Review

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The Role of Vaginal Microbiota Dysbiosis and Inflammation in Reproduction and Pregnancy Outcomes

Xiang Li[1,*], Jianzhen Zhao[1], Shuzhan Li[2]

[1]Department of Gynecology and Obstetrics, Tianjin Medical University General Hospital, 300052 Tianjin, China
[2]Department of Biological Therapy, Tianjin Medical University Cancer Institute & Hospital, 300060 Tianjin, China
*Correspondence: lxdemail2023@163.com (Xiang Li)
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The human vagina harbors various types of microorganisms, and the normal female vaginal microbiota is in a dynamic balance ecosystem, with *Lactobacillus* as the predominant organism. Vaginal microbiota dysbiosis is influenced by disordered hormone regulation, autoimmune imbalance, and pathogen invasion. This dysbiosis not only adversely affects women's health and fertility but also has a negative impact on the development of babies during pregnancy, especially in terms of inflammatory responses and complications. The inflammatory response within the vagina is the first to reflect vaginal microbiota dysbiosis. Therefore, understanding the mechanisms by which host inflammatory responses triggered by changes in the microbiota lead to disease progression is critical for prevention and treatment strategies. In this review, we conducted a search of the PubMed electronic databases for studies published before August 2023 with keywords "vaginal microbiota", "inflammation", "reproductive", "fertility", and "pregnancy". We also manually searched relevant references from retrieved manuscripts and review articles. We aim to summarize the research focused on inflammation and complications induced by dysbiosis of the vaginal microbiota and the impact on female fertility and pregnancy outcomes.

Keywords: vaginal microbiota; inflammation; female genital tract; immune response

Introduction

The vaginal microbiota plays a crucial role in maintaining vaginal health and preventing disease. A healthy vaginal microbiome is typically dominated by *Lactobacillus*, especially *Lactobacillus curvatus*. The presence of non-*Lactobacillus*-dominated vaginal microbiota increases the risk of developing bacterial vaginosis (BV) [1]. A healthy vaginal microbiota, dominated by normally resident microorganisms, serves as a protective barrier against pathogens. However, an imbalance in the vaginal microbiota can lead to inflammatory responses and disruption by pathogens, resulting in vaginal dysbiosis (Fig. 1). This condition can have several clinical implications, including a higher susceptibility to genital infections, increased risk of preterm birth, and adverse outcomes in assisted reproduction [2].

Vaginal dysbiosis significantly affects women's fertility and pregnancy outcomes. The vaginal microbiota can influence women's hormone levels, immune response, and metabolism [3–5]. Vaginal dysbiosis can lead to various diseases, including female infertility and serious pregnancy complications [6,7]. The dysbiosis of the vaginal microecological system is associated with the development of vaginitis, cervicitis, endometritis, pelvic inflammatory disease, human papillomavirus (HPV) infection, polycystic syndrome, uterine adhesions, cervical lesions, and gynecological malignant tumors [8]. During pregnancy, vaginal dysbiosis is also linked to adverse outcomes such as premature rupture of membranes, preterm birth, diabetes, and chorioamnionitis [9].

In this review, we have summarized the impact of vaginal microflora dysbiosis and inflammation on female fertility and pregnancy outcomes. By systematically evaluating a series of related studies, we aimed to gain a deeper understanding of the microbial factors influencing female reproductive health. By identifying and understanding the risk factors that result from vaginal dysbiosis, physicians and researchers can better prevent and treat the associated conditions, thereby improving women's reproductive health and pregnancy outcomes.

Vaginal Dysbiosis Induces Inflammation and Infertility

Endometriosis

The prevalence of endometriosis (EMs) among women of reproductive age is approximately 10–15% and is one of the main causes of infertility [10]. EMs is associated with a downregulation of *Lactobacillus* abundance, which can lead to persistent immunological dysregulation and the development of a chronic inflammatory state, as well as promote angiogenesis and cell adhesion [11].

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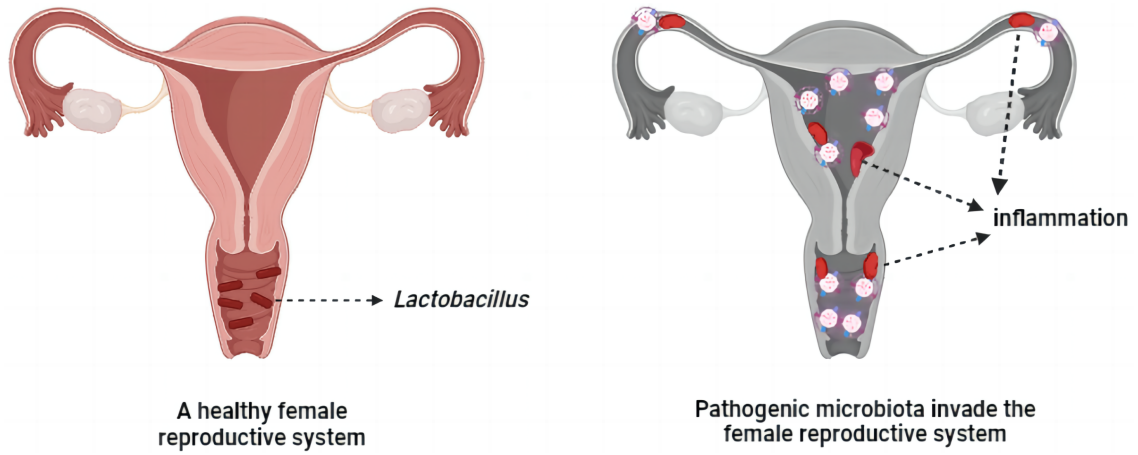

Fig. 1. The main microbiota in the healthy female reproductive system (left) and pathogenic microbiota that invaded and caused inflammation (right). Created with BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates.

Regulating the vaginal microbiota through antibiotics or probiotics may serve as a treatment or prevention for EMs [12]. In the vaginal environment of patients with infertility due to EMs, there is a decrease in *Lactobacillus*, an increase in bacterial diversity, and a prevalence of anaerobic bacteria. Therefore, adjusting the abundance of *Lactobacillus* in the vagina could be a prospective therapeutic approach to improve infertility in EMs [13]. Analysis of laparoscopic surgical samples has revealed a link between the vaginal microbiota and EMs; women with EMs have a higher presence of infectious bacteria in the vagina, and there is a significant correlation between the abundance of *Lactobacillus* in the vaginal microbiota and infectious bacteria [14]. Effective management of EMs often involves hysterectomy, and investigating drugs that target the vaginal microbiota may lead to the development of less invasive and highly effective treatments.

Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder that affects women of reproductive age. Research has shown that there is a dysregulation of the vaginal microbiota in patients with PCOS. The abundance of *Lactobacillus crispatus* in the vaginal microbiota of patients with PCOS is reduced, while the abundance of *Mycoplasma* and *Prevotella* is higher [15]. *Prevotella* is a potential causative agent of many inflammatory diseases [16] and is closely related to BV [17]. The reduced abundance of *Lactobacillus* in the vaginal microbiota of patients with PCOS has been associated with a higher risk of various adverse pregnancy outcomes, vaginitis, infertility, miscarriage, stillbirth, preterm birth, and repeated implantation failure [18]. Salah *et al*. [19] found that the prevalence of BV in patients with PCOS reached 42.5%. Patients with PCOS may be in a chronic inflammatory state.

Pelzer *et al*. [20] found an increase in Interleukin 8 (IL-8) expression in the vaginal secretions of PCOS patients, suggesting an inflammatory condition in the vagina. The increase in local vaginal chemokines such as IL-8 and IL-18 was associated with the type of vaginal microbiota, and the level of IL-8 was inversely correlated with the number of *Lactobacillus* [20]. Anahtar *et al*. [21] studied the relationship between different community state types (CSTs) and inflammation markers and found that IL-8 and IL-1β were significantly higher in CST IV than in CST I, and IL-8 was significantly elevated in CST III. Therefore, PCOS may cause vaginal microecological dysfunction by locally regulating the levels of inflammatory factors and changing the structure of the vaginal microbiota. Most current studies are cross-sectional and cannot specifically elucidate the causal relationship between the development of PCOS and vaginal microbiota dysbiosis. However, the analysis of PCOS using multi-omics techniques is expected to be a promising direction [22].

Vaginitis and Pelvic Inflammatory Diseases

Previous studies have shown that 40% of patients undergoing *in vitro* fertilization and embryo transfer (IVF-ET) have abnormal microbiota in their reproductive tract [23]. Infections and imbalances of bacteria, mycoplasma, and chlamydia in the vagina are associated with vaginitis and pelvic inflammatory disease [24,25]. The primary cause of infertility is tubal factor. Tubal dysfunction can develop from both acute and chronic inflammation. In the case of an infection, adhesions, damage to the tubal mucosa, or blocked tubal transportation can lead to tubal injury [26].

Persistent, chronic inflammation resulting from imbalanced vaginal microbiota can reduce the openness and cause obstruction of the fallopian tubes. It can also alter the anatomical structure and function of the female reproductive tract, leading to complications such as ectopic pregnancy, chronic pelvic pain, and even female infertility [27]. This condition is considered one of the primary causes of early adverse pregnancy.

Endometritis

Traditionally, the uterine cavity was considered a sterile environment. However, recent studies have revealed the presence of microbial colonization of the uterine cavity, with *Lactobacillus* and *Anaplasma* being the dominant species in the normal uterine cavity microbiota [28]. These studies have also shown that the translocation of vaginal microbiota to the uterus regulates the composition of the uterine microbiota. Furthermore, the synchronization of vaginal and uterine microbiota changes with age, and the translocation of pathogens to the vagina can lead to endometritis symptoms [29].

Chronic endometritis is significantly associated with changes in the vaginal microbiota, and the study of the vaginal flora is likely to aid in the diagnosis of endometritis [30]. The implantation of the embryo into the endometrium is the most important event that determines the success of IVF-ET [31]. Chronic inflammation affects the secretion of endometrial glands, causing local infiltration of inflammatory cells and exudation of inflammatory mediators, resulting in cytotoxicity. This cytotoxicity is detrimental to sperm survival and embryo implantation [32].

Recurrent Implantation Failure (RIF)

A decrease in the proportion of *Lactobacillus* in the vagina or disturbance of vaginal microecology can lower embryo implantation and pregnancy rates [33]. *Atopobium* and *Gardnerella* can form biofilms in the vagina, preventing *Lactobacillus* from colonizing the surface of the luminal epithelium and reducing the expression of lactic acid, which indirectly affects the embryo implantation process [34]. Additionally, the metabolites of the vaginal microbiota can influence the success rate of implantation. The changes in the composition of vaginal metabolites in patients with RIF may be caused by changes in the composition of microorganisms, which may be one of the important mechanisms leading to the pathogenesis of RIF [34]. Previous studies have reported that glycerophospholipids and benzopyrans are metabolites found at low levels in RIF patients. Benzopyrans, which act as selective estrogen receptor modulators, have been shown to influence endometrial tolerance [35]. However, the expression of benzopyrans is significantly reduced in RIF patients, which may contribute to the occurrence of infertility [36].

Vaginal Microecological Characteristics and Pregnancy Outcome

Characteristics of Vaginal Microbiota during Pregnancy

The composition of the vaginal microbiota in pregnancy is characterized by a higher abundance of *Lactobacillus spp.* and greater stability throughout the entire pregnancy [37]. Low levels of *Lactobacillus* can lead to excessive inflammation, while *Lactobacillus* is effective in preventing the negative consequences of inflammation during pregnancy [38]. Research has shown that *Lactobacillus crispatus* is the dominant vaginal microbe in women who have given birth at full term, while *Lactobacillus iners* is the dominant vaginal microbe in women who have miscarried [39].

Changes in hormones, immune cells, and cytokines during pregnancy alter the immune system of the vaginal mucosa, leading to a shift in the balance between Th1 and Th2 cells. This imbalance reduces immunity and increases susceptibility to opportunistic infections caused by conditionally induced pathogens, posing a high-risk factor for pregnancy outcome [40]. Recent research has shown a reduced abundance of *Lactobacillus spp*. and increased α diversity in first-trimester miscarriage [41]. *Lactobacillus*-depleted vaginal microbiota also appears to be a risk factor for ectopic pregnancy.

Premature Rupture of Membranes and Preterm Birth

Vaginal dysbiosis is associated with preterm rupture of membranes. A high-risk microbiota, characterized by a reduced abundance of *Lactobacillus*, is a contributing factor to preterm rupture of membranes [42]. Reduced vaginal *Lactobacillus* is present before membrane rupture in approximately one-third of cases compared to term births [43]. Studies have shown that premature rupture of membranes is associated with the complexity of the vaginal microbiota, and the presence of *Mollicutes* in the vaginal flora has been found to be associated with gestational age [44].

Preterm birth is associated with abnormalities in the vaginal microbiota during early pregnancy, characterized by significantly lower levels of *Lactobacillus curvatus*. Additionally, *Lactobacillus iners* has been associated with premature birth due to dysbiosis of the intravaginal environment [45]. An increased positivity of *Mycoplasma urealytium* is also a risk factor for preterm birth [46]. One of the predisposing factors for premature rupture of membranes is the secretion of large amounts of endotoxin by the causative organism, leading to an overproduction of inflammatory factors and the release of cyclooxygenase and phospholipase enzymes, which in turn increases prostaglandin synthesis [47].

Chorioamnionitis

Chorioamnionitis (CAM) is a disease in which bacteria directly invade the fetal membranes, umbilical cord, or placenta, resulting in inflammatory symptoms in the uterus [48]. It is a significant intrauterine infection in pregnant women that can result in adverse pregnancy outcomes, such as preterm labor, miscarriage, neonatal asphyxia, and fetal lung and gastrointestinal tract injury [49]. The most common route for microbes to cause this infection is by ascending from the vagina [50], and there is a notable correlation between ascending infection of the vaginal microbiota and CAM [51]. CAM is typically caused by bacteria entering

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the uterine cavity from the vagina or cervix and then passing through the opening of the cervix into the uterine and amniotic cavities. Normally, the mother's defense mechanisms prevent bacterial infections from entering the uterine cavity. However, factors such as cervical laxity, trauma, and preterm labor can suppress the defense mechanism, increasing the risk of infection [48].

Genital mycoplasmas, particularly the *Ureaplasma* species [52], are the most common microorganisms found in the amniotic cavity. Increased vaginal microbial complexity is also a significant clinical risk factor for CAM [51], with causative bacteria including gram-negative (e.g., *Escherichia coli* and *Klebsiella*) and gram-positive (e.g., *Staphylococcus aureus* and *group B streptococci*) bacteria [53]. A trial of oral probiotics to prevent bacterial vaginitis showed a lower incidence of CAM in the probiotic group [54]. The vaginal microbiota can also be used to assess the risk of CAM in preterm infants [55].

Gestational Diabetes

Gestational diabetes mellitus (GDM) is a common complication in pregnant women, with a prevalence rate of approximately 1.5%–4% [56]. Excessively high blood glucose and estrogen levels in pregnant women change the vaginal microbiota, resulting in vaginal dysbiosis and inflammation [57]. GDM increases the risk of adverse pregnancy outcomes, which can have serious implications for the health of both the mother and the infant [58,59]. The abnormally high levels of estrogen in pregnant women with GDM cause physiological changes in the vaginal mucosa, increasing the permeability of the vaginal epithelium and weakening the local mucosal barrier function.

In addition, high blood glucose levels in GDM lead to a significant accumulation of glycogen in the vaginal epithelium. This causes mucosal congestion, edema, and increased vaginal secretions. Consequently, pathogens can more easily invade, reducing the population of dominant *Lactobacillus* and allowing other pathogens to proliferate. This disrupts the vaginal microecological balance, leading to vaginal dysbiosis [60]. GDM patients also experience abnormal humoral and cell-mediated immunity, and vaginal microbiota disorders exacerbate the degree of inflammation [61]. In GDM patients, the peripheral blood levels of cluster of differentiation 4 ($CD4^+$), $CD4^+/CD8^+$, and NK cells were reduced, and there was a significant imbalance of Th1/Th2 cells, increasing the risk of pregnancy termination [62].

Vaginal Dysbiosis and the Immune Response

Characteristics of the Vaginal Microbiota and Evaluation Indicators

The dynamics of the microorganisms in the vaginal microbiota constitute the vaginal microbiome (VMB), which varies in composition based on factors such as racial differences and geographic location [63]. The microbiota in the vagina is mainly comprised of *Lactobacillus*, which accounts for approximately 95% [64]. Next-generation 16S rRNA high-throughput gene sequencing technology has identified five major CSTs for the microorganisms in the vagina, with four CSTs being dominated by different *Lactobacillus* species (*L. crispatus*, CST I; *L. gasseri*, CST II; *L. iners*, CST III; and *L. jensenii*, CST V). CST IV is characterized by a significant proportion of obligate anaerobic bacteria, including *Atopobium*, *Gardnerella*, *Prevotella spp*., and other bacterial species [65]. These CSTs are capable of producing lactic acid [66] and maintain a lower pH environment (3.0–4.5) in the vagina. The presence of *Lactobacillus* on the epithelial surface prevents the adherence of pathogenic bacteria, thus aiding in the prevention of reproductive tract diseases such as bacterial vaginitis.

Assessing the vaginal microecology in women of childbearing age involves two main aspects: morphological and functional evaluations. Morphological assessments encompass flora density, diversity, dominant organisms, pathogenic microorganisms, and inflammatory responses. On the other hand, functional assessments mainly focus on the detection of secretions and biochemical indices, including pH, leukocyte esterase, leukocytes, bacilli, hydrogen peroxide, sialidase, and β-glucuronidase. The Nugent scale can be used for this purpose, where scores of 0–3 indicate normalcy, 4–6 represent a transitional type for BV, and scores $\geq$7 indicate BV-positive [67]. Sequencing of the 16S rRNA gene amplification and the application of the Dirichlet multinomial mixtures (DMM) model can also be utilized. This involves DNA extraction and amplification of 16S rRNA fragments to sequence the bacterial genome of vaginal secretions. It is used to identify the dominant vaginal microbiota and other constituent genera, as well as to determine the type of CST based on the DMM model [68].

Immune Response in Vaginal Dysbiosis

Vaginal Microbiota and Innate Immunity

The dysbiosis of the vaginal microbiota is primarily prevented and controlled by three factors. First, the vaginal tissue barrier prevents the invasion of most pathogens by forming tight barriers. Second, innate immune cells within the vagina, such as dendritic cells, macrophages, natural killer cells, and neutrophils, recognize, bind, and destroy pathogenic bacteria in the inflamed area by recognizing Toll-like receptors [69], NOD-like receptors [70], and major histocompatibility complexes (MHCs) [71]. Finally, cytokines, chemokines, and antimicrobial peptides are released to combat dysbiosis [72]. Vaginal mucus serves to lubricate the vagina and contains various components such as cytokines, chemokines, and antimicrobial peptides, which play a crucial role in defending against bacterial, fungal, and viral invasion. For example, it secretes tumor necrosis factor-α (TNF-α), GM-CSF, and IL-8 to recruit

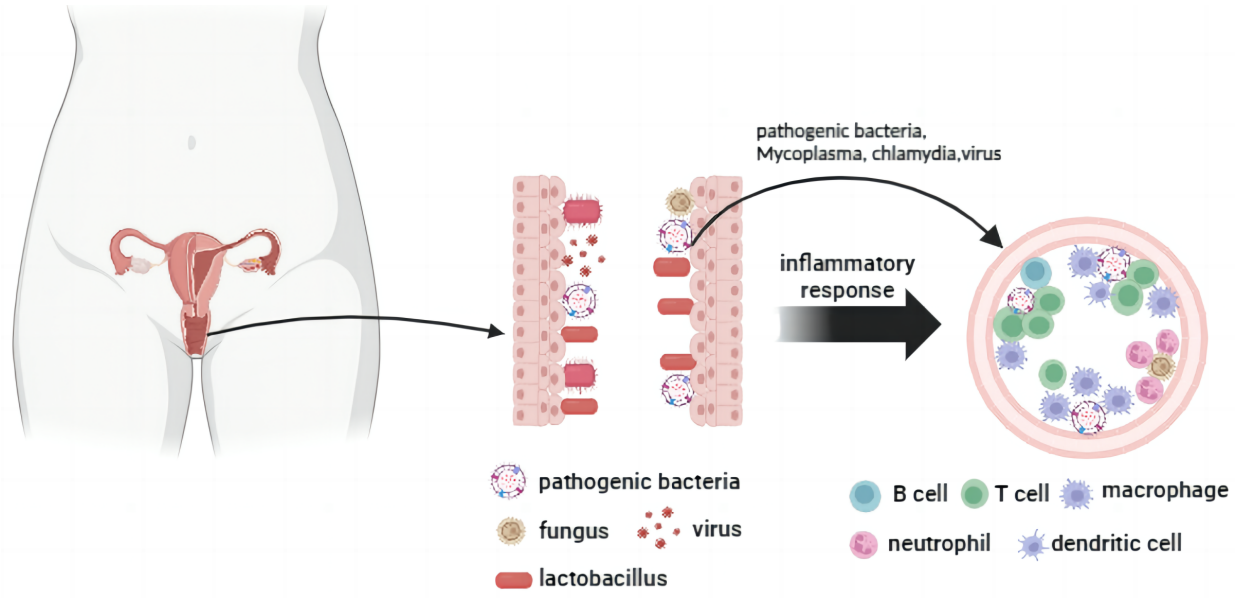

Fig. 2. The relationship between immune response and inflammation in the vaginal defense system. Created with BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates.

and activate immune cells and induce differentiation [73]. Furthermore, the natural vaginal microbiota contributes to vaginal homeostasis by producing lactate and hydrogen peroxide, further enhancing the action of antimicrobial peptides [74].

Vaginal Microbiota and Adaptive Immunity

Neutrophils, macrophages, classical dendritic cells, NK cells, and mast cells play a crucial role in regulating adaptive immunity in the female vagina [75]. Antigen-presenting cells present antigens to T cells to induce adaptive immunity, and T cells and B cells receive signals to target pathogens. $CD8^+$ T cells are the primary T lymphocytes, while B cells are observed in the vagina as aggregates or follicle-like structures [76]. Immune cell movement and activation are closely governed by pattern recognition receptor (PRR) expression and modulated by endocrine signaling throughout the vagina [77]. $CD4^+$ T cells that generate IL-17 [78] and IL-22 [79] are essential in the vaginal mucosa's antimicrobial immune response to pathogen invasion Fig. 2.

Inflammatory Vaginal Microbiota and Therapy

Inflammatory Vaginal Microbiota

Bacterial Microbiota

Bacterial vaginitis is typically caused by the invasion of foreign bacteria that disrupt the balance of microorganisms. *Gardnerella* is one of the most common pathogens of BV, with the greatest biofilm-forming ability and virulence of the pathogens associated with BV [80]. *Atopobium* [81], *Prevotella* [82] and *Mobiluncus curtisii* [83] have been shown to be associated with vaginal inflammation. *Lactobacillus vaginalis* prevents the invasion of other dangerous bacteria by secreting antibiotic compounds. Estrogen delivered into the vagina can modify the vaginal mucosa's local immune response by regulating the composition and stability of the vaginal microbiota [84]. Antimicrobial peptides (AMPs) play a key role in maintaining the barrier function and defending the host by regulating the structure of vaginal flora [85]. *Atopobium* increases the mucus associated with the vaginal epithelial membrane, triggering an inflammatory and immune response. This can also impact female reproductive health by increasing the expression of cytokines and AMPs associated with the disruption of the vaginal barrier, such as changes in the expression of CCL20, hBD-2, IL-1β, IL-6, IL-8, and TNF-α [86].

Candida

Candida can primarily colonize vaginal tissues via adhesins, causing vulvovaginal candidiasis. Neutrophils play a key role in fighting the inflammatory response caused by *Candida* infection. During fungal invasion, neutrophils infiltrate at high levels, aggregating and amplifying the inflammatory response [87]. For defense against *Candida*, neutrophil activation can also generate neutrophil extracellular traps (NETs) [88]. NETs can regulate the inflammatory response and promote T-cell activation through the activation of IL-1 family cytokines while inducing Th2 cells to express IL-4 and activate neutrophil adhesion [89]. NETs can also induce the production of IL-1β and IL-18 in macrophages, resulting in the perpetuation of an inflammatory environment [90]. The NOD-like receptor protein 3 (NLRP3) inflammasome is a key component of the inflammasome complex. Mannan on the surface of *Candida albicans* binds to the Toll-like receptor 4 (TLR4) receptor of

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vaginal epithelial cells, leading to the production of S100A8 and IL-1β by the NLRP3 inflammasome and the recruitment of neutrophils to trigger acute inflammation [91,92].

Mycoplasma and Chlamydia

Mycoplasma and *Chlamydia* are pathogenic microorganisms that can cause various diseases, including urethritis and vaginitis [93]. They can be detected in the vaginal secretions of patients with pelvic inflammatory disease [94]. It has been shown that these microorganisms can affect the vaginal microecology and promote the occurrence of inflammation [95]. The inflammatory damage caused by *Mycoplasma* and *Chlamydia* leads to increased expression of Th17 cells and their inflammatory factors [96], along with an increase in proinflammatory factors and a decrease in anti-inflammatory factors.

Mycoplasma adheres to vaginal epithelial cells, causing chronic inflammation. Macrophages partially clear the infection [97]. Additionally, *Mycoplasma* infection induces innate immunity via lipid-associated membrane proteins (LAMP), a collection of *Mycoplasma* surface lipoproteins that cause an inflammatory response by binding to TLR receptors. LAMP stimulates the nuclear factor kappa-B (NF-κB) pathway mainly through TLR1, TLR2, and TLR6, causing monocytes and macrophages to be recruited into invaded mucosa and causing inflammation [98]. Infection with *Chlamydia trachomatis* is also a risk factor for cervicitis, pelvic inflammation, and infertility [99].

HPV Infection

An increased variety of vaginal microbiota and a decreased presence of *Lactobacillus* are significantly associated with a higher risk of HPV infection [100]. Vaginal microbiota dominated by non-*Lactobacillus* or *Lactobacillus iners* is linked to a 3- to 5-fold increased risk of prevalent HPV [101]. A large retrospective study and a K14-HPV16 transgenic mouse model indicate that HPV E7 oncoproteins inhibit host defense peptides by interacting with the NF-κB and *Wnt*/β-catenin signaling pathways. The HPV E7 oncoprotein reduces the expression of elafin and S100A7 by promoting the NF-κB and *Wnt*/β-catenin signaling pathways. This leads to the cleavage of host defense peptides that support *Lactobacillus* survival, resulting in the development of vaginitis [102].

Therapy of Vaginal Dysbiosis

Oral Probiotic Therapy

The principle of action of probiotic preparations for the treatment of vaginal inflammation involves the balanced regulation of vaginal microbiota by beneficial bacteria. Research suggests that oral probiotics, particularly *Lactobacillus*, can colonize the vagina through the rectum. Short-term oral probiotics in patients with recurrent BV are better tolerated and reduce the rate of BV recurrence and the risk of *Gardnerella vaginalis* transitions up to 11 months after treatment [103]. Treatment with oral probiotics in combination with antibiotics has been found to be more effective in preventing vaginitis recurrence [104].

Microbiota Transplantation

Vaginal microbiota transplantation (VMT) consists of transferring the entire microbiota from a healthy donor vagina to a recipient's vagina to restore microbial variety and normal composition. This is mainly done by transplanting *Lactobacillus,* which produces H_2O_2, bacteriocins, and other bacteriostatic chemicals to inhibit the growth of pathogenic microorganisms [105]. *Lactobacillus* also produces lactic acid in collaboration with vaginal epithelial cells, creating an acidic environment in the vagina with a pH of 4.0–4.5. This plays a vital role in maintaining vaginal health and defending against external infections [106]. *In vitro* studies have shown that *Lactobacillus* isolated from the vagina of healthy women can inhibit the adhesion of *Gardnerella* and even replace *Gardnerella* already adherent to the vaginal epithelium [107].

Lactobacillus vaginal treatment has shown good safety and efficacy in patients with BV, as well as the ability of *Lactobacillus* to colonize the vagina. Transplantation of healthy rat vaginal microbiota into the vagina of BV model rats restored the morphology of their uterine tissues, reduced the concentration of inflammatory factors such as serum IL-6, IL-8, and TNF-α, and had a significant therapeutic and restorative effect on bacterial vaginal infections caused by dysfunctional vaginal microbiota in rats [108]. Scientists in Israel have shown that vaginal flora transplantation has a beneficial ameliorative effect in the long-term treatment of recurrent and antibiotic-resistant bacterial vaginitis [109].

Antibiotic Drugs

The treatment of BV usually involves oral antibiotics or antibiotic-based vaginal douches. Although these treatments can be effective in the short term, they are associated with a high recurrence rate. Studies have indicated an 80% likelihood of BV recurrence within 9 months of antibiotic treatment [80]. Furthermore, antibiotics can also affect *Lactobacilli*, leading to a temporary aseptic state in the vagina. However, this is more likely to cause a loss of resistance to foreign pathogens, triggering vaginal microbiota dysbiosis and infection with pathogenic bacteria [110].

Conclusions

Dysbiosis of the female vaginal microbiota is associated with the abundance of a wide range of microorganisms that can contribute to the development of a variety of female reproductive tract disorders and complications. Multiple physiological and behavioral factors associated with the vaginal microbiota can lead to a cascading effect of chronic inflammation, genital epithelial barrier damage,

and increased risk of other infections. Next-generation sequencing technologies have provided new insights into the abundance and function of the vaginal flora, the homeostasis of which is relevant to maintaining the health of the intravaginal environment. The inflammatory response in the vagina is the first indicator of vaginal microbiota dysbiosis. Understanding the mechanisms by which host inflammatory responses triggered by changes in the microbiota lead to disease progression is critical for prevention and treatment strategies.

Current research on the vaginal microbiota focuses on bacterial community diversity, epidemiology, genomics, and the association between the vaginal microbiota and reproduction. In the future, emphasis should be placed on the role of the vaginal microbiota in predicting, diagnosing, and treating diseases. Studies on the vaginal microbiota must consider the effects of different races, socioeconomic backgrounds, behaviors, and environment on women.

Author Contributions

XL, JZZ and SZL: Conceptualization, Methodology, Data curation, Writing—Original draft preparation. XL: Supervision, Review and Editing. JZZ and SZL: Review and Editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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