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Review Article

The Detrimental Impact of Dysbiosis in Gynecology and Obstetrics, Alongside the Positive Role of Probiotics in Prevention and Treatment: A Review Article

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Abstract

Reproductive tract microbiome dysbiosis contributes to various gynecological and obstetric issues, including vaginal infections, adverse pregnancy outcomes, endometriosis, pelvic pain, sexually transmitted diseases, vulvodynia, and pelvic organ prolapse. Probiotics offer a promising approach to mitigating these problems through mechanisms such as microbiome regulation, immune system strengthening, antioxidant effects, and production of anti-mutagenic compounds. Common probiotics used to modulate reproductive dysbiosis include: *Limosilactobacillus reuteri* RC-14, *L. fermentum*, *L. gasseri*, *L. rhamnosus*, *L. acidophilus*, *L. crispatus*, *L. casei*, *L. salivarius*. Given the increasing prevalence of antibiotic resistance and associated limitations, probiotics represent a valuable therapeutic strategy; however, further research is required to optimize strain selection and dosage for specific conditions. Investigations should consider diverse populations, varying dosages, and different routes of administration (e.g., oral vs. vaginal suppositories) to determine the optimal approach for maximizing therapeutic benefits. The aim of the this study is to review the detrimental impact of reproductive tract microbiome dysbiosis on various gynecological and obstetric conditions, while also exploring the positive role that probiotics may play in the prevention and treatment of these conditions. The review seeks to evaluate how dysbiosis contributes to vaginal infections, adverse pregnancy outcomes, endometriosis, pelvic pain, sexually transmitted diseases, vulvodynia, and pelvic organ prolapse, as well as to assess the mechanisms through which probiotics may mitigate these problems, including microbiome regulation, immune system strengthening, antioxidant effects, and production of anti-mutagenic compounds.

Keywords: Dysbiosis, Microbiome, Probiotics, Obstetrics, Gynecology

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Introduction

The human body is a place with abundant concentration and diversity of microbes. These microorganisms populate any body organ and system, including the skin, gastrointestinal (GI), urogenital, oropharyngeal, and respiratory tracts. Microbes can be classified as beneficial, known as the microbiota, or harmful, known as pathogens..
They reside in or on the human body, maintaining a state of homeostasis with one another. Whenever the balance of the microbiota and pathogen is disrupted, a condition known as "dysbiosis", infection or disease occur. Today, it has been well understood that this imbalance is the main underlying cause of several inflammatory, infectious and malignant disorders. Accordingly, the discovery of probiotics, discussed in subsequent sections, has revolutionized both preventive and therapeutic medicine [1, 2].
The female reproductive system is one of the human body organs that is most tightly linked with microbiota balance. As soon as the microflora composition of the genital tract is changed, certain essential functions are impaired. In fact, successful human reproduction is influenced by the microbiota balance, and microbiome plays a role in reproductive cyclicity, pregnancy and delivery [3, 4]. On the other hand, disruption of the female genital microflora composition (dysbiosis) also leads to genital infections and the subsequent consequences like infertility. Thus, microbiota imbalance can be a trigger for several gynecological and obstetric events [5, 6].
Probiotics are live microorganisms that, in sufficient quantities, confer a health benefit on the host [7]. Probiotics offer a valuable approach to modulating microbiota dysbiosis and, with specific strains and dosages, can shift the microbiota towards a healthier state [8]. Their use is favored over antibiotics as long-term probiotic use avoids the serious side effects, particularly disruption of the natural microbiome, associated with antibiotics [9]. In addition, probiotics benefit female reproductive health by reducing gynecological diseases and strengthening vaginal immunity [10].Several review studies have examined the role of the female reproductive tract microbiome and gynecological disorders. Doroftei et al. (2023) reviewed the adverse impacts of microbial alterations in the vagina, cervix, and endometrium on pregnancy outcomes. Their narrative review analyzed studies from 2010-2023, finding that low levels of Lactobacillus species and core microbiota members can lead to eubiosis-to-dysbiosis transitions, impairing metabolic and endocrine network homeostasis [11]. Blancafort and Llácer (2023) reviewed the effect of probiotics on fertility outcomes and their capacity to improve the feminine genital tract microbiota, especially addressing the 50% of women with bacterial vaginosis who are asymptomatic [12]. Souza et al. (2023) systematically reviewed the influence of vaginal microbiome and Lactobacillus species on female fertility, analyzing 18 studies encompassing 2,011 women and concluding that fertile women exhibited dominance of Lactobacillus species while infertile women showed dysbiotic profiles [13]. Xholli et al. (2023) explored the relationship between gut microbiota and endometriosis, revealing altered gut microbiota in endometriosis patients, including reduced diversity, microbial composition imbalances, and increased pathogenic bacteria [14]. Kobayashi (2023) reviewed the role of gut and reproductive tract microbiota in endometriosis pathogenesis, highlighting how dysbiosis leads to estrobolomic and metabolomic changes that may contribute to disease development [15]. Wu et al. (2022) systematically reviewed disturbances in vaginal microbiome composition related to HPV infection and cervical carcinogenesis, finding higher alpha diversity in patients with HPV infection, cervical lesions, and/or cancer compared to controls [16].
Despite extensive research in this field, there remain significant gaps in the comprehensive understanding of dysbiosis impact across the full spectrum of gynecological and obstetric disorders, as well as the precise role of probiotics in prevention and treatment. Most existing studies have focused on specific aspects of the microbiome-disease relationship, with fewer studies comprehensively examining both the detrimental effects of dysbiosis and the positive role of probiotics in a single review. Furthermore, a complete understanding of the specific mechanisms of probiotic effectiveness, optimal

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strain selection, and appropriate dosage for specific conditions still requires further investigation. The present study aims to fill these gaps.

Methods

Microbiota dynamics of the female reproductive tract

Similar to any human body organ, the female reproductive system has its own micro-niche composition with regular interpersonal variations. In fact, the vaginal microbiome is a dynamic ecosystem, which depends upon the host factors and their interplay with the environment for example, ethnicity, seasonal cycles, or climate can influence every individual's vaginal microbiome. Moreover, age, menstrual cycle, pregnancy, menopause, and other hormonal changes of a female affect the spatio-temporal diversity of the reproductive tract microbiota [5, 17].

Defining a healthy female reproductive tract (FRT) microbiota is challenging. The female neonate acquires vaginal microflora shortly after birth. During the course of a female's life, the vagina is exposed to hormonal changes, sexual activity, constant secretions and medication use. Moreover, the composition of microbiota differs in various anatomical sites of the reproductive tract. For example, the quantity of endometrial bacteria is significantly lower than that of vaginal bacteria. It means that the cervix probably serves as a partial barrier for ascending microflora. However, microbial communities that inhabit the vagina of a healthy nonpregnant female predominantly consist of four *Lactobacillus* species (*L. crispatus*, *L. iners*, *L. jensenii* or *L. gasseri*). Lactobacillus species are significant in maintaining normal pH through the production of lactic acid and regulation of glycogen metabolism. Moreover, they can provide an acidic and antimicrobial environment through production of bacteriocins and hydrogen peroxide, which protect against the invading pathogens. However, other vaginal microbiome of a healthy female of reproductive age includes several aerobic and facultative or obligate anaerobic species, including *Gardnerella*, *Prevotella*, *Atopobium*, and *Mobiluncus*; the dominance of these pathogens in the vagina of a female is usually associated with increased mucosal inflammation through increasing pro-inflammatory cytokines and numbers of CD4+ T-cells, disruption of epithelial barrier, and production of immunomodulatory metabolites [18, 19]. On the other hand, the microbiota composition of the vulva consists of *Lactobacillus* along with several other genera including *Corynebacterium*, *Staphylococcus* and *Prevotella*, which resemble the vaginal, skin and fecal commensals [20].

In the menstruation period, the composition of vaginal microbiota depends upon estrogen levels, with overall increase in *Gardnerella vaginalis* abundance and decrease in *Lactobacillus* species (except for *L. iners*) [21]. During pregnancy, the microbial composition alters as a decrease in the abundance and composition of the vaginal microbiome occurs to enable sufficient fetal development, while maintaining maternal health. The richness and diversity of vaginal commensals of a pregnant female vary according to gestation progression. Nevertheless, a change towards a *Lactobacillus*, Actinomycetes and Bacteroidetes-dominated community occurs in order to preserve the vaginal immunity [22, 23]. On the other hand, a change occurs in the vaginal bacterial community after pregnancy, with a significant decrease in abundance and diversity of *Lactobacillus* species. In fact, postpartum vaginal commensals resemble the gut microfloral communities and this alteration usually persists up to one year after the end of pregnancy [24, 25]. And last, but not least, the vaginal microbiome alteration during menopause is on behalf of decreased abundance of *Lactobacilli* and increased amount of other bacterial species. This occurs as a result of estrogen loss which causes vaginal atrophy and decreased immunity [26-28].

In general, any change in the urogenital microfloral profile of an individual is associated with certain infections and diseases, mentioned as follows:

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Role of microbiome in fertility and pregnancy outcome

The female microbiota affects almost all stages of reproduction, including gametogenesis, fertilization, embryo migration, implantation and parturition. Thus, any alteration in the commensals composition may lead to infertility and detrimental pregnancy outcome.

Vaginal microbiota and chorioamnionitis

Intra-amniotic infection (IAI), also known as chorioamnionitis (CAM), has also been determined to be associated with a deranged vaginal microbiome. It has been demonstrated that decrease of *L. crispatus* amount and increase of certain anaerobic groups are related to occurrence of chorioamnionitis. Moreover, prediction of the severity of CAM may also been feasible through vaginal flora analysis [29-31].

Vaginal microbiota and fertility

Today, the endometrial cavity is no longer assumed to be sterile, rather, it has been demonstrated to be populated with a variety of microorganisms. The presence of commensals within the FRT has been demonstrated to contribute in reproductive health and fertility. It has been shown that dysbiosis plays an important role in infertility and restoration of endometrial and vaginal microbiota could increase the success of reproductive techniques in infertile couples and improve the reproductive outcome [32, 33].

On the other hand, it has been demonstrated that vaginal dysbiosis is tightly associated with the occurrence of intrauterine adhesion (IUA), which is a significant underlying cause of amenorrhea, repeated miscarriages and infertility [34].

Vaginal microbiota and preterm birth

Vaginal dysbiosis has been suggested to serve as a cause for preterm birth (i.e. delivery before 37 weeks' gestation). In general, it has been demonstrated that the vaginal richness, diversity, and evenness of microbiota is decreased during pregnancy in those females with subsequent preterm labor; this alteration occurs between the first and second trimesters. An increase in the abundance of *Gardnerella* and a decrease in the abundance of *Lactobacillus* species have been demonstrated in the vaginal commensals of a female with preterm delivery [35, 36].

Vaginal microbiota and premature rupture of membranes

Premature rupture of membranes (PROM) is another adverse pregnancy outcome that may lead to preterm labor, low birth weight, fetal loss and even life-threatening maternal and neonatal septicemia. PROM is associated with endometrial and vaginal infections like bacterial vaginosis, which is the result of the shift from Lactobacilli dominance to a mixed microflora including *G.vaginalis* [37-40].

Vaginal microbiota and miscarriage

It has been recently demonstrated that the FRT dysbacteriosis can play a role in miscarriage and pregnancy loss. The underlying mechanism might be attributed to the disequilibrium in the Th1/Th2 immune response posed by the microbial imbalance. On the other hand, genital infections which are main causes of pregnancy loss are per se precipitated by the change in the bacterial microflora of the FRT [41-43].

Role of probiotics in fertility and pregnancy outcome

Probiotic effects on pregnancy are debated. One study found no impact on preterm birth or pregnancy length versus placebo [44]. However, evidence increasingly supports probiotic benefits; one recent systematic review suggests combined antibiotics/probiotics may improve outcomes in PPROM cases [45]. Probiotics may be linked to longer pregnancies, increased birth weight, reduced chorioamnionitis, and improved vaginal flora. Specifically, oral probiotics containing Clostridium may help prevent preterm birth before 32 weeks [46]. A daily 6-month *Ligilactobacillus salivarius* intervention in pregnant women with recurrent miscarriage or infertility, abnormal vaginal flora, and pH increased pregnancy success rates by 56% while

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decreasing vaginal pH and increasing vaginal lactobacilli [7]. Common probiotics used to modulate reproductive dysbiosis include: *L. reuteri* RC-14, *L. fermentum*, *L. gasseri*, *L. rhamnosus*, *L. acidophilus*, *L. crispatus*, *L. casei, L. salivarius* [47]. Also, probiotics can influence fertility by:

1. Improving sperm parameters, testicular health, and testosterone levels through antioxidant effects;

2. Supporting a healthy vaginal microbiome and preventing bacterial vaginosis (BV) and inflammation [48].

Role of microbiome in female genitourinary infections

Female genital and sometimes gut dysbiosis is tightly linked with abundant adverse reproductive health outcomes like sexually transmitted diseases and other genitourinary infections.

Bacterial vaginosis

BV is a common vaginal infection in women [49]. in females of reproductive age. This condition is also associated with dysbiosis. In fact, decreased lactobacilli abundance can lead to reduced lactic acid production and increased vaginal pH, which can result in increased load of anaerobic and facultative-anaerobic bacteria like *G. vaginalis*, Bacteroidetes, *Mobiluncus*, and *Prevotella* species [50, 51].

Sexually transmitted infections

Not only BV, but also other sexually transmitted infections (STIs) are closely related to vaginal dysbacterosis. These STIs include *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, human papillomavirus (HPV), herpes simplex virus (HSV) and human immunodeficiency virus (HIV). As a matter of fact, lactic acid has an inhibitory impact on STIs through modulation of cervicovaginal epithelial cell functions and exertion of immunomodulatory effects. Thus, decreased lactic acid production as a result of dysbiosis and decreased lactobacilli diversity and abundance can lead to decreased protection against STIs [52-54]. On the other hand, loss of lactobacilli dominance can be followed by an increased risk of HPV infection, persistence, and the associated cervical malignancies [55-58]. In addition, dysbiosis may decrease body defense against HIV infection and promote HIV disease progression, which per se facilitates other STIs occurrence and persistence [59-61].

Endometritis and pelvic inflammatory disease

There are sparse reports that are suggestive of the relative similarity of the upper FRT and the lower FRT microbiota. This would be the result of ascending microbial seeding of the uterine cavity with vaginal commensals. Thus, dysbiosis seems to play an important role in acute or chronic endometritis [62]. On the other hand, STIs that seem to be the result of dysbiosis are the main contributors to upper genital tract infections or pelvic inflammatory diseases (PID). In fact, Lactobacillus species can protect the host against STIs and the consequent PID [63-66].

Role of probiotics in female genitourinary infections

Probiotics in various forms of dietary supplements, capsules, and vaginal suppositories have beneficial effects on the vaginal environment through various means:

1. Reducing vaginal PH by producing lactic acid and hydrogen peroxide;

2. Producing antimicrobial compounds and stimulating the immune system;

3. Inhibiting the attachment of pathogenic bacteria by adhering probiotics to the vaginal epithelium;

4. Using the same nutrients as pathogens [49].

A meta-analysis study by Wang, Z., et al. (2019) showed that probiotics could have a potential effect in relieving BV [67]. Due to the dynamic environment of the genital tract and the risk of local infections, probiotics are recommended for both women susceptible to recurrent urogenital infections and healthy women to help prevent

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genital mucosal superinfections [68].**Role of microbiome in gynecological cancers**

Alteration of the female gut and vagina microbiome may lead to the onset or progression of gynecologic cancers like endometrium, cervical and ovarian malignancies. For example, elevated level of Proteobacteria and Firmicutes phylum bacteria, namely *Atopobium* and *Porphyromonas*, is associated with endometrial cancer, increased level of *C. trachomatis*, *Lactobacillus* and *Mycobacterium* have been reported in ovarian cancer, and high loads of human papillomavirus, Fusobacterial and *Sneathia* species are accompanied by cervical cancers. Moreover, vaginal and vulvar cancers have also been linked to gut and vaginal dysbiosis [69, 70]. Furthermore, disruption of estrogens metabolism by the commensals imbalance may predispose to breast cancer [71].

Role of probiotics in gynecological cancers

Probiotic bacteria may reduce cancer risk through several mechanisms, including the production of anti-mutagenic compounds, degradation of carcinogens, induction of apoptosis, and modulation of both carcinogenic compound concentrations and the host immune response. In cervical cancer management, probiotics contribute by enhancing immunity, balancing the vaginal microbiome, and decreasing the risk of secondary infections [72]. Furthermore, long-term administration of *Lactiplantibacillus plantarum* LS/07 induces immunomodulation, potentially decreasing tumor necrosis factor (TNF)- α and increasing CD4(+) T-Cells levels [73].

Role of microbiome in other gynecological disorders

Endometriosis and chronic pelvic pain

Endometriosis is the presence of endometrium-like tissue outside the uterine cavity. This chronic inflammatory condition has been deemed to be the result of microbiome alteration. In fact, gut dysbiosis (with increased levels of Proteobacteria, *Streptococcus*, Enterobacteriaceae and *Escherichia coli*) leads to a change in estrogen metabolism and the resultant increase in levels of circulating estrogen, which is the underlying pathogenic mechanism for endometriosis. Moreover, decreased abundance of *Lactobacillus* species and increased abundance of anaerobes like *Prevotella*, *Atopobium*, *Mobiluncus*, and *Gardnerella* species are associated with vaginal dysbiosis, stimulation of the immune system and the consequent inflammation and endometriosis [26, 74, 75].

On the other hand, chronic pelvic pain (CPP) is another inflammatory condition with endometriosis being one of the causes. This annoying syndrome, which considerably affects the quality of life, has also been observed to be associated with alterations of the vaginal and rectal microbiome profiles [76, 77].

Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) is the most prevalent endocrinopathy in females of reproductive age, which mainly results from insulin resistance (IR). Females with PCOS exhibit ovarian cysts, anovulation/menstrual irregularity, and hyperandrogenism, and occasionally overweight, insulin resistance, anxiety and depression. Furthermore, it is sometimes associated with follicular dysplasia, abortion or infertility [78].

It has been suggested that alteration of the phylogenetic profile of the gut commensals may have a role in the evolution of PCOS. However, the association between vaginal microbiota and PCOS has not yet been established. Studies have demonstrated a lower diversity of stool microbiota, with decreased abundance of *Lactobacillus* species, namely *L. crispatus* and the increased abundance of *Mycoplasma* and *Prevotella* in females with PCOS. Moreover, the abundance of GABA-producing bacteria like *Parabacteroides distasonis*, *Bacteroides fragilis* and *E. coli*, is also increased which is associated with increased serum luteinizing hormone (LH) to follicle stimulating hormone (FSH) ratios. This type of dysbiosis reveals a potential gut–brain axis in PCOS. This disturbance in gut microbiota increases the gut mucosal permeability and

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consequently increased passage of lipopolysaccaride (LPS) from Gram-negative colonic bacteria into the systemic circulation. This leads to the immune system activation and the resultant interference with insulin receptor function, androgen production by the ovaries and impaired follicle development [79-81].

Vulvodynia

Dysbiosis has also been suggested to contribute to the onset of vulvodynia, also known as idiopathic vulvar pain. This is perhaps the result of altered immune inflammatory response caused by the changed microbiota composition and abundance. In fact, females with low-diversity microbiota are more likely to develop vulvodynia, compared with those women with high-diversity microbiomes [82, 83].

Pelvic organ prolapses

Pelvic organ prolapse (POP) is a prevalent female syndrome presenting with various manifestations like uterine prolapse, rectal bladder prolapses, and anterior and posterior vaginal wall bulge. It has been demonstrated that vaginal dysbiosis has an impact on the occurrence of female POP; it means that the inflammation and fluctuations of estrogen levels caused by vaginal microecology disruption may be a trigger for POP [84, 85].

Role of probiotics in other gynecological disorders

PCOS-related insulin resistance may be mitigated by specific probiotics. For example, a 12-week supplementation with "*Lactobacillus acidophilus*", "*Lacticaseibacillus casei*", and "*Bifidobacterium bifidum*" significantly lowered Sex Hormone Binding Globulin (SHBG) and serum insulin levels in one study [86]. While a systematic review found that probiotics did not significantly reduce insulin and fasting blood glucose (FBG), even small reductions in these markers offer health advantages [87]. Furthermore, prior studies indicate that probiotic use exceeding 12 weeks leads to weight and fat loss in obese women [88]. Furthermore, daily intake of 100 mg of "Lactobacillus gasseri" reduced Visual Analog Scale (VAS) pain more effectively than a placebo in women with endometriosis [89]. Probiotics, by reducing immune responses and proinflammatory cytokines, alleviate inflammation and discomfort. They may also promote endometriotic lesion regression through Natural killer cell activation [90].

Association of sex behaviors and vaginal microbiome

an association has recently been demonstrated between vaginal commensals and sexual behaviors. As previously mentioned the vaginal microbiota contribute to in the development and persistence of STIs; this per se has a significant impact on sexual relationship [91]. On the other hand, it has been demonstrated that sexual practices affect the vaginal microbiota profile in women with various sexual orientation and behaviors. For example, inconsistent condom use, new or multiple numbers of sexual partners and homosexual affair have been shown to lead to decreased lactobacilli abundance and increased diversity and abundance of anaerobic bacteria including *G. vaginalis*; this is followed by increased risk of BV. Moreover, high-risk sexual behavior like female sex work is associated with increased diversity of the vaginal microbiome and decreased abundance of Lactobacillus species, which is the cornerstone of several gynecological infections and disorders [92-94].

Association of contraceptives and the female reproductive tract microbiome

It has been demonstrated that different contraceptives have various effects on the composition of FRT microbiota and vaginal health. For example, women who are on intramuscular injectable depot-medroxyprogesterone acetate (DMPA-IM) or oral contraceptives (OCPs) for contraception are at decreased risk of BV incidence and recurrence, mainly due to the increase in Lactobacillus levels [95, 96]. This is in contrast with copper or levonorgestrel intrauterine device (IUD) users who are at increased risk of BV as a result of alteration in the

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vaginal bacterial composition [97-99].**Supporting and Conflicting Studies**

Multiple studies have confirmed the important role of *Lactobacillus* species in maintaining vaginal health. Zierden et al. demonstrated that *Lactobacillus* crispatus-dominated microbiota was associated with stronger cervicovaginal mucus barrier function, while polymicrobial communities increased permeability. This suggests that microbial composition plays a crucial role in preventing bacterial ascension, with potential implications for preterm birth risk [100]. Similarly, Takano et al. (2023) evaluated how various *Lactobacillus* species inhibit *Candida albicans* growth, biofilm formation, and epithelial adhesion, identifying lactate as a key factor in suppressing *C. albicans* biofilms and hyphal transition [101]. Rahman et al. (2023) showed that estrogen significantly influences Lactobacillus and *G. vaginalis* colonization, with mice treated with 17β-estradiol exhibiting increased glycogen levels supporting Lactobacillus colonization, whereas progesterone alone failed to restore microbial balance [102].

However, some studies have reported conflicting findings. Mao et al. (2023) investigated the association between vaginal and cervical microbiome dysbiosis and uterine fibroids, finding no significant difference in overall microbial diversity between women with fibroids and healthy controls, although alpha diversity was negatively correlated with the number of fibroids Mao [103]. Zhang et al. (2024) reviewed the relationship between vaginal microbiota, human papillomavirus (HPV) infection, and cervical cancer, highlighting that while vaginal dysbiosis (characterized by reduced *Lactobacillus* abundance and increased microbial diversity) contributes to HPV persistence and cervical lesion progression, the specific mechanisms and causal relationships remain complex [42]. Additionally, Wu et al. (2022) reported that *L. iners* may exert either protective or pathogenic effects on different HPV-related diseases, suggesting variability in the role of specific *Lactobacillus* species [16].

Conclusion

This review article highlights the essential impact of dysbiosis on various obstetric and gynecological disorders. Thus, it seems that restoration of female normal microflora through probiotics can be used as a preventive and therapeutic target for several reproductive diseases. This can be true for all challenges including reproductive failures and gynecological cancers. Given the unclear mechanisms of action and inconsistent findings on effective strains and doses, further research is needed to determine the impact of probiotics on women's health, particularly in conditions like gynecological cancers.

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Author's contribution:

All the authors contributed to the conception and design of the study. MA Z, B F, and F R drafted the first version of the manuscript. All authors approved the final version.

List of abbreviations

GI: Gastrointestinal , FRT: Female Reproductive Tract, CAM: Chorioamnionitis, IUA: Intrauterine Adhesion, PROM: Premature Rupture Of Membranes, BV: Bacterial Vaginosis, STIs: Sexually Transmitted Infections, HPV: Human Papillomavirus, HSV: Herpes Simplex Virus, HIV: Human Immunodeficiency Virus , PID: Pelvic Inflammatory diseases, PCOS: Polycystic ovary syndrome, LPS: lipopolysaccaride, POP: Pelvic Organ Prolapse, SHBG: Sex Hormone Binding Globulin, FBG: Fasting Blood Glucose, VAS: Visual Analog Scale, DMPA-IM: Depot-

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Medroxyprogesterone Acetate, OCPs: Oral Contraceptives, IUD: intrauterine device.

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