *et al.,* 2016). The condition of bacterial vaginosis is linked to unfavorable pregnancy outcomes such as spontaneous early birth, endometritis following cesarean section, and second trimester miscarriages (Işik *et al.,* 2016). This underscores the significance of reviewing the literature on the subject. Patients typically complain of having a bad odor coming from their vagina, along with other clinical symptoms like burning or pain when micturition (Khedkar and Pajai, 2022). Increased vaginal discharge is a more prevalent indicator of bacterial vaginosis, despite being less specific. These indicators were found in 73% and 92% of patients, respectively, in studies involving symptomatic patients (Chen *et al*., 2021). Forty-five percent of research participants with irritating symptoms (pain, burning, and itching) might have been misdiagnosed with vaginitis from other conditions if symptoms alone had been used to confirm diagnosis and therapy (Mondal *et al*., 2023). Many risk factors, such as sexual activity (though it is not considered a STD), douching, and the lack of vaginal lactobacilli, have been linked to an increased susceptibility to BV (Esber *et al*., 2015). Although BV in and of itself may not always result in serious complications, it is associated with unfavorable outcomes like an increased risk of acquiring HIV and other STDs (Sousa *et al*., 2023). Furthermore, BV is associated with pregnancy complications like low birth weight and preterm birth, underscoring the importance of appropriate management (Garcia *et al.,* 2024).

Diagnosis

The diagnosis of BV is typically based on clinical criteria, including the Amsel criteria, and microscopic examination of vaginal fluid (Bhujel *et*

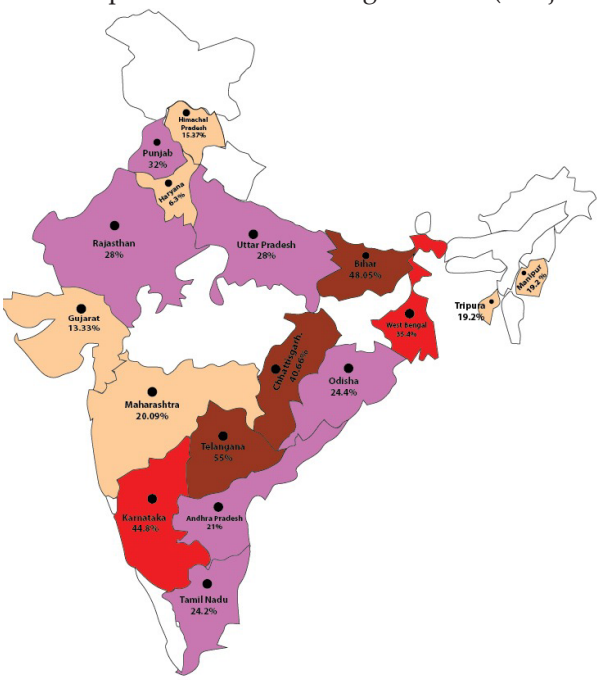

Fig. 1. Prevalence map of Bacterial vaginosis in India

al., 2021). Antibiotics are usually prescribed as part of treatment; metronidazole and clindamycin are the most often prescribed medications. Unfortunately, BV frequently returns even after successful treatment. A greater understanding of BV's effects on women's reproductive health is urgently needed, given the disease's complexity and frequency (Menard and Bretelle, 2012). Given that many BV-affected women do not exhibit any symptoms and that only 34% of women are sensitive to amine odor and 56% to increased discharge. A predominant granular micro flora with uncountable bacteria all over the slide, covering epithelial cells (clue cells) was diagnosed as 'full bacterial vaginosis'. As previously mentioned, areas that had a mixture of BV-like flora and normal-looking microflora expressing lacto bacillary morphotypes were categorized as "partial BV" (Donders *et al.,* 2010). Vaginal secretions stained with Gram's stain can be used to diagnose bacterial vaginosis. There are now two developed methods of interpretation. The more recent approach by Nugent and colleagues. Gram's stain can be used to identify clue cells. It may be easier to interpret such vaginal deliveries if clue cells are combined with reduced lactobacilli morphotypes on Gram's stain. When large numbers of *Gardnerella vaginalis*, *Prevotella* sp., *Bacteroides* sp., *Mobiluncus* sp., and *Mycoplasma hominis* replace normal lactobacilli, an ecological disorder known as bacterial vaginosis (BV) results. According to Amsel, smears are used in the clinical diagnosis when there is a combination of features such as fishy odor, uniform, grey, watery vaginal discharge, pH above 4.5, and typical findings during fresh wet mount examination of vaginal fluid (e.g., "clue cells") (Redelinghuys *et al.,* 2020). On Papanicolaou smears, clue cells and alterations in flora can also be found; however, these techniques have not shown to be as specific for bacterial vaginosis as alternative means of detection. Although more quick diagnostic techniques have been developed, they are primarily used for research to identify women who have bacterial vaginosis. The foundation of these tests is the identification of bacterial metabolic products in the vaginal secretions of vaginosis-affected women. Three examples of these tests are enzymatic analysis for proline aminopeptidase, thin-layer chromatography for putrescine and cadaverine, and gas-liquid chromatography for the detection of succinic acid (Discacciati *et al*., 2006). The ecosystem of the normal vagina is extremely complex. Lactobacilli make up the majority of the bacterial flora, but a wide range of aerobic and anaerobic bacteria can also be found; many of these are linked to bacterial vaginosis when found in higher concentrations. The amount of bacteria in the vaginal ecosystem of BV patients increases significantly (10^9 to 10^{11}/g of secretion) from the normal range of 10^5 to 10^6/g of secretion (Lamont *et al*., 2011). Since there isn't a single bacterium that inhibits lactobacilli and generates succinate to start the anaerobic over growth, *Gardnerella*, other anaerobes, and maybe genital mycoplasma could be involved in the full-blown syndrome's development (Amabebe and Anumba, 2018).

Pathophysiology

The stratified squamous nonkeratinized epithelium that constitutes the vaginal mucosa is covered by cervicovaginal secretion. The vaginal mucosa gets oxygen, glucose and other nutrients from underlying submucosal tissues through diffusion due to the limited blood supply. As a result, a somewhat anaerobic habitat condition is established. There is a complex microbial population in the vagina that lives in symbiosis with the host (Pekmezovic *et al*., 2019). The whole habitat, or vaginal microbiome, is therefore made up of bacteria, their genes, and the natural environment. *Lactobacillus* species grow in the anaerobic environment of the tent and produce various antimicrobial compounds such as lactic acid, hydrogen peroxide (H_2O_2) and bacteriocins, thus contributing to a healthy gut microbiome and offering defense against invading pathogens. *Lactobacillus* species are the main source of L-lactic acid and D-lactic acid, which keep the pH of the environment below 4.5 (Witkin *et al.,* 2013). Whereas epithelial cells contain 20% of L-lactic acid (Boskey *et al*., 2001). According to this finding, H_2O_2 is not a space killer for maintaining the pyramidal microbiome homeostasis. *Lactobacillus* synthesizes bacteriocins, antimicrobial peptides that penetrate the micro-membrane of non-natural microorganisms. In addition, they can adhere to epithelial cells and compete with other microbial cells for attachment sites. This discovery is significant because the pathogen's adhesion to epithelial cells is the initial and essential step towards infection. Notably, the degree of protection provided to the vaginal ecosystem depends on the dominant species of *Lactobacillus*. For instance, dysbiosis and low stability are usually related to the vaginal microbiota dominated by *L. iners*.

Conversely, *L. crispatus*, which produces D- and L-lactic acids, improves the health and high stability of the vaginal community. Unlike other Lactobacillus species, D-lactic acid-which is more significant than L-lactic acid-cannot be produced by *L. iners*. *Atopobium*, *Mobiluncus*, *Gardnerella*, *Prevotella*, *Bifidobacterium*, *Sneathia*, *Leptotrichia*, and certain new bacteria in the Clostridiales order known as BV-associated bacteria (BVAB 1-3) are among the facultative or obligate anaerobic microbes that are present in higher concentrations in Bifidobacterium-associated bacteria (BVB) cases. Out of the vaginal samples obtained from women with BV, *Gardnerella* is the most frequently found microbe (Petrova *et al*., 2015). An imbalance of the naturally occurring vaginal flora, which is characterized by an increase in the total number of bacteria present as well as a change in the most common type of bacteria present, is the cause of bacterial vaginosis. The predominant species in the normal vaginal microbiota is *Lactobacillus* (Hartmann *et al*., 1987). A decrease in the total quantity of lactobacilli is linked to bacterial Vaginosis (Coudray and Madhivanan *et al*., 2020). Though exact causes are unknown, *Gardnerella vaginalis* is thought to be the initial cause of most bacterial vaginosis infections. *Gardnerella* vaginosis forms a biofilm, which then fosters the growth of other opportunistic pathogen (Verstraelen and Swidsinski, 2019). Moreover, *G. vaginalis* generates vaginolysin, that plays a role in BV pathogenesis by inducing cell death by forming pores in the human cells through the p38 mitogen-activated protein kinase pathway with the aid of CD59 (Patterson *et al*., 2010). *Gardnerella* virulence is increased by the cholesterol-dependent cytolysin vaginolysin, which starts intricate signalling cascades that cause target cell lysis. *Gardnerella* can efficiently compete with *Lactobacillus* for dominance in the vaginal environment because it possesses the virulence elements that enable it to cling to host epithelial cells. It is thought that the growth of often latent vaginal anaerobes that form symbiotic associations with *Gardnerella* is the cause of the symptoms of bacterial Vaginosis (Baruah *et al*., 2014). *Gardnerella vaginalis* was the only species known to exist in the genus for around forty years. Up to thirteen new species, including *G. leopoldii*, *G.piotii*, and *G.swidsinskii* have been identified in more recent times (Kairys *et al*., 2024). Because bacterial vaginosis makes it possible for other vaginal pathogens to enter the upper genital tract, it is linked to a higher chance of contracting STIs in the future. The presence of enzymes that weaken the host leukocytes' defenses against infection and the increased release of endotoxins that promote the production of prostaglandins and cytokines in the vagina are also caused by bacterial Vaginosis (Hu *et al*., 2021). Women with higher concentrations of *G. vaginalis* compared to those with healthy vaginal microbiota experience displacement of healthy vaginal *Lactobacilli* like *L. crispatus*, leading to the initiation of BV biofilm production. BV involves a constantly changing imbalance of multiple types of microorganisms, with the formation of biofilms being necessary (Fig. 2). The cell-cell signaling mechanism known as quorum sensing (QS) controls the constant population density inside a biofilm. Different bacteria produce different QS signals, such as autoinducers (AIs), diffusible signaling factors (DSF), hydroxyl-palmitic acid methyl esters (PAME), indole, and N-acetyl homoserine lactones (AHLs) (Pena *et al*., 2019). Depending on the bacterial structure and activity, bacterial infections release a range of proteins that are controlled by QS, which enables them to take control of the host's immune system and promote pathogenesis through multiple secretory systems (T1-T7 and T9) (Swidsinski *et al*., 2005). The three phases of BV biofilm formation are primary adhesion, accumulation, and dispersion. It has been demonstrated that *G. vaginalis* is the most prevalent vaginal anaerobe. Its biofilm is highly resistant to lactic acid and hydrogen peroxide, upsetting the equilibrium of the normal vaginal ecology. Consequently, an abnormal decline in *Lactobacilli* is seen along with the growth of BV-associated or opportunistic pathogens. In addition to promoting aggregation, biofilm formation shields the microbial community from the host's immune system and antibiotics (Zhao *et al*., 2023). The release of bacteria andthe spread of disease are facilitated by the dispersion step. When grown on tissue-culture-treated polystyrene, strains of *G. vaginalis* obtained from infected women exhibit a thicker biofilm than some BV-associated anaerobes (*P. bivia*, *M. mulieris*, *A. vaginae*, *Veillonella*, *Peptostreptococcus*, and *Peptoniphilus*) (Pleckaityte, 2020). Vaginal epithelium is cytotoxically affected by the *vly* gene, a pore-forming toxin that is a member of the cholesterol-dependent cytolysins (CDCs). In biofilms, BV-associated *G. vaginalis* expresses low amounts of *vly*, which may help suppress the host immune response. After that, vaginal sialidase (neuraminidase) is produced, which is in charge of

breaking down the mucosal barrier, creating carbon sources for bacterial growth, and facilitating bacterial attachment. The presence of fimbriae and *G. vaginalis*'s capacity to produce sialidase and vaginolysin may aid in the biofilm's formation. The production of sialidase may result from sialic acid on the epithelial surface activating the sialidase gene. The concentration of *G. vaginalis* must reach a threshold in order to activate the sialidase gene, according to another theory.When exposed to sialidase, epithelial tissues block subterminal sugars, which increases the virulence of other bacteria linked to BV by facilitating their attachment (Liu *et al*., 2023). By creating an immunoregulatory environment, *Lactobacillus crispatus*, which generates both D- and L-lactic acid isomers, was found to be the healthiest *Lactobacillus* species that excludes HIV and bacteria linked to BV. Women with BV-associated microorganisms may easily contribute to HIV acquisition because they have a 13-fold increased risk due to higher *Prevotella bivia* concentrations and produce more CD4 T cells (HIV target cells). HPV infection is more likely to occur in women with BV. Women with HPV who have completely destroyed their *Lactobacillus* vaginal milieu are twice as likely to contract oncogenic HPV (Martius and Eschenbach, 1990). We know very little about the pathophysiologic mechanisms through which bacterial vaginosis can result in premature membrane rupture and/or preterm labor. A high concentration of virulent bacteria in the vagina, as in bacterial vaginosis, would increase the likelihood of membrane colonization (Sturm-Ramirez *et al*., 2000).

Role of cytokines in pathogenesis

High cytokine levels in genital secretions are more likely to be detected when STDs and other conditions, like vaginal douching or BV, disturb the flora and genital mucosa, making it more susceptible to bleeding. High levels of either TNF-α or IL-1b in cervical secretions were four times more common in women with BV than in those without infection. By activating the LTR promoter region, TNF-α and IL-1b can both increase HIV replication. Given the elevated cytokine levels in genital secretions, BV may have a substantial impact on HIV local replication, raising the risk of HIV infection. One of the potential biological explanations for why women with a changed vaginal flora are more susceptible to HIV infection is the induction of elevated proinflammatory cytokine concentrations in BV (Weissenbacher *et al*., 2010). The production of pro and anti-inflammatory cytokines in the vagina, however, does not seem to be significantly impacted by BV. Higher level of IL-10 were found in BV patients. In contrast, IL-12 was not detected. The concentrations of IL-6, IL-10, and IL-12 were measured with a commercial ELISA (Mitchell and Marrazzo *et al*., 2014). Cervicovaginal cytokine levels in BV have been measured by many workers, with varying degrees of success. According to the most of studies, women with BV have higher IL1β and lower SLPI. Numerous studies have also measured IL6 and IL8, with far more inconsistent

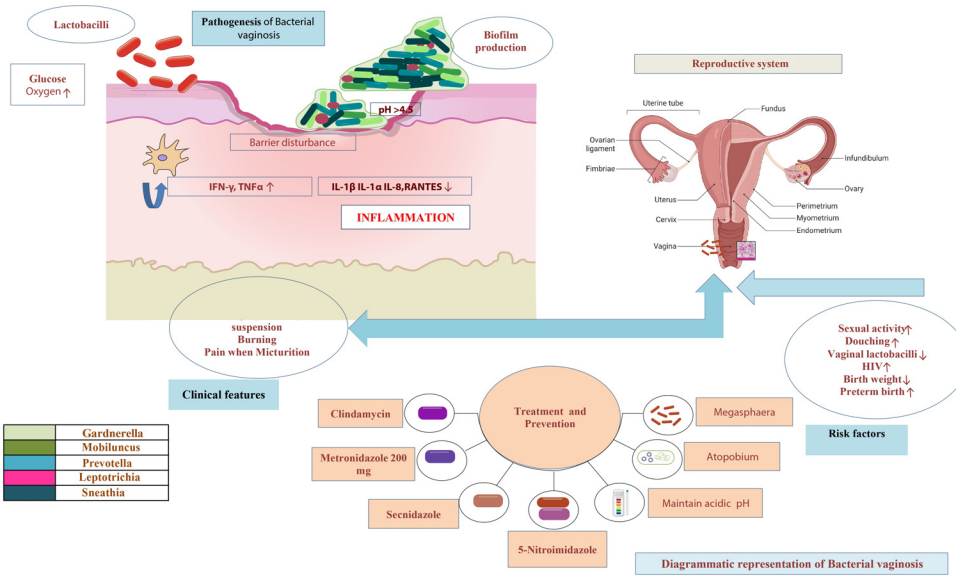

Fig. 2. Pathogenesis of Bacterial vaginosis

findings. A large number of these studies assessed pregnant women, whose vaginal cytokines are noticeably higher than those of non-pregnant women (Garcia *et al*., 2019). Only IP-10 production declines when basolateral tissue is inoculated with *G. vaginalis*, whereas cytokine secretion (IL-1β, IL-1ra, eotaxin, and IL-12) increases. It is believed that the cytopathogenic effect of vaginolysin protects the growth of *G. vaginalis* by eliminating host immune cells and components (neutrophils, cytokines, etc.). However, the inhibitory proinflammatory response might be caused by the cytokine IL-1ra. Higher levels of CD59 are found on the basolateral surface of the vaginal epithelium, which facilitates vly-mediated permeabilization and the release of lactate dehydrogenase (Eade *et al*., 2012). A large number of the analytes that were measured were below the limit of detection (IL-2, IL2-Rα, IL-3, IL-4, IL-5, IL-9, IL-12p40, IL-15, IL-16, IL-17, IL-18, eotaxin, IFN-α2, FGF-β, GM-CSF, MCP-1, MCP-3, MIG, Mip-1α, SCF, SCGF-β, TNF-α, TNF-β, TRAIL, and HGF. Other cytokines (IL-1β, IL-7, IL-10, and IL-13) were below 50 pg/ml in all conditions, indicating that the examined epithelia do not produce significant amounts of these cytokines at rest or as part of their immune response to BVAB. The cytokines IL-1RA, IL-6, IL-8, IP-10, RANTES, VEGF, Gro-α, and MIF, on the other hand, were recovered in ng/ml concentrations from certain conditions, suggesting that they are the main constituents of baseline or stimulated epithelial cytokine production. Comparing the concentrations of these analytes under BVAB and *L. johnsonii* conditions, it is found that the commensal *Lactobacillus* strain inhibited the cytokine responses from FRT epithelium more than the BVAB. The fold expression shading showed that BVAB increased the analytes IL-6, IL-8, G-CSF, IP-10, Mip-1β, RANTES, and Gro-α more than commensal lactobacilli did in all three epithelial lines. Additionally, when compared to the other bacteria tested, the BVAB *Atopobium vaginae* produced stronger cytokine responses from every type of epithelial cell, with certain chemokines reaching ng/ml concentrations under *A. vaginae*-stimulated conditions. Notably, it was found that End1 epithelial cells produced more cytokines than the other two types of reproductive cells. Following inoculation with *A. vaginae*, but not with the commensal *Lactobacillus* species *L. johnsonii* (Hanna *et al*., 2006). The mechanisms of disease in preterm labor and delivery have also been linked to other cytokines (IL-6, IL-10, IL-16, IL-18, colony stimulating factors (CSFs), and macrophage migration inhibitory factor (MIF)) and chemokines (IL-8, monocyte chemotactic protein-1 (MCP-1), epithelial cell-derived neutrophil-activating peptide-78, and Regulated on Activation Normal T cell Expressed and Secreted, or RANTES). Because of the cytokine network's redundancy, preventing preterm delivery in the context of infection requires more than just blocking one factor. One important cytokine for the maintenance of pregnancy is believed to be interleukin-10. In fact, compared to tissues from the first and second trimesters, the placentas of patients who are at term and not in labor produce significantly less IL-10, indicating that IL-10 down-regulation is a physiological phenomenon that promotes an inflammatory state around the time of labor onset. The regulation of inflammation-related preterm parturition has also been linked to IL-10. IL-10 expression was, in fact, lower in placental tissues from preterm labor and chorioamnionitis-complicated pregnancies than in placental tissues from normal controls. Crucially, IL-10 suppressed the expression of COX-2 mRNA in cultured placental explants from preterm labor deliveries, but not in those from term labor. This suggests that the mechanisms governing the inflammatory response during term and preterm parturition may differ (Cristofori *et al*., 2021). BV is regarded as a dysbiosis that frequently manifests clinical symptoms. The host immune response and a multitude of proinflammatory microbes can both contribute to this condition. High concentrations of immune mediators, including interleukin (IL)-8, IL-6, IL-1α, IL-1β, IL-12p70, and TNFα, have been found in vaginal samples from females with BV. For example, *L. crispatus* is linked to a significant decrease in IL-12 (p70), IL-8, IL-1β, and IL-1α, as well as a marked increase in gamma-induced protein 10 (IP-10). However, the analysis of vaginal swabs indicates that G. vaginalis is associated with an increase in IL-12 (p70), IL-8, IL-1β, and IL-1α and a decrease in IP-10. *A. vaginae* is linked to both an increase and a decrease in the same factors as *G. vaginalis*. High concentrations of *Prevotella* spp. have been found in females with higher levels of IL-1β, IL-8, and interferon (IFN)-γ. It is confirmed that IL-36G has a critical effect on BV-affected women. Consequently, women with BV have higher levels of IL-36G in their vaginal samples. The immune system's reaction to BV and other illnesses may be significantly influenced by IL-36G (McDonald *et al*., 2007).

Management

Antibiotics are widely used to treat bacterial vaginosis, even though up to 30% of cases resolve on their own. Whether it taken orally or vaginally, both of these methods function effectively. Pregnant women can use both methods without risk. Ten to fifteen percent of females may require additional treatment if the first round of antibiotics does not improve their condition. Since there is no risk of partner transmission and the condition is not considered a sexually transmitted infection, partners do not require treatment. Recurrences have been shown to occur in as many as 80% of women who receive therapy. If a patient continues to have symptoms, a second round of antibiotics is frequently given. A 2009 Cochrane study found some preliminary but insufficient evidence that probiotics could be used to prevent or treat bacterial vaginosis. Previous research suggests that pregnant women who exhibit signs of bacterial vaginosis should start taking clindamycin before week 22 in order to reduce the likelihood that labor will start before week 37. It is not entirely clear whether screening or treating bacterial vaginosis in the general population can reduce the risk of negative outcomes like preterm birth. Women who exhibit symptoms should be tested and treated for bacterial vaginosis, even though asymptomatic women may not be screened for it at this time. Clindamycin is believed to be safe for pregnant women to take either orally or vaginally. Mehta's systematic study found that therapy among male partners did not prevent recurrent bacterial vaginosis. For seven days, 200 mg of metronidazole is taken orally three times a day. For five days, metronidazole gel (0.75% of 5 g) is applied intravaginally once daily for full treatment. For five days, clindamycin is typically administered intravaginally as a gel (2% of 5 g) once daily. It has been demonstrated that vaginal application once daily for five days can prevent obstetric issues. Concurrent attendance by sexual partners is also recommended. According to a study, these drugs cure 80% of patients (Nyirjesy *et al.*, 2018). The U.S. Food and Drug Administration (FDA) authorized secnidazole in 2017 for use as a single oral dose to treat bacterial vaginosis. A next-generation 5-nitroimidazole, secnidazole has long been used to treat bacterial and parasitic infections. A single-dose clindamycin vaginal gel was authorized by the FDA in 2021 to treat bacterial vaginosis in females 12 years of age and up. Because of its ease of use and favorable effects on patient compliance, the addition of a single-dose therapy was praised (Ling *et al.*, 2010). By using barcoded pyrosequencing and PCR-DGGE fingerprinting, the bacterial diversity of the vaginal microbiota can be examined. These two molecular analytical techniques are widely used to match vaginal phylotypes like *Lactobacillus*, *A. vaginae*, uncultured *Sneathia* sp., *Fusobacterium nucleatum* subsp., uncultured *Eggerthella* sp., and uncultured *Megasphaera* sp. However, because more phylotypes were identified using pyrosequencing analysis than PCR-DGGE fingerprinting, the bacterial communities identified using this method were more diverse than those determined using PCR-DGGE analysis. In order to make up for the PCR-DGGE method's inability to detect small populations in the microbiota, pyrosequencing offered a high-throughput method for analyzing 16S rRNA gene sequences and thoroughly exploring bacterial diversity in various microhabitats. The total amount of bacterial diversity in the vagina could not be revealed by band richness because PCR-DGGE could only identify the predominant microbiota. Using the UniFrac algorithm for clustering analysis, it was discovered that the two groups' cluster profiles were comparable. Two clusters were created from the samples in the CN group and the BV group, respectively (Darbandi *et al.*, 2022). It is essential for keeping the population of BV-associated bacteria at low levels and lowering the risk of infections by pathogenic microorganisms to maintain an acidic vaginal pH, which is maintained by lactobacilli and other lactic acid-producing bacteria. Additionally, it is likely that the low pH in the vaginal cavity facilitates the lysis of exfoliated epithelial cells and increases the amount of glycogen released into the vaginal lumen for lactobacilli to use. Moreover, lactobacilli produce a proteins with antibacterial activities known as bacteriocins (Plummer *et al.*, 2021). Supplying a supplementary means of upholding their supremacy. It is unclear if *Atopobium*, *Megasphaera*, and *Leptotrichia* species, among others, can successfully replace lactobacilli in suppressing the growth of bacteria linked to BV. Lactic acid does not affect lactobacilli, but it specifically inactivates bacteria that are part of the BV microbiota. Therefore, it stands to reason that the presence of any lactic acid-producing bacteria, not just lactobacilli, would predominate in the vagina and prevent the development of BV. Metronidazole is the most often prescribed oral treatment for BV in both pregnant and non-pregnant women. Individual

cure rates for a 500 mg metronidazole course administered twice daily for seven days range from 84% to 96%, while cure rates for a 2g single dose of metronidazole are 54-62% (Deborah *et al*., 2002).

CONCLUSION

Bactrial vaginosis is a very common disease but general public is not aware of this. Despite predominance, the primary cause of this disorder is a decrease in *Lactobacillus* population in the vaginal tract, which varies by geographic location.In addition to dysbiosis, BV raises the risk of STIs by increasing the chance of co-infection among infected women. BV risk factors include advanced age, lack of literacy, having several sexual partners, and not using contraception. Improved analytical tools like multi-state Markov models and structural equation modeling are crucial for understanding the connection between BV and sexual correlates. More research employing the "omics" technique might provide additional information. Because of the complexity of the infection and the patient's risk behaviors, the recovery path in BV may not be as clear-cut as it seems; however, more thorough research can help manage BV.

ACKNOWLEDGEMENT

We extend our heartfelt gratitude to our respective institutions Era University (NP, VK and FH), PCPS College of Pharmacy (SK), Yessthetics Face Clinic (SSC), Amity University (SA), and Kashi Institute of Technology (SKV) for their continuous support and encouragement throughout the completion of this review article.

Conflict of Ineterst

There is no conflict of interest.

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