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Effects of contraceptive choice on vaginal microbiome: current evidence and perspectives

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ABSTRACT

Lactobacillus species are the most significant bacteria present in the vaginal microbiome, as they protect the female reproductive system against infections by, for example, releasing protective substances and regulating vaginal pH. The disrupted vaginal ecosystem may lead to bacterial vaginosis, which is the term for inflammation of the vagina because of the overgrowth of naturally present bacteria. Many factors may influence the microbial ecosystem of the vagina, not only the contraceptive methods but also lifestyle and diet. Evaluation and summing up of the current knowledge of the influence of different contraceptive methods on the vaginal ecosystem and reproductive health is the aim of this review article. Combined oral contraceptives may be linked to the stability of the vaginal microbiota and lead to a lower risk of bacterial vaginosis (BV). Progesterone-only methods, such as depot medroxyprogesterone acetate, may increase microbial diversity and cause shifts in the *Lactobacillus* dominant ecosystem. Some older contraceptive methods, such as copper intrauterine devices, are known to increase the risk of BV and other bacterial infections, for instance, Actinomyces. Condoms are shown not to influence the vaginal ecosystem and keep it stable. It is crucial to say that the use of different hormonal and non-hormonal contraceptive methods is not indifferent to sexually transmitted infections (also HIV), as they alter vaginal mucosa, leading to being prone to infections. As the interactions between contraceptive use and the vaginal microbiota are complex, it is essential to conduct long-term, multi-center studies, which may allow doctors in personalized contraceptive counseling.

Keywords: vaginal microbiome, hormonal contraception, bacterial vaginosis, *Lactobacillus* species

1. INTRODUCTION

The vaginal microbiota is a complicated and dynamic ecosystem. Maintaining the balance of this ecosystem plays a key role in the health of a woman's reproductive system (Buchta, 2018). This article must define what bacterial

vaginosis is. Bacterial vaginosis is "a vaginal inflammation resulting from an overgrowth of naturally occurring vaginal bacteria." Some researchers highlighted that the right microbiota prevents women from having bacterial dysbiosis and has a role in the fertilization process during pregnancy (Younes et al., 2018). *Lactobacillus* species are the main ingredient of the physiological vaginal microflora. Their role is complex, as they produce and release some protective factors, for example, lactic acid and hydrogen peroxide, which have an antimicrobial effect and protect from colonization by pathogens.

Bordorff et al., (2014) documented during their research that the vaginal microbiome dominated by *Lactobacilli* species reduced the risk of sexually transmitted diseases, also HIV, in African women. However, the microbiological balance can be disturbed by several factors, including the use of drugs, infections, and contraception. This review examines current evidence on how different contraceptive choices—oral contraceptives, injectable and implantable progestins, intrauterine devices (IUDs), and intravaginal rings—affect the vaginal microbiome, highlighting implications for women's health and future contraceptive development (Klebanoff et al., 2017).

2. METHODS

We used PubMed, Cochrane Library, and Google Scholar databases to gather the information needed for this review article and then performed the review of literature available on these platforms in December 2024. The authors aimed to find the relevant articles which analyzed the influence of different contraceptive methods on the vaginal microbiota. We used Medical Subject Headings (MeSH) terms and specific keywords during searching for relevant information, including contraceptive use, vaginal microbiota, and bacterial vaginosis. Also, to ensure that the authors included the essential literature, citation tracking was applied. During the research, we took into consideration only articles in English. The authors assessed every article to determine if it was relevant and whether its quality was high enough to be applied in this review. We included only peer-reviewed studies with direct relevance to the article topic. We believe that this approach ensured comprehensiveness and validity.

3. RESULTS AND DISCUSSION

Effect of hormonal contraception on the vaginal microbiome

Hormonal contraceptives, including oral contraceptive pills (OCPs), injectables, and hormonal intrauterine systems (IUS), have been shown to alter the vaginal microbiome by modulating estrogen and progesterone levels. These hormones can influence the vaginal epithelial environment, glycogen deposition, and consequently, the microbial composition (Brotman et al., 2014; Jespers et al., 2017). Studies have indicated that combined oral contraceptives (COCs) tend to promote a *Lactobacillus*-dominant microbiota, which may be connected to the reduced risk of vaginal inflammation (bacterial vaginosis) and sexually transmitted infections (STIs) (Brooks et al., 2017; Vodstrcil et al., 2013). In contrast, the use of depot medroxyprogesterone acetate (DMPA), a progestin-only injectable, has been linked to microbial dysbiosis characterized by a reduction in *Lactobacillus* spp. and an increase in anaerobic bacteria (Achilles et al., 2018; Gosmann et al., 2017).

The ECHO trial and related studies have raised concerns about the use of DMPA in populations at high risk for HIV due to its potential to alter the vaginal mucosal barrier and immune function (Morrison et al., 2015; Birse et al., 2017). However, not all studies show consistent outcomes, suggesting that factors such as host genetics, sexual behavior, and regional microbiota profiles may modulate these effects (Ata et al., 2021).

Intrauterine Devices and Vaginal Microbiome Disruption

Non-hormonal intrauterine devices (IUDs), especially copper IUDs (Cu-IUDs), have been consistently linked with disruptions in the vaginal microbiome and an elevated risk of bacterial vaginosis (BV) (Daniel et al., 2023; van de Wijgert and Jespers, 2017). The insertion and long-term presence of a Cu-IUD can act as a mechanical irritant to the cervicovaginal mucosa, altering the reproductive tract's physical and immunological barrier functions. Additionally, the copper ions released by the device may have antimicrobial properties that selectively influence bacterial populations, potentially reducing protective *Lactobacillus* species while promoting the overgrowth of anaerobic, BV-associated microorganisms such as *Gardnerella vaginalis*, *Atopobium vaginae*, and other members of the polymicrobial BV biofilm (Brooks et al., 2017). As an effect of this imbalance, vaginal pH rises, which can be prone to secondary infections.

In the case of hormonal intrauterine systems, the scientists think that levonorgestrel-releasing intrauterine system has a more stabilizing influence on the vaginal ecosystem. The continuous release of levonorgestrel leads to localized endometrial suppression, which not only results in reduced menstrual bleeding but also diminishes the influx of iron-rich menstrual blood—a known substrate

for BV-associated bacteria. By reducing menstrual flow, the LNG-IUS may help maintain a more favorable vaginal environment for the dominance of beneficial *Lactobacillus* species, particularly *Lactobacillus crispatus*, which is associated with lower rates of BV and sexually transmitted infections (Bastianelli et al., 2021).

However, the effect of the LNG-IUS is not universally positive. Some women may still experience dysbiosis or microbial shifts after its insertion, possibly due to individual host factors, baseline microbiota composition, or variations in immune responses (Ata et al., 2021). These inconsistencies highlight the complexity of host-microbiome-contraceptive interactions and the need for more personalized approaches in contraceptive counseling and selection.

Contraceptive Vaginal Rings and Local Microbiome Stability

Vaginal rings, such as the NuvaRing, are a form of hormonal contraceptive that provides a unique route of administration by delivering a combination of estrogen and progestin directly into the vagina mucosa. In contrast to oral contraceptives, which need to be absorbed and metabolized by the liver, vaginal rings release relatively consistent local hormone levels meanwhile almost not influencing hormonal balance.

This localized mode of delivery allows for more targeted hormonal effects on the vaginal environment, potentially influencing the microbial ecosystem distinctly. Despite their widespread use and user-friendly characteristics, including monthly application and low failure rates with typical use, the impact of vaginal rings on the vaginal microbiome has not been as extensively studied as other contraceptive methods, such as oral contraceptives or intrauterine devices.

Preliminary evidence suggests that vaginal rings may contribute to the maintenance of a *Lactobacillus*-dominant vaginal microbiome, which the scientists generally considered protective against bacterial vaginosis (BV), sexually transmitted infections (STIs), and reproductive tract inflammation. The stable and sustained hormone delivery provided by the ring may promote epithelial integrity and enhance glycogen deposition in the vaginal lining, thereby supporting the growth of beneficial *Lactobacillus* species, particularly *Lactobacillus crispatus*. These bacteria maintain low vaginal pH and create an environment where bacteria are not able to resist by producing lactic acid and hydrogen peroxide. Like everything in nature, not all the characteristics of a vaginal ring are positive.

Some researchers have reported a potential increase in fungal colonization, particularly by *Candida* species, among users of vaginal hormonal rings (Muhleisen and Herbst-Kralovetz, 2016). The possible mechanism may be a modulation of immune response in the mucosa by reducing neutrophil activity and altering cytokines levels, which may, in total, make mucosal cells unable to defend against opportunistic fungi. Moreover, the presence of the vaginal ring may be a place where bacteria form biofilm, which may influence microbial balance. Because data about the influence of the vaginal rings on the vaginal microbiome are pretty narrow and sometimes not clear enough, it is crucial to conduct long-term and multi-centered studies. It is essential to take into consideration some factors that may interact with hormonal delivery systems, such as genetics, immune system status, sexual behavior, and microbial status, before using these contraceptive methods. *Lactobacillus* predominating vaginal ecosystem is significant in keeping it far from infection and overall, in having good reproductive health.

Menstrual Cycle, Contraception, and Microbial Fluctuations

During the menstrual cycle, female sex hormones fluctuate, causing the menstrual cycle. But also, this occurs to have an impact on the composition of the vaginal microbiota and its stability. These cyclical changes, driven primarily by estrogen and progesterone, are known to influence the vaginal epithelial environment and immune responses, thereby shaping microbial dynamics. In particular, the rise in estrogen levels during the follicular phase and at ovulation has been strongly associated with an increased abundance of beneficial *Lactobacillus* species. This is connected mainly to estrogen's role, which is a promotion of the thickening of one of the vaginal mucosa layers, which is the epithelium, and also stimulating glycogen accumulation within epithelial cells. The glycogen, which is a polysaccharide composed of many glucose molecules, after being broken down into simpler sugars, like glucose, serves as a nutrient source for *Lactobacillus*, supporting their dominance and contributing to a low vaginal pH, which helps prevent colonization by pathogenic bacteria.

A dynamic microbiota may result from hormonal shifts that naturally occur in the different phases of the menstrual cycle. Nonetheless, transient dysbiosis may accompany these changes during the cycle, which makes the vaginal mucosa prone to inflammation. Hormonal contraceptives, especially those that modulate or suppress ovulation and, thereby, blunt hormonal peaks and troughs, may contribute to more stable microbial communities in the vagina. By maintaining relatively constant hormone levels, these

contraceptives can minimize the hormone-driven fluctuations that affect microbial balance and potentially reduce the risk of recurrent BV episodes (Kenneally, 2024). Further research into the mechanisms by which hormonal regulation affects the vaginal ecosystem could enhance our understanding of how to maintain optimal vaginal health across different contraceptive regimens.

Clinical Implications and Susceptibility to Infections

Disruptions to the vaginal microbiome caused by specific contraceptive methods can significantly increase a woman's vulnerability to various genital infections, including HIV, human papillomavirus, and herpes simplex virus type 2 (Gosmann et al., 2017). The changes in the vaginal microbial ecosystem often facilitate these infections, compromising mucosal integrity and immune defense. In particular, the depletion of beneficial *Lactobacillus* species—especially *Lactobacillus crispatus*—has been linked to a pro-inflammatory vaginal environment. This state of chronic low-grade inflammation can impair the epithelial barrier and reduce its protective function, making it easier for pathogens to invade and establish infection (Srinivasan et al., 2015).

Lactobacillus crispatus plays a critical role in maintaining vaginal health by producing lactic acid, hydrogen peroxide, and bacteriocins, which help maintain a low vaginal pH. A low pH creates a vaginal environment that is inhospitable for harmful bacteria. When this species is absent or replaced by anaerobic bacteria commonly related to bacterial vaginal inflammation (BV), such as *Gardnerella vaginalis*, the risk of acquiring sexually transmitted infections increases markedly. While hormonal contraceptive methods—particularly combined oral contraceptives (COCs)—are often associated with a more stable and *Lactobacillus*-dominant vaginal microbiome and thus may offer some degree of protection against infections and BV, this is not universally the case. The protective effects can vary based on the hormonal composition, dosage, and individual host factors.

On the other hand, non-hormonal contraceptive methods, including copper intrauterine devices (IUDs), may disrupt the vaginal microbial equilibrium in some users. Copper IUDs have been associated with an elevated risk of BV and microbial dysbiosis, possibly due to their pro-inflammatory effects and the mechanical influence of the device itself (Pettifor et al., 2009; Borgdorff et al., 2015). Given these findings, clinicians should carefully consider the patient's history of vaginal infections or dysbiosis when recommending contraceptive options. For women with a history of recurrent BV or other microbiome imbalances, it may be prudent to avoid non-hormonal devices like copper IUDs in favor of methods that are less likely to disrupt the vaginal microbial community. The wise contraceptive counseling for a particular woman may contribute to the good health of the female reproductive system and is an essential factor in the prevention of many conditions.

Lifestyle Factors

Lifestyle factors such as diet, exercise (its type and frequency), and sexual activity, can also influence the vaginal microbiome. For example, a study by Gajer et al. (2012) found that a vegetarian diet and intense exercise appeared to lead to vaginal microbiome alterations and loss of *Lactobacillus* species. Moreover, non-hormonal contraception and unprotected sexual activity increased the incidence of vaginal inflammation and BV by disturbing the vaginal microbiota and reducing *Lactobacillus* plenty. So, to sum up, there are strong correlations between lifestyle factors and the vaginal microbiota, which for sure are not entirely explored, and still need to be analyzed. The study's summary key points are presented in Table 1.

Table 1. Key Summary Points of the Study

Hormonal Contraceptives and Vaginal Microbiome
- Combined oral contraceptives (COCs) support a <i>Lactobacillus</i>-dominated microbiome, reducing the risk of bacterial exclusion (BV) and sexually transmitted diseases. - Depot medroxyprogesterone acetate (DMPA) may cause dysbiosis, reduce <i>lactobacillus</i> and increase anaerobic bacteria, which may increase the risk of HIV infection.
Intrauterine Devices (IUDs)
- Copper intrauterine devices are more likely than other methods to cause bacterial vaginosis and vaginal dysbiosis, which are caused by mechanical damage or the influence of copper. - The levonorgestrel-releasing intrauterine device may stabilize the vaginal microbiome and reduce menstrual bleeding by supporting <i>Lactobacillus crispatus</i>. However, results vary from person to person.
Vaginal Rings

• Potentially maintain a microbiota dominated by <i>Lactobacillus</i> bacteria. • May weaken immune defenses, potentially increasing <i>Candida</i> colonization or promoting biofilm formation.
Menstrual Cycle and Microbial Fluctuations
• Hormonal changes (especially estrogens) influence the growth of <i>Lactobacillus</i> bacteria through the production of glycogen. • Hormonal contraceptives can stabilize the vaginal microflora by inhibiting natural hormonal fluctuations.
Lifestyle Factors
• A vegetarian diet and vigorous exercise can lower <i>Lactobacillus</i> levels. • Non-hormonal contraception and unprotected sex are associated with an increased incidence of BV.

4. CONCLUSIONS

It is significant to understand the effects of different contraceptive methods on the vaginal microbiota, to prevent infections and generally to maintain the well-being of female reproductive health. The vaginal microbiota acts as a defensive shield against pathogens and modulates immune response. A *Lactobacillus*-dominated microbial profile—especially one dominated by species such as *Lactobacillus crispatus*—is associated with a lower risk of bacterial vaginosis (BV), sexually transmitted infections (STIs), and adverse reproductive outcomes, including preterm birth. Consequently, contraceptive methods that support or maintain this beneficial microbiota are of high clinical value and doctors should prioritize them when appropriate.

Hormonal contraceptives, particularly combined oral contraceptives (COCs), have been consistently shown in the literature to promote or maintain a stable, *Lactobacillus*-rich vaginal microbiome. That may be thanks to the estrogen part of the COCs, as estrogens make glycogen more available for the cells of the vaginal epithelium, which promotes the growth of *Lactobacillus* bacteria. These microbiota-stabilizing effects not only reduce the incidence of BV and vulvovaginal candidiasis but may also confer protection against more serious infections such as HIV and HPV. Furthermore, hormonal methods like the levonorgestrel-releasing intrauterine system (LNG-IUS) have also demonstrated a generally favorable impact, though individual responses can vary. In contrast, non-hormonal methods, such as copper intrauterine devices (Cu-IUDs), have been associated with higher rates of microbial dysbiosis, likely due to increased menstrual bleeding and inflammation, which may alter vaginal pH and create an environment conducive to anaerobic pathogens like *Gardnerella vaginalis* and *Atopobium vaginae*.

The changes in the microbial ecosystem may lead women to have recurrent BV and other gynecological infections and complications. In practice, that means the need for more careful choosing and recommending these devices, especially in women with a history of recurrent BV. A progestin-only injectable method, depot medroxyprogesterone acetate (DMPA), has a more extensive influence. For instance, it may elevate the risk of STI. Nonetheless, factors such as genetics, sexual activity, hygiene practices, and composition of the vaginal microbiota before using DMPA may modulate the influence of DMPA. While DMPA remains a valuable contraceptive tool, doctors should weigh its effects on the microbiome in the context of individual risk profiles. The vaginal ring and other localized hormonal delivery systems appear to provide a more stable hormonal environment with potentially less systemic immune modulation. Preliminary evidence suggests they may help sustain a *Lactobacillus*-dominant microbiota; however, data are still limited, and some long-term and multi-center studies are needed to clarify these outcomes fully. Given the multifaceted interaction between contraceptive methods and the vaginal microbiome, clinicians should adopt a patient-centered approach when recommending contraceptives.

Beyond considerations of efficacy, side effects, and personal preference, the potential microbiological consequences should be discussed, particularly in women who are immunocompromised, at high risk for STIs, or have a history of recurrent BV or vulvovaginal candidiasis. Finally, further studies are unavoidable in translating emerging microbiome research into actionable clinical recommendations. Conducting long-term, randomized, and multicenter studies is crucial to understanding real correlations fully. What is worth mentioning is that the study should assess a diverse population, favorably all around the world, from different sociocultural backgrounds. In conclusion, this article shows that contraceptive methods influence not only reproductive autonomy but also the microbial ecosystem of the vagina.

Author's Contribution

Justyna Kuciel- Conceptualization, review, editing, investigation, methodology

Dominik Tomczak- Methodology, investigation, visualization, supervision

Maria Mrocza- Conceptualization, visualization, resources,

Kinga Erasmus- Review, data curation, investigation

Roksana Hrapkowicz- Resources, writing- rough preparation, data curation

Agnieszka Czernecka- Visualization, data curation, investigation

Kinga Świła- Review, visualization, formal analysis

Patrycja Pysz- Supervision, writing- rough preparation, data curation

Marek Borecki- Review and editing, formal analysis, supervision

Karolina Jałocha- Resources, writing- rough preparation, formal analysis

Project administration- Justyna Kuciel

Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this study are present in the paper.

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