

Role of Vaginal Microbiota in Women's Reproductive Health and Diseases

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I. Introduction

■ Definition of vaginal microbiota

The vaginal microbiota is a diverse and dynamic ecosystem consisting of microorganisms such as bacteria, fungi, and viruses [1-6]. Lactobacillus species are the most common bacteria found in the vagina and produce lactic acid, which helps maintain a low pH and prevent the overgrowth of pathogenic microorganisms [7]. Other bacteria like Gardnerella vaginalis, Prevotella, Mobiluncus species, and fungi such as Candida can also be present in the vaginal microbiome [6, 8]. Viruses such as Herpes Simplex Virus can also be found in the vagina and may lead to infection if present in high amounts [9]. The composition of the vaginal microbiome is influenced by various factors like age, sexual activity, antibiotics and other medications, diet and lifestyle, and hormonal fluctuations [4, 5]. The microbiome's primary function is to maintain a healthy pH balance, which can prevent the overgrowth of pathogenic microorganisms that may cause infections [6]. Lactobacilli are the predominant bacterial species in the vaginal microbiota and play a crucial role in promoting women's reproductive health [7]. They produce lactic acid, which helps maintain an acidic environment in the vagina, and antimicrobial peptides that promote immune tolerance, supporting a healthy vaginal microbiota. Dysbiosis of the vaginal microbiota, a disturbance in the composition and diversity of microorganisms, can lead to various reproductive health problems such as bacterial vaginosis, urinary tract infections, and sexually transmitted infections [6, 8]. Dysbiosis can also increase the risk of adverse outcomes in pregnancy, including preterm birth and low birth weight [10]. Therefore, maintaining a healthy balance of vaginal microbiota is critical for good reproductive health [6-8].

■ Overview of the role of vaginal microbiota in women's reproductive health and diseases

The role of the vaginal microbiota (VMB) in women's reproductive health and diseases is an area of active research. The VMB is a complex community of microorganisms that play important roles in maintaining homeostasis in the female genital tract. Evidence suggests that an imbalance in the VMB, such as an overgrowth of less beneficial bacteria, may lead to poor reproductive and gynecologic health outcomes [11]. The VMB is also believed to be important for maintaining the health of the vagina and preventing the transmission of sexually transmitted infections. Research is ongoing to better understand the role of the VMB in health and disease and to develop methods to maintain the balance of the VMB to improve women's health and prevent or treat disease [12]. The VMB has been linked to numerous reproductive and gynecologic conditions, such as bacterial vaginosis, vulvovaginal candidiasis, pelvic inflammatory disease, and preterm birth. Additionally, research indicates that the VMB can be manipulated to improve health outcomes and prevent or treat certain conditions. In addition to promoting reproductive health, the vaginal microbiota can also play a role in reducing the risk of sexually transmitted infections (STIs). Several studies have found that a healthy vaginal microbiota with high levels of lactobacilli can reduce the risk of acquiring or transmitting STIs,

such as HIV, gonorrhea, and chlamydia. Additionally, research indicates that the presence of certain bacterial strains in the vagina can help protect against the development of cervical cancer. These findings underscore the importance of maintaining a healthy vaginal microbiota for women's overall reproductive health [13].

II. Role of Vaginal Microbiota in Women's Reproductive Health

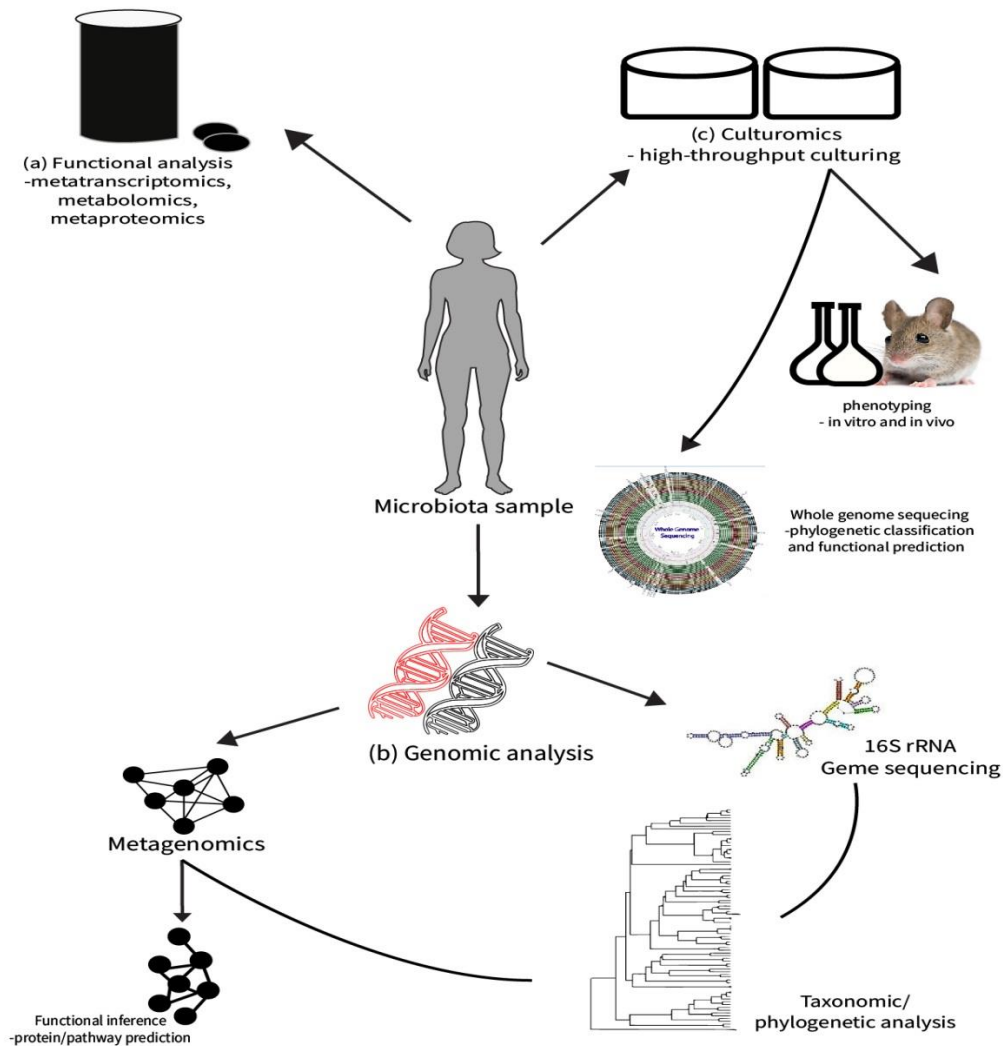
■ Impact of vaginal microbiota on fertility

The role of the vaginal microbiome in female fertility has become an increasingly important area of research. Studies have shown that the composition of the vaginal microbiome can have a direct impact on reproductive health and fertility, both positively and negatively. An imbalance in the composition of the vaginal microbiome, such as bacterial vaginosis or sexually transmitted infections, can lead to inflammation and damage to the reproductive organs, resulting in infertility [14]. Conversely, the presence of certain bacteria, like *Lactobacillus* species, can promote a healthy vaginal environment and enhance fertility [15]. The vaginal microbiota is essential for women's reproductive health, and it can have a major impact on different aspects of fertility, such as ovulation, implantation, and pregnancy outcomes. The vaginal microbiota helps to maintain a healthy pH balance, which can reduce the risk of pathogenic microorganisms taking over, leading to infections. An imbalance of the vaginal microbiota can lead to bacterial vaginosis, which has been linked to a higher risk of infertility. Women with bacterial vaginosis may have decreased chances of getting pregnant and a higher risk of miscarriage [16].

The composition of the vaginal microbiota also influences the success rates of fertility treatments, such as artificial insemination and in vitro fertilization (IVF). Research has shown that women with healthy vaginal microbiota have higher success rates with IVF than those with dysbiosis. Dysbiosis of the vaginal microbiota has been linked to some fertility-related conditions, such as endometriosis, polycystic ovary syndrome (PCOS), and pelvic inflammatory disease (PID) [17]. Additionally, dysbiosis can lead to reduced sperm quality and motility, negatively impacting male fertility.

A healthy vaginal microbiota dominated by *Lactobacillus* species has been associated with improved fertility outcomes, such as higher rates of successful embryo implantation and reduced risk of miscarriage. *Lactobacillus* species produce lactic acid, which helps maintain an acidic environment in the vagina that inhibits the growth of pathogenic microorganisms. Moreover, lactobacilli can produce antimicrobial peptides and promote immune tolerance, which supports healthy vaginal microbiota [18]. Other factors that can impact the composition of the vaginal microbiota and potentially affect fertility include sexual activity, hygiene practices, the use of antibiotics or other medications, and hormonal fluctuations. For example, the use of certain antibiotics can disrupt the balance of vaginal microbiota and lead to conditions such as yeast infections or bacterial vaginosis [19].

The vaginal microbiota is a critical component of female fertility, and its composition can have a significant impact on various aspects of reproductive health. The presence of certain bacterial species, such as *Lactobacillus*, can have a positive effect on fertility outcomes, while an imbalance of the vaginal microbiota can have an adverse impact. Factors such as antibiotics, hormonal changes, and sexual activity can also alter the composition of the vaginal microbiome and thus affect fertility. To better understand the relationship between the vaginal microbiome and female fertility, and to develop new treatments to improve reproductive health outcomes, it is essential to gain a better understanding of its role in fertility [14-19].



▪ **Influence of vaginal microbiota on pregnancy and labor**

In recent years, a significant amount of research has been conducted on the impact of vaginal microbiota on pregnancy and labor. It is believed that the composition of a woman's vaginal microbiome can have a significant effect on the outcome of pregnancy and labor. Certain bacteria present in the vagina have been found to predict preterm or spontaneous labor, while others are protective against it [20]. The presence of certain *Lactobacillus* species has also been linked to a lower risk of preterm labor and delivery [21]. Various factors, such as pregnancy hormones, medications, lifestyle habits, and sexual activity, can affect the composition of the vaginal microbiome. Therefore, it is crucial to be aware of how the vaginal microbiota can impact pregnancy and labor and to monitor any changes that could potentially upset the delicate balance.

During delivery, the vaginal microbiota also plays a role in the colonization of the newborn's gut microbiota. The baby is exposed to the mother's vaginal microbiota during birth, which can help to establish a healthy gut microbiota and protect against the development of certain allergies and diseases. However, if the mother's vaginal microbiota is imbalanced or contains harmful bacteria, this can increase the risk of infection in the newborn [22].

Pregnancy Hormones

Pregnancy hormones are hormones that are released by the placenta during pregnancy and play an important role in influencing the development of the fetus and the mother's body. They can also influence the vaginal microbiome, which is the community of bacteria, fungi, and other microorganisms that live in the vagina [23, 24]. During pregnancy, the levels of certain hormones, such as progesterone and estrogen, increase, which in turn can cause changes in the vaginal microbiome [23]. This can lead to an increase in pathogenic microorganisms, which can cause vaginal infections, preterm labor, and other complications during pregnancy [23, 25]. In addition, the pH of the vagina can also be affected by pregnancy hormones, which can lead to an imbalance in the vaginal microbiome and cause infections [23, 25]. Changes in the vaginal microbiome can also affect the labor process, as certain bacteria can stimulate the production of certain hormones that can help induce labor.

The vaginal microbiota can also affect the labor process. Certain bacterial species, such as *Lactobacillus*, are known to stimulate the production of certain hormones that can help induce labor [1, 23]. In addition, the presence of certain bacteria in the vaginal microbiome can also affect the duration of labor, as certain bacteria can help to reduce the amount of time that it takes for a baby to be born [1, 23]. Furthermore, changes in the vaginal microbiome during pregnancy may influence the mother's risk for preterm labor or other labor complications [23, 25]. Therefore, maintaining a healthy vaginal microbiome throughout pregnancy can help to reduce the risk of labor complications, and increase the chances of successful and safe delivery [23-25]. Other hormones produced during pregnancy include human chorionic gonadotropin (hCG) and relaxin, which are involved in maintaining the corpus luteum, preparing for childbirth, and

loosening ligaments and joints [23]. Oxytocin is another hormone produced during pregnancy that is involved in the initiation of labor by stimulating uterine contractions [1, 23]. Recent studies have also shown that oxytocin receptors are present in the vagina and that oxytocin can affect the vaginal microbiota by promoting the growth of *Lactobacillus* bacteria [1, 23].

Medications

Medications can affect the vaginal microbiome, and certain medications can increase the risk of vaginal infections, preterm labor, and other complications during pregnancy. Antibiotics, antifungals, anti-virals, and other medications can all affect the vaginal microbiome [26]. Some antibiotics are known to disrupt the balance of the microbiome, while anti-fungal and anti-viral medications can help to restore balance [27]. Pregnant women should talk to their doctor before taking any medications, as some medications can harm the vaginal microbiome. Additionally, some medications, such as contraceptives, can also affect the vaginal microbiome, and women should be aware of this when considering taking any medications during pregnancy. Certain medications, such as antibiotics, can also disrupt the balance of the vaginal microbiome, leading to the overgrowth of certain bacteria and the undergrowth of others, which can lead to infections. In addition to antibiotics, other medications can also affect the composition of the vaginal microbiota during pregnancy and potentially impact pregnancy outcomes [28]. For example, some studies suggest that prenatal corticosteroids, which are commonly used to prevent preterm labor and improve fetal lung maturity, may alter the vaginal microbiota and increase the risk of vaginal infections. Other medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), have been associated with an increased risk of miscarriage and preterm birth. Pregnant women need to discuss any medication use with their healthcare provider to determine if there are any potential risks or alternatives available [27].

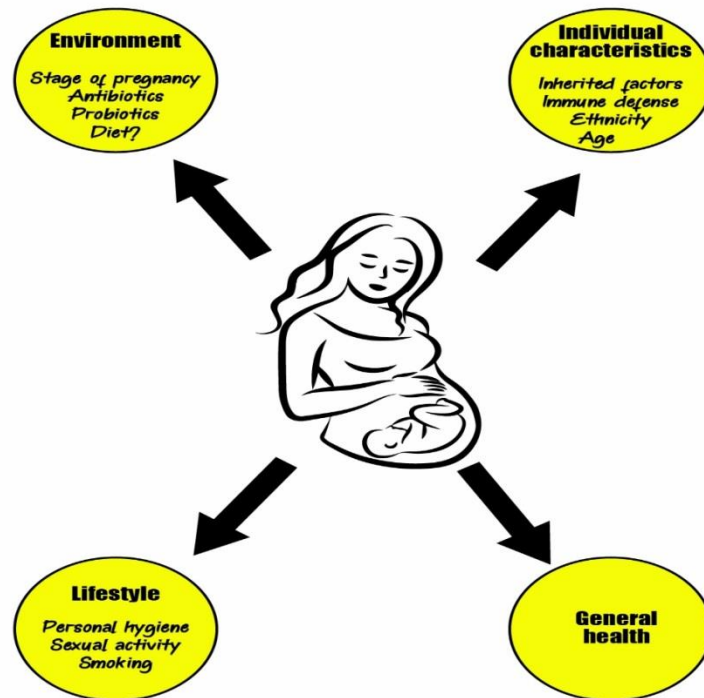
Lifestyle Habits

Lifestyle habits have a significant influence on the vaginal microbiota and, consequently, on pregnancy and labor. Poor lifestyle habits, such as inadequate nutrition, smoking, and excessive alcohol consumption, can affect the composition of the vaginal microbiome. Additionally, certain medications, such as antibiotics, can also influence the vaginal microbiota and can lead to adverse pregnancy outcomes. Factors such as stress, lack of physical activity, and poor hygiene can also contribute to an imbalanced vaginal microbiota, which can lead to complications with pregnancy and labor [29]. During pregnancy and labor, lifestyle habits can significantly impact the composition of the vaginal microbiota. Smoking has been linked to an altered vaginal microbiota composition, which can increase the risk of preterm labor and low birth weight. Poor sleep and stress can also impact the vaginal microbiota by altering hormonal levels and immune function. Maintaining good hygiene practices, such as using mild and fragrance-free personal care products, can help promote healthy vaginal microbiota. On the other hand, engaging in unprotected sex with multiple partners can increase the risk of sexually transmitted infections

that can negatively impact the vaginal microbiota, ultimately leading to adverse pregnancy outcomes [30].

Sexual Activity

Sexual activity can significantly affect the composition of the vaginal microbiota during pregnancy and labor. This is because sexual intercourse can introduce new bacteria into the vagina, which may disrupt the delicate balance of the vaginal microbiota. However, it is important to note that not all sexual activity harms the vaginal microbiota. Engaging in sexual activity with a consistent partner who is free from sexually transmitted infections can help maintain a healthy balance of vaginal bacteria [31]. Conversely, having unprotected sex with multiple partners can increase the risk of sexually transmitted infections, which can harm the vaginal microbiota and lead to adverse pregnancy outcomes [31, 32]. Therefore, it is essential to practice safe sex and take appropriate measures to prevent sexually transmitted infections during pregnancy. In addition to safe sex practices, it is also recommended to limit the number of sexual partners, use water-based lubricants or natural oils like coconut oil or olive oil, and maintain good hygiene practices [31]. By taking steps to maintain a balanced vaginal microbiota, women can reduce the risk of adverse pregnancy outcomes [31, 32].



▪ Role of vaginal microbiota in postpartum care

The vaginal microbiome is a crucial factor when it comes to postpartum care [33]. Research has shown that the composition of the vaginal microbiome can have a direct impact on the outcome of the pregnancy and the onset of labor [34]. Certain types of bacteria in the vagina can be indicative of preterm or spontaneous labor, while other bacteria can work to protect against it [35]. Additionally, the presence of certain *Lactobacillus* species has been linked to a lower risk of preterm labor and delivery [36]. To ensure a healthy balance of bacteria in the vaginal microbiome, postpartum care should focus on implementing lifestyle changes such as eating a balanced diet, exercising regularly, avoiding smoking and alcohol, and using lubricants and condoms during sexual activity [37]. Furthermore, it is essential to discuss any medications or treatments that could affect the composition of the vaginal microbiome with a healthcare provider before starting those [38].

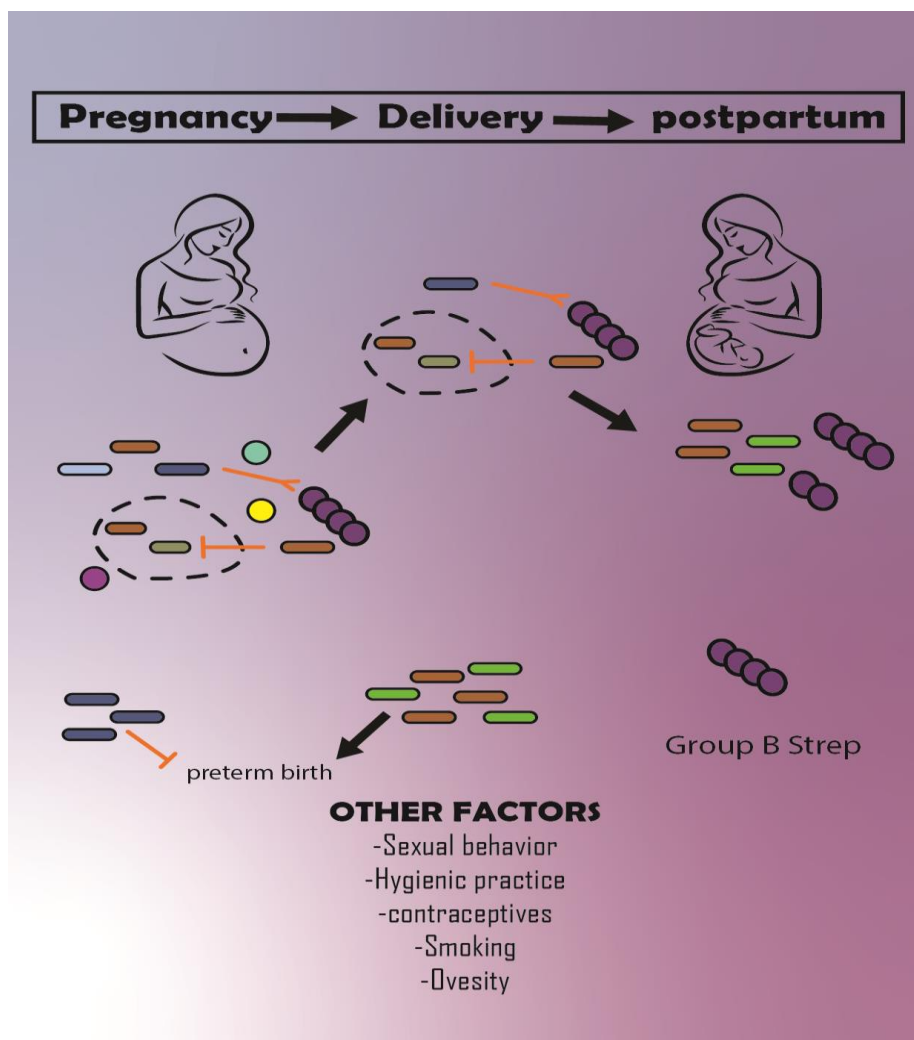
The role of the vaginal microbiota in postpartum care is critical, as it undergoes significant changes during pregnancy and childbirth. Restoring the natural balance of bacteria is crucial after delivery, as disruptions can lead to infections and other complications [33]. In the first few weeks postpartum, the vaginal microbiota is in a state of transition due to a rapid decrease in estrogen and progesterone levels. This decrease can cause a reduction in beneficial lactobacilli, which maintain the acidic environment of the vagina. Insufficient lactobacilli levels can cause the vagina to become more alkaline, enabling harmful bacteria to grow, leading to infections like bacterial vaginosis or urinary tract infections [35].

To help restore the natural balance of the vaginal microbiota after delivery, healthcare providers may recommend certain postpartum care practices. These may include avoiding the use of harsh soaps or douches, which can disrupt the balance of bacteria in the vagina, and using only water or a block of mild, fragrance-free soap for cleaning [33]. Women may also be advised to wear breathable cotton underwear and avoid tight-fitting clothing, which can trap moisture and promote the growth of harmful bacteria [37].

A key aspect of postpartum care involves maintaining the balance of the vaginal microbiota, and probiotics may be recommended for this purpose. Probiotics contain live bacteria that can stimulate the growth of beneficial bacteria in both the gut and vagina, and are available in various forms such as oral supplements, vaginal suppositories, or creams [34]. The composition of the vaginal microbiota can change after childbirth due to various factors such as hormonal changes, stress, or antibiotic use, which can have a significant impact on recovery and overall health [36]. Certain bacteria such as *Lactobacillus* species can support postpartum healing and immune function and may help prevent infections.

Additionally, breastfeeding can also have an impact on the composition of the vaginal microbiota. Breast milk contains prebiotics and probiotics that can help establish a healthy gut microbiome in newborns, which can in turn affect the composition of the vaginal microbiota in breastfeeding mothers [34].

In postpartum care, healthcare providers may recommend probiotics, which are supplements containing live bacteria that can help replenish the vaginal microbiota and promote a healthy balance of bacteria [33]. Women may also be advised to avoid certain products that can disrupt the vaginal microbiota, such as harsh soaps, douches, and scented hygiene products [33]. Postpartum care should also include monitoring the vaginal microbiome to ensure that it remains balanced. This includes regular tests to check for the presence of vaginal infections, such as bacterial vaginosis and yeast infections [37]. Additionally, it is important to be aware of any changes in the vaginal microbiome that could be indicative of a more serious health issue. If any changes are noticed, it is important to consult with a healthcare provider and seek treatment as soon as possible [33]. Finally, postpartum care should also include regular vaccinations, such as influenza and tetanus vaccines, to help protect the mother and baby from serious illnesses [37].



III. Dysbiosis of Vaginal Microbiota

▪ Definition of vaginal dysbiosis

[39] Stated that vaginal dysbiosis is a bacterial imbalance in the vagina, characterized by a decrease in beneficial bacteria like *Lactobacillus* and an increase in potentially pathogenic bacteria, fungi, and parasites. It can lead to several health issues, including vaginal infections, pelvic inflammatory disease, and infertility, and can increase the risk of sexually transmitted infections and HIV transmission [40]. Vaginal dysbiosis can be caused by several factors, including hormonal changes, smoking, douching, and antibiotic use [41]. Symptoms of vaginal dysbiosis may include abnormal vaginal discharge, itching, burning, pain during urination or intercourse, and an unpleasant odor [40]. Diagnosis of vaginal dysbiosis is usually performed through a physical exam and laboratory testing such as a wet mount or culture test to detect abnormal bacteria or fungi [40]. Treatment of vaginal dysbiosis typically involves the use of probiotics and other medications to restore bacterial balance and reduce the risk of infection [39]. Lifestyle changes such as avoiding douching and wearing loose-fitting clothing may also help. In more severe cases, medical treatment such as antibiotics or antifungal medication may be necessary to address the underlying infection [40]. An acidic environment dominated by the presence of *Lactobacillus* species is typically a sign of a healthy vagina, but when the number of *Lactobacillus* species decreases and pathogenic bacteria such as *Gardnerella vaginalis* and *Atopobium vaginae* increase, vaginal dysbiosis can occur [42]. Symptoms of this condition can include itching, burning, discharge, and a foul smell. Additionally, it can increase the likelihood of developing certain vaginal infections such as bacterial vaginosis or yeast infections. To diagnose vaginal dysbiosis, a swab test of the vaginal microbiota is performed. Treatment for this condition can involve lifestyle changes and the use of probiotics orally or topically, or it can require medical treatment such as antibiotics or antifungal medication in more severe cases. [40].

▪ Causes of Vaginal Dysbiosis

Causes of vaginal dysbiosis may include bacterial vaginosis (BV), desquamative inflammatory vaginitis (DIV), candidiasis, and fungemia. BV is a disorder caused by an abnormal increase of certain types of bacteria in the vagina [43-45]. DIV is an inflammation of the vagina due to an imbalance of healthy bacteria [44]. Candidiasis is a contamination caused by an overabundance of the yeast species *Candida*, which is normally found in the vagina [43, 45]. Fungemia is an infection of the bloodstream caused by the presence of *Candida* fungi [44]. All of these conditions can lead to a disruption in the customary vaginal ecosystem, resulting in vaginal dysbiosis [43]. Symptoms of vaginal dysbiosis can include abnormal vaginal discharge, itching, burning, and discomfort during sexual intercourse [43, 44]. Treatment for vaginal dysbiosis normally involves a combination of medications and lifestyle changes to restore the balance of beneficial bacteria in the vagina [43, 44].

Several factors may contribute to the development of vaginal dysbiosis, such as changes in hormones, a weakened immune system, or a change in the balance of bacteria in the vagina. Other factors that can lead to an imbalance of bacteria in the vagina are the use of antibiotics, douching, and sexual activity. Additionally, some types of contraceptives, such as spermicides and diaphragms, can increase the risk of developing vaginal dysbiosis [43, 44].

Causes of vaginal dysbiosis can include a variety of unique factors, such as exposure to certain chemicals, changes in the pH balance of the vagina, and an increase in the number of sexual partners. Additionally, certain medications, such as antibiotics and steroids, can increase the risk of developing vaginal dysbiosis. Other risk factors include smoking, stress, and a weakened immune system [43, 46]. In addition to the traditional causes of vaginal dysbiosis, research has identified some new factors, such as the use of certain types of lubricants that may also increase the risk [47, 48].

▪ **Effects of vaginal dysbiosis on women's reproductive health**

Vaginal dysbiosis is a disruption of the normal balance of microorganisms in the vagina, which can have significant negative effects on a woman's reproductive health. Studies have shown that dysbiosis can lead to an increased risk of pelvic inflammatory disease, bacterial vaginosis, recurrent urinary tract infections, sexually transmitted infections, preterm birth, low birth weight, infertility, endometriosis, endometrial cancer, and other adverse pregnancy outcomes [47, 48]. When the balance of vaginal microbiota is disrupted, it can lead to a range of negative consequences. One of the most common effects of vaginal dysbiosis is an increased risk of vaginal infections, including bacterial vaginosis and yeast infections, which can cause discomfort, itching, burning, and abnormal discharge. Recurrent or severe vaginal infections can also increase the risk of preterm labor, miscarriage, and postpartum infections [49, 50].

Additionally, vaginal dysbiosis can affect fertility and increase the risk of complications during pregnancy. The vaginal microbiota plays an important role in protecting the reproductive tract against infection and maintaining a healthy environment for fertilization and implantation. When this balance is disrupted, it can lead to inflammation and damage to the reproductive tissues, which can impair fertility and increase the risk of complications such as ectopic pregnancy and preterm birth. Additionally, dysbiosis has been linked to an increased risk of sexually transmitted infections (STIs) and HIV transmission. Women with vaginal dysbiosis are more likely to acquire STIs, including HIV, because the changes in the vaginal microbiota can weaken the natural defenses of the reproductive tract, making it more vulnerable to infection [51].

Pelvic Inflammatory Disease

Pelvic Inflammatory Disease (PID) is a dangerous infection that affects the female reproductive organs and can have long-lasting serious consequences. It is caused by bacteria, like Chlamydia, gonorrhea, and other sexually transmitted infections, when they move from the vagina or cervix, up through the uterus and into the fallopian tubes, ovaries, or other areas of the reproductive

system. Symptoms of PID can include abdominal discomfort and tenderness, fever, abnormal vaginal discharge or bleeding, pain during sexual intercourse, and pain when urinating. In some cases, PID may have no symptoms at all. Chlamydia trachomatis is the most common sexually transmitted organism associated with PID, but not all cases of PID test positive for it. When present, signs and symptoms of PID can include abdominal pain, fever, abnormal vaginal discharge, and dyspareunia [52-55]. Diagnosis of PID typically involves a physical examination, laboratory tests to identify the presence of bacterial infections, and imaging tests, such as ultrasound or CT scans, to evaluate the extent of the infection. Without treatment, PID can lead to long-term damage to the reproductive organs, such as infertility, or even death [52-54]. Chronic pelvic pain and ectopic pregnancy, where the fertilized egg implants outside the uterus, are also potential complications of untreated PID. Furthermore, the inflammation and scarring caused by PID can increase the risk of complications during pregnancy, such as preterm labor and miscarriage.

Treatment for PID commonly includes antibiotics to get rid of the bacteria and other types of supportive treatment. It is essential to take the full course of antibiotics to make sure that the infection is gone. In some cases, hospitalization may be needed to give intravenous antibiotics and provide pain management. People who have PID should have their sexual partners tested and treated to avoid a re-infection. Doctors may give empiric treatment for PID to women who meet certain criteria, and those with excessive vomiting, high fever, symptoms of sepsis, or who cannot tolerate oral medications may be prescribed to be admitted for treatment [52].

PID can be prevented by avoiding risky sexual behaviors, getting tested and treated for STIs, using condoms correctly and consistently, and receiving the HPV vaccine. Good hygiene is also important, and any signs or symptoms of PID should be reported to a doctor. Individuals need to seek medical attention if they experience any symptoms of PID or if they suspect they may have been exposed to an STI. PID can have serious long-term effects, so it is crucial to be aware of the signs, take preventative measures, and seek prompt treatment if necessary [52, 55, 56].

Preterm Birth

Preterm birth is a widespread health concern that impacts millions of babies globally, resulting in high infant mortality rates and long-term complications for the affected child [57]. Short cervix in the second trimester of pregnancy, bacterial vaginosis, and vaginal dysbiosis are identified as risk factors for preterm birth [58]. Vaginal dysbiosis is characterized by an imbalance in the vaginal microbiota, leading to adverse reproductive health outcomes, including an increased risk of preterm birth, small-for-gestational-age births, and infections [59]. The disruption of the proportion of vaginal bacteria can predispose women to bacterial vaginosis and preterm birth [60]. The presence of *Gardnerella vaginalis*, one of the harmful bacteria causing bacterial vaginosis, is associated with an elevated risk of preterm birth due to the inflammatory response it triggers [59].

Treatment for preterm birth often involves antibiotics, while probiotics may also be beneficial in preventing preterm birth and restoring the balance of vaginal bacteria [57]. Good hygiene practices such as avoiding douching and using mild, fragrance-free soaps can help prevent vaginal dysbiosis and reduce the risk of preterm birth [58]. Sexual practices, such as using condoms and limiting sexual partners, can also help prevent the transmission of harmful bacteria that can disrupt the vaginal microbiota [60]. Women who experience symptoms of dysbiosis, such as abnormal vaginal discharge or odor, should seek medical attention to prevent complications and promote a healthy pregnancy [61]. The vaginal microbiota is a complex ecosystem of bacteria that helps maintain the health of the female reproductive system, and the prevention and treatment of dysbiosis are critical in reducing the risk of preterm birth.

Endometriosis

Endometriosis is a chronic and estrogen-dependent gynecological condition affecting about 10% of reproductive-age women. It is characterized by the presence of endometrial tissue outside the uterus, which causes inflammation and pain [62]. Recent research has identified vaginal dysbiosis, an imbalance in the vaginal microbiota, as a possible risk factor for endometriosis [63]. The dysbiosis is associated with an increased abundance of certain bacteria, such as *Gardnerella vaginalis*, *Prevotella bivia*, and *Atopobium vaginae*, and decreased abundance of beneficial bacteria, such as *Lactobacillus* species [63]. Dysbiosis in the reproductive microbiota, including the vaginal, cervical, and uterine microbiota, has also been associated with fertility issues, pregnancy loss, and recurrent pregnancy loss, as well as endometriosis-related pain [62].

Certain hormonal contraceptives have been found to influence the composition of the vaginal microbiome, with progesterone-only contraceptives leading to increases in *Gardnerella vaginalis* and *Prevotella bivia* and combined contraceptives leading to increases in *Atopobium vaginae*. Endometriosis is associated with significant impairments in health-related quality of life and is linked to an increased risk of developing other gynecologic and non-gynecologic conditions, including ovarian cancer, infertility, depression, anxiety, and chronic pelvic pain [62]. Endometriosis can also increase the risk of miscarriage and preterm birth [64].

While there is no cure for endometriosis, treatments are available to manage symptoms and improve quality of life. These treatments include pain medication, hormonal therapy, and surgery to remove endometrial tissue. Additionally, lifestyle interventions such as diet and exercise may be beneficial in managing endometriosis symptoms [62]. Maintaining a healthy vaginal microbiota through good hygiene practices, such as avoiding douching and using mild, fragrance-free soaps, may help reduce the risk of vaginal dysbiosis and the potential development of endometriosis [63]. Recent research has also suggested that magnetic resonance imaging (MRI) may be a useful tool for diagnosing deep infiltrating endometriosis. A systematic review and meta-analysis published in 2021 found that MRI had high sensitivity and specificity for detecting deep infiltrating endometriosis, with a pooled sensitivity of 0.87 and a pooled specificity of 0.94 [65].

Endometrial Cancer

Endometrial cancer is a prevalent type of gynecologic cancer that affects the inner lining of the uterus. A combination of genetic and lifestyle factors can contribute to the development of this cancer, including obesity, diabetes, hormone replacement therapy, and endometriosis. Vaginal dysbiosis, which is an imbalance in the vaginal microbiota, can increase the risk of endometrial cancer due to decreased levels of beneficial bacteria like *Lactobacillus crispatus* and *Lactobacillus jensenii* that are associated with vaginal health. Dysbiosis can also cause an increase in harmful bacteria and alter the vaginal pH, both of which can lead to endometrial cancer. Furthermore, studies have suggested that serum levels of Human Epididymal Protein 4 (HE4) can serve as a prognostic marker for endometrial cancer [66, 67].

Women with endometrial cancer may also experience abdominal pain, pelvic pain, and changes in urination or bowel habits [68]. Women should also be aware of the potential risk factors associated with vaginal dysbiosis, including the use of certain vaginal products, douching, and the regular use of antibiotics [69]. Additionally, women should be aware of the potential long-term risks of endometrial cancer, such as an increased risk of other types of cancer, including ovarian and cervical cancer, as well as a higher risk of developing blood clots and other cardiovascular disease. Finally, women should be aware of the importance of regular screenings for endometrial cancer, as early diagnosis is key to successful treatment and improved outcomes [68].

It's important for women to know that there are various options for treating endometrial cancer, including surgery, radiation, and hormone therapy. Depending on the stage of cancer, a combination of these treatments may be recommended. In addition to treatment, lifestyle changes can help reduce the risk of endometrial cancer, such as maintaining a healthy weight, eating a balanced diet, exercising regularly, and avoiding smoking. Finally, women should be aware that regular screenings are important for detecting endometrial cancer early so that treatment can be started as soon as possible [68].

Moreover, vaginal dysbiosis can also cause changes in the pH of the vagina, which can lead to vaginal dryness and irritation, as well as an increased risk of bacterial and fungal infections. It can also cause discomfort, pain, and embarrassment, and can lead to psychological distress. To maintain a healthy balance of microorganisms in the vagina, it is important to practice good hygiene and to use protective barriers, such as condoms, during sexual activity. Treatment options for vaginal dysbiosis may include dietary changes, probiotic supplementation, and topical or oral medications. It is essential to speak to a healthcare provider to determine the best course of action because the effects of dysbiosis on reproductive health vary from woman to woman [67, 69].

IV. Role of Vaginal Microbiota in Women's Diseases

■ Impact of vaginal microbiota on sexually transmitted infections

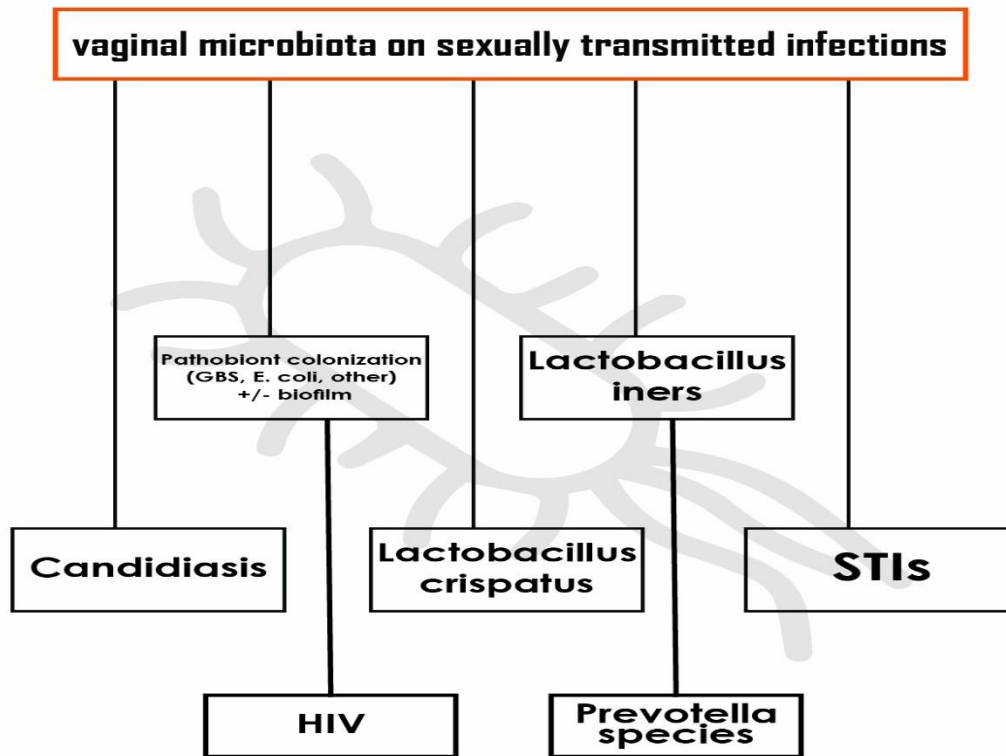
Sexually transmitted infections (STIs) remain a major public health challenge worldwide, with millions of new cases diagnosed annually. The vaginal microbiota has a critical role to play in both preventing and acquiring STIs [70]. A healthy vaginal microbiota is predominantly made up of *Lactobacillus* species, which generate lactic acid, preserve an acidic pH, and create a barrier against pathogens. An imbalance or dysbiosis in the vaginal microbiota can increase vulnerability to STIs. Various studies have indicated that the composition of the vaginal microbiota can significantly influence the likelihood of contracting STIs like HIV, herpes, chlamydia, gonorrhea, and syphilis [16]. There is a strong association between abnormal vaginal microbiota or dysbiosis and a heightened risk of STI acquisition, and alterations in the vaginal microbiota due to factors such as antibiotics, hormonal contraception, and sexual activity can modify STI acquisition risk [71].

Research has demonstrated that certain characteristics of the vaginal microbiota, such as reduced diversity or the presence of specific bacteria, can affect the risk of acquiring STIs. Furthermore, the presence of certain bacteria in the vaginal microbiota, such as *Lactobacillus*, can help reduce the risk of acquiring STIs. Studies have shown that *Lactobacillus crispatus* and *Lactobacillus jensenii* in the vaginal microbiota are associated with a decreased risk of acquiring STIs, including chlamydia, gonorrhea, and HIV [71]. In contrast, vaginal dysbiosis is associated with an increased risk of acquiring STIs, particularly bacterial vaginosis (BV), which is characterized by a decrease in *Lactobacillus* species and an increase in pathogenic bacteria [70]. Dysbiosis can alter the vaginal pH, making it less acidic and more hospitable to pathogens, and can lead to inflammation and disruption of the vaginal epithelium, which can increase susceptibility to infection. Additionally, certain pathogenic bacteria, such as *Gardnerella vaginalis* and *Prevotella* species, can produce enzymes that degrade the mucus layer of the cervix, further increasing the risk of STI acquisition [70-72].

It is important to consider the potential impact of lifestyle, environmental, and product-related factors on the composition of the vaginal microbiota when managing STI risk. Certain lifestyles and environmental factors, such as smoking and douching, may affect the composition of the vaginal microbiota and increase the risk of acquiring STIs [16, 71]. The use of certain products, such as spermicides and lubricants, may also alter the vaginal microbiota and increase the risk of acquiring STIs. Additionally, research has indicated that the use of certain types of hormonal contraception, such as the combined oral contraceptive pill, can alter the vaginal microbiota and increase the risk of acquiring STIs [16, 70].

Strategies for preventing and treating vaginal dysbiosis may help reduce the risk of STI acquisition. Probiotics, particularly those containing *Lactobacillus* species, may help restore healthy vaginal microbiota and reduce the risk of STIs. Additionally, maintaining good hygiene practices, such as avoiding douching and using mild, fragrance-free soaps, may also help prevent

vaginal dysbiosis. Research is ongoing to better understand the role of the vaginal microbiota in the risk of acquiring STIs and to identify effective interventions to reduce the risk [16, 70, 71].



▪ **Effect of vaginal microbiota on bacterial vaginosis**

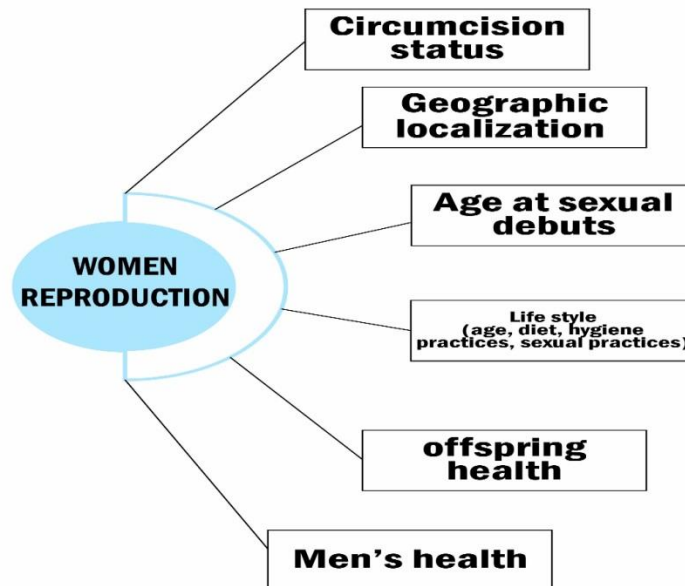
BV is a prevalent vaginal infection among women all over the world and is caused by an array of different factors. These can include changes to the microbial balance of the vagina due to sexual activity, hormonal fluctuations, and other environmental causes. The vaginal environment is made up of several microorganisms, including bacteria, which play a key role in keeping the vagina healthy [73]. Lactobacillus species are usually the most dominant type of bacteria in a healthy vaginal environment, as they generate lactic acid and other compounds that help keep the vagina's pH low and inhibit the growth of other bacteria [15, 74].

In women with BV, there is a decrease in the abundance of Lactobacillus species, which are beneficial bacteria that produce lactic acid, maintain an acidic pH, and create a barrier against pathogens. Instead, there is an increase in the abundance of anaerobic bacteria, such as Gardnerella vaginalis, Prevotella spp., and Atopobium vaginae, which contribute to the

development of BV [49]. The decrease in *Lactobacillus* species and the increase in anaerobic bacteria in BV patients result in an elevated vaginal pH level, which can lead to vaginal inflammation and an increased risk of acquiring sexually transmitted infections (STIs) and other vaginal infections [31].

The effect of the vaginal microbiota on BV is complex, but it is known to have some impact on the prevalence and severity of the condition. The composition of the vaginal microbiota is a key factor in determining the risk of BV. In addition to the shift in the vaginal microbiota, several other factors can influence the risk of BV, such as sexual activity, hormonal changes, the use of certain medications, and the presence of STIs. These factors can disrupt the balance of the vaginal microbiota, leading to an increase in the prevalence of BV [31, 73].

BV has been associated with a range of negative pregnancy outcomes, including premature birth and an enhanced vulnerability to HIV and other STIs [75]. For this reason, it is essential to diagnose and treat BV to reduce the potential for these issues. Treatments for BV generally include antibiotics, probiotics, or other medications to reestablish the balance of the vaginal microbiome. Studies have proposed that restoring the equilibrium of the vaginal microbiome, particularly by augmenting the presence of *Lactobacillus* species, can help to avert and treat BV. Probiotics containing *Lactobacillus* strains have demonstrated some encouraging results in diminishing the reoccurrence of BV and enhancing vaginal health. In addition, other approaches such as antibiotics, antimicrobial agents, and vaginal pH regulators may also be effective in restoring the balance of the vaginal microbiome and treating BV [76].



▪ **Influence of vaginal microbiota on urinary tract infections**

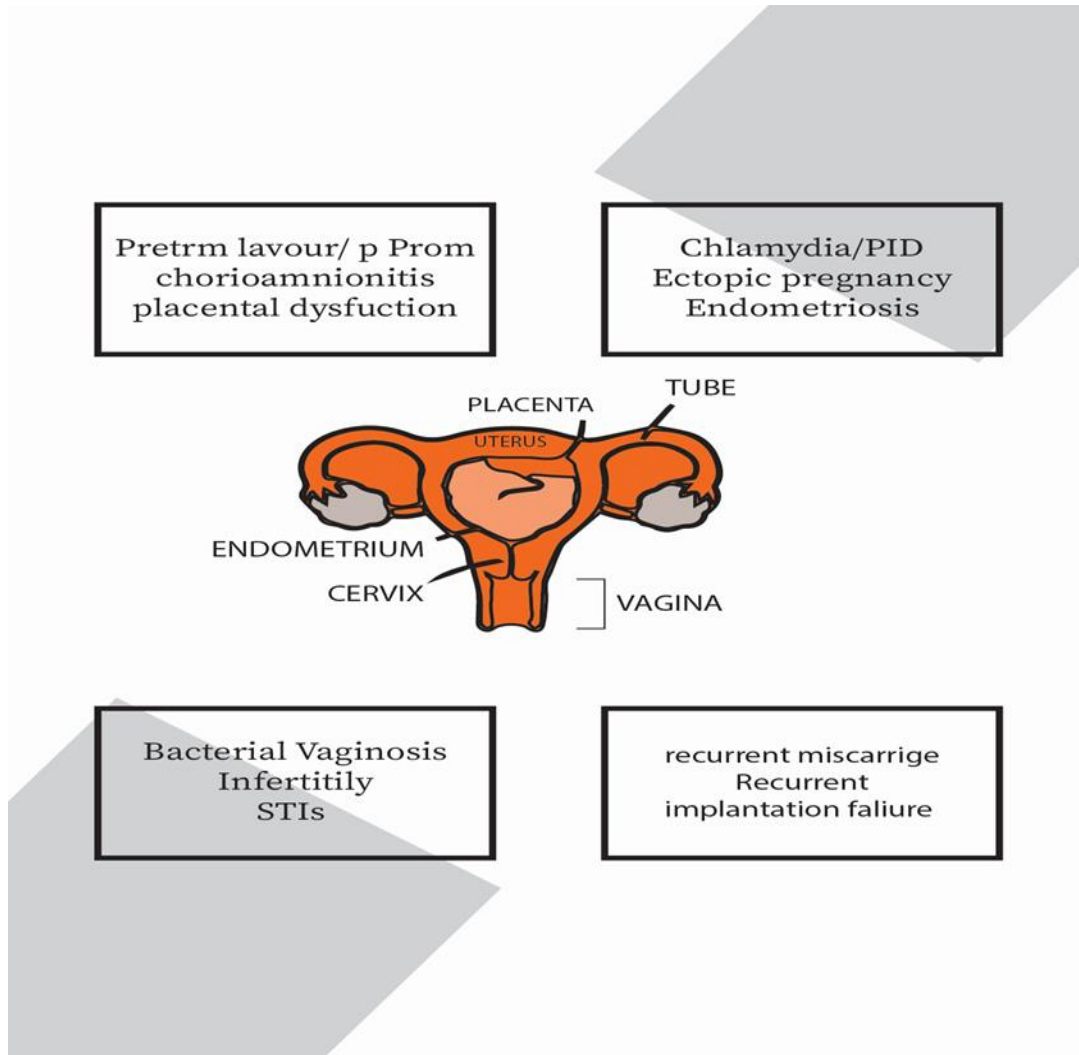
Urinary tract infections (UTIs) are common bacterial infection that affects millions of people worldwide, with around 150 million cases reported each year [77, 78]. While certain risk factors such as female gender, prior UTI, sexual activity, diabetes, and catheter use have been linked to increased UTI risk [79], recent studies have suggested that the composition of the vaginal microbiota also plays an important role in UTI development and progression. Women with recurrent UTIs are more resistant if their vaginal microbiota is in balance, with certain species of bacteria such as *Lactobacillus* being beneficial in preventing UTIs. Conversely, an overgrowth of harmful bacteria due to the presence of species like *Candida albicans* in the vagina can increase the risk of UTI [80, 81].

The vaginal microbiota is dominated by *Lactobacillus* species, which produce lactic acid and other compounds that help to maintain an acidic environment and inhibit the growth of harmful bacteria. When the vaginal microbiota is disrupted, through factors such as antibiotic use, hormonal changes, or sexual activity, the risk of developing UTIs can increase [81]. This is because the loss of protective *Lactobacillus* species can allow pathogenic bacteria, such as *E. coli*, to colonize the vaginal and urinary tract, leading to infection [82].

Furthermore, alterations in the female urinary microbiota have also been associated with the development of bladder disease. The risk of UTIs increases with age, and postmenopausal women may experience changes in the composition of their vaginal microbiota [78]. The diagnosis of UTI can be challenging due to the absence of symptoms or atypical presentations, but common symptoms include dysuria, frequency, and urgency. UTI diagnosis is typically confirmed with a urine culture [79].

Antibiotics are the mainstay of treatment for UTIs, but proper management also includes lifestyle modifications to promote healthy vaginal microbiota. These modifications include avoiding douching, limiting sexual intercourse, and drinking plenty of fluids. Additionally, probiotics containing *Lactobacillus* strains have been shown to help reduce the risk of UTIs, as well as improve symptoms and overall vaginal health. Cranberry has also been studied for their potential protective effects against UTIs, and further research is needed to examine these potential benefits [83].

Overall, the influence of the vaginal microbiota on UTIs highlights the importance of maintaining a healthy balance of microorganisms in the vaginal and urinary tract and the potential benefits of probiotic interventions in reducing the incidence and severity of UTIs. Proper hygiene, urinating after sexual intercourse, and drinking plenty of water are other UTI prevention strategies that can help reduce the risk of developing UTIs [77, 79].



V. Recent Developments in the Field

Summary of newly published review papers

Recent studies indicate that the vaginal microbiota is a crucial factor in women's reproductive health and diseases. It affects fertility, pregnancy, labor, and postpartum care, and imbalances can lead to various infections, including sexually transmitted infections, bacterial vaginosis, and urinary tract infections [84]. A recent review paper delves into the role of vaginal microbiota in women's reproductive health and diseases. It defines the vaginal microbiota and its role in reproductive health, explores dysbiosis of the vaginal microbiota, and analyzes the microbiota's impact on women's diseases [85]. The paper also cites research indicating that the composition of the vaginal bacterial community is dynamic, with changes reported after delivery that may

lead to a decrease in *Lactobacillus* species and an increase in gram-negative anaerobes [85, 86]. Furthermore, bacterial colonization modulates host immunity. Recent reviews underscore the importance of comprehending the role of the vaginal microbiota in women's health, and more research is needed in areas such as the migration of *Listeria monocytogenes* from the gut to the vagina. Altering the VMB to be dominated by lactobacilli may be linked to better health outcomes [85, 87]. To develop effective treatments, it is critical to understand the role of the vaginal microbiota in women's reproductive health and diseases. Future research should investigate the microbiota's impact on fertility and pregnancy, as well as its role in the development of infections and other diseases [84, 85].

▪ Overview of current research and trends

The role of vaginal microbiota in women's reproductive health and diseases has been the subject of much research in recent years. The composition of the vaginal microbiome has been found to be associated with reproductive outcomes, including fertility, pregnancy, labor, and postpartum care. Dysbiosis of the vaginal microbiome can lead to a variety of conditions, including bacterial vaginosis, sexually transmitted infections, and urinary tract infections.

Current studies have been dedicated to comprehending the significance of the vaginal microbiome in women's reproductive health and ailments. Through the analysis of data gathered from extensive studies, researchers have gained valuable knowledge on how the vaginal microbiome affects fertility, pregnancy, labor, and postpartum care. Furthermore, they have thoroughly investigated the connection between the vaginal microbiome and sexually transmitted infections, bacterial vaginosis, and urinary tract infections.

Recent developments in the field have focused on the use of probiotics to re-establish a healthy microbiome, as well as the role of the microbiome in the development of certain diseases. New techniques such as metagenomics and metatranscriptomics have been employed to better understand the microbial communities present in the vaginal microbiome. Additionally, the use of machine learning and artificial intelligence is enabling researchers to gain deeper insights into the relationship between the vaginal microbiome and women's health.

In summary, the investigation of the vaginal microbiome's influence on women's health and diseases remains a continual process. With the accumulation of additional data and advancements in technology, further revelations are inevitable. This will ultimately improve comprehension of the vaginal microbiome's role in women's health and possibly lead to novel remedies for various ailments [88].

VI. Conclusion

■ Summary of the Main Points

The article presents an overview of the crucial role played by vaginal microbiota in maintaining women's reproductive health and preventing diseases. It highlights the impact of vaginal microbiota on fertility, pregnancy, labor, and postpartum care, as well as the consequences of vaginal dysbiosis on reproductive health. Additionally, it discusses the role of vaginal microbiota in common women's diseases such as sexually transmitted infections, bacterial vaginosis, and urinary tract infections. The paper also covers recent developments in the field and recommends areas for future research to deepen our understanding of vaginal microbiota and its role in women's reproductive health [89].

To advance our understanding of the vaginal microbiota, the paper recommends future research to investigate the impact of specific bacterial species on vaginal microbiota and their potential use as biomarkers for predicting or monitoring women's reproductive health. It also suggests exploring the role of microbiota in the development of endometriosis and examining the impact of vaginal dysbiosis on the immune system and its potential involvement in the pathogenesis of inflammatory diseases. Additionally, the paper recommends investigating the impact of vaginal microbiota on menopausal transition and related symptoms and exploring the potential of probiotics, prebiotics, and synbiotics in maintaining a healthy vaginal microbiota.

Other research gaps identified by the paper include understanding the impact of external factors such as oral contraceptives, antibiotics, douching, sexual practices, and lifestyle on vaginal microbiota and conducting longitudinal studies to track the temporal dynamics of vaginal microbiota during different phases of a woman's life. By addressing these research gaps, we can develop new diagnostic and therapeutic approaches to improve women's health outcomes [84].

In conclusion, this review paper highlights the crucial role played by the vaginal microbiota in women's reproductive health and diseases. The findings presented in the paper could guide researchers and healthcare practitioners toward developing more effective diagnosis, prevention, and treatment strategies to promote women's reproductive health.

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