

Probiotics and their potential use in treating infertility in human

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ABSTRACT

Background:

Nowadays, there is a lot of focus on the use of probiotics as an alternative therapy for a number of human diseases, including those of the gastrointestinal tract, particularly colorectal cancer, cardiovascular conditions, hyperlipidemia, and cases of high blood pressure. Nevertheless, infertility as it relates to the. Not enough attention was paid to the microbiome and the potential function of probiotics in easing infertility issues, particularly in IVF patients with male or female characteristics.

Main body:

In this review, we tried to draw the attention of researchers in the medical settings to the importance of the forthcoming role of probiotics use in elucidating the role of the microbiome in infertile patients. The hope is to attain the best performance of both male and female reproductive systems and to shed some light on infertility problems.

Conclusion:

Before considering probiotics as an alternative treatment, more in vivo research is still required to address numerous probiotic-related issues, including correct administration, precise functional strains, dosage requirements, application methods, duration of treatment, and interaction with antibiotics.

Keywords:

Probiotics, bacterial vaginosis, lactobacillus species, increasing fertility, infertility.

I. Background :

The need for various natural resources that can be utilised as substitutes for traditional foods

and can be included into diets is urgent due to the demand for healthy food on a worldwide scale. Created in the therapeutic and nutraceutical industries. The usage of probiotics, which has attracted significant interest over the past 15 years [1], is the greatest option for this endeavour. The purpose of using probiotics is to have a healthy lifestyle by enhancing one's internal microbiota [2] and to identify the most effective microorganism or group of bacteria for enhancing health preventing/treating certain disorders [3]. The correct kind of beneficial bacteria can help you reach this goal. The word probiotics, which is a combination of "Pro: for, bios: for," has a long history dating back to the Greek and Latin cultures life" [4]. Elie Metchnikoff, a Nobel Prize laureate who lived in the early 20th century, emphasised the benefits of fermented milk for both general body health and the gut microbiota. He was given the title "father of probiotics" based on his early observations. Probiotics are defined as microorganisms and/or compounds released from living microorganisms to bestow greater health either directly or indirectly or to stimulate the growth of others by Lilly and Stillwell in 1965 [5]. After that, the definition of probiotics had been changed to include the good bacteria that help the body's microbiome. The Food and Agriculture Organization came up with the most recent definition of probiotics (FAO) Live microorganisms, which, when administered in sufficient proportions, provide a health benefit on the host, were defined in 2002 to be: The International Scientific Association for Probiotics and Prebiotics (ISAPP) participant scientists highlighted the prior probiotics idea put forth by the FAO in October 2013. This emphasised the development of the idea of prebiotics and related crucial part in assisting probiotics in playing the expected role. Non-digestible carbohydrates known as

prebiotics include numerous substances, including fructo- oligosaccharides (FOS) and inulin, promote the growth of probiotic microorganisms. They encourage the growth of good bacteria rather than bad.

Synbiotics are probiotics and prebiotics together, and they have a synergistic effect [7]. Probiotics are widely known for their ability to increase immunity [8], eradicate harmful bacteria by preventing colonisation [9], prevent infection, and enhance overall gastrointestinal tract (GIT) health [10]. Recently, focus has been placed on how probiotics affect the skin, oropharynx, and vaginal tract, among other areas of the body. The World Health Organization claims that (WHO), "A disorder of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of frequent unprotected "sexual activity," is how infertility is defined. As the percentage of male and female infertility increases, a global worry is emerging [11]. According to epidemiological research, about 10% of people in reproductive age worldwide experience infertility issues [12]. Since infertility is a complicated problem and the vaginal microbiome may be the least of their concerns, counselling an infertile couple is a struggle for any doctor. But the vagina is regarded as a key research site, according to the suggestions made by the "Human Microbiome Project" (HMP) in the USA in 2007. The human body's bacterial microbiota [13]. Today, it is well known that the female vaginal tract contains specific strains of helpful bacteria. The solution to many infertility issues lies in the tract.

According to studies, *Lactobacillus* species predominate in the vagina [14]. Because the vaginal microbiome (VMB) imbalance that causes female infertility may alter the sperm parameters inside the female reproductive tract, the beneficial effect of probiotics on fertility does not clearly distinguish between males and females [15]. The effects of probiotics on fertility and their contribution to fecundity promotion could be considered from two perspectives. The possible anti-oxidant effects of probiotics on sperm parameters, testicular histology, and testosterone level; first, male fertility;

Second, female fertility and the impact of probiotics on bacterial vaginosis therapy, vaginal bacterial balance maintenance, and consequent effects on inflammation reduction. Probiotics' effects on menopause infections, pregnancy difficulties, and assisted reproductive technology

(ART) should also be taken into account.

Mechanisms of action of probiotics

The most well-studied probiotic bacteria, *Lactobacilli* spp., exhibit multiple methods to safeguard the vaginal environment disease-causing agents. The following are the most important ones: [16] production of lactic acid, which lowers pH to 3.5-4.7 and contributes to indirect pathogen inhibition by effectively acid cervico-vaginal human mucus ([17, 18] production of bacteriocins, which are antimicrobial peptides (AMP) and proteins, produced as a response to an imbalance of vaginal microbiome, to protect the host against microbial invasion ([19, 20] blocking the uptake of lactic acid by bacteria) *Lactobacilli* bacteria's displacement and exclusion competition with vaginal pathogens [17]; their stimulation of immunomodulation mechanisms [21]; and

nisms by inducing H₂O₂ production, activating the innate immune system, and promoting anti-inflammatory action [22].

Intestinal health and male fertility

Male infertility was brought on by obesity and ageing. It has been observed that there is a substantial proportionate association between male subfertility and fat. Obese men reportedly have a larger percentage of poor-quality sperm [23]. In men who were discovered to have reduced sperm count and motility, testosterone deficit is another adverse effect of obesity [24]. However, irreversible testosterone decline is connected to ageing in men. In addition to poorer spermatogenesis, this lack of testosterone is accompanied by increased body fat, decreased libido, and decreased sexual activity [25].

Probiotic effects on testicular histopathology, oxidative stress, testosterone levels, and sperm quality.

Around 50% of the infertility issue is caused by male infertility caused by low sperm parameters [26]. Obesity is one of the main variables influencing sperm parameters and in particular histopathology. A high-fat diet significantly reduces the anti-oxidant action and increases oxidative stress [27]. The quality of sperm and, consequently, the capacity for fertilisation may suffer from an increase in reactive oxygen species (ROS) [28]. A second study that used a combination of the results from the first to support a vaginal tablet formulation of

three chosen probiotic strains (*Lactobacillus brevis*, *L. salivarius*, and *L. plantarum*) was utilised to treat bacterial vaginosis in order to investigate probiotics ability to protect sperm quality from harmful ROS. It has been demonstrated that this probiotic combination prevented sperm lipid peroxidation and preserved the viability and motility of human sperm [19].

Numerous studies examined the negative impact of obesity on male fertility in mouse models and the beneficial role of probiotics in battling the harmful effects of a high-fat diet. Ibrahim and others [29] utilise male mice model to investigate how probiotics improve their poor fertility. Only the serum levels of cholesterol increased significantly in mice fed a high-fat diet. Sperm parameters (count, motility, and morphological abnormalities), as well as the atrophy and degeneration of seminiferous tubules, triglycerides, low-density lipoprotein, high-density lipoprotein, and testosterone. The relative weight of the testes and the length of the penis, however, remained unaffected. Using selenium-enriched probiotics dramatically lessened the harmful effects of hyperlipidemia by reducing testicular tissue injury and improving sperm quality and testosterone levels. They came to the conclusion that probiotics high in selenium increase male fertility in a high lipid state. Probiotics' antioxidant and preventive benefits against sperm damage were investigated by Chen et al. [30] caused in rats by a high-fat diet. To assess oxidative stress, sperm count, motility, viability, and DNA integrity, they fed the test group a high-fat diet. They observed a notable increase in oxidative stress and lipid peroxidation as well as a notable decrease in sperm quantity, motility, viability, and DNA stability. In male rats fed a high-fat diet supplemented with probiotics, all the adverse effects of every test parameter were reversed. The fact that the test group's sperm DNA damage was much lower than the control group's, but still greater than the test group's, suggests that probiotics partially offset the negative effects of a high-fat diet on sperm DNA level. Probiotics may be an alternate treatment for eliminating certain types of bacteria, according to a new study by Dardmeh et al.

Obesity has negative effects on the quality of semen. To determine the impact of probiotics (*Lactobacillus rhamnosus*) on sperm kinematic characteristics, testicular weight, lipid profiles, and reproductive hormones such as follicle

stimulating hormone (FSH), luteinizing hormone (LH), and testosterone, the study was conducted on male mice. They discovered that *Lactobacillus rhamnosus* reduces the weight of mice given a high-fat diet. Additionally, male mice fed a fat-rich diet supplemented with probiotics preserved some sperm indicators including motility and reproductive hormones.

Probiotics may enhance male fertility positively either directly or indirectly, according to their hypothesis. The immediate result enhances spermatogenesis and maturation, while the indirect impact eliminates the negative effects of obesity and increases overall anti-oxidant power. Not alone does fat decrease testosterone levels; ageing is another factor that lowers the amount of testosterone in the blood that is circulated.

Probiotic *Lactobacillus reuteri* may prevent testicular shrinkage caused by obesity and age-related variables in male mice, according to Poutahidis et al. [31].

Testicular tissue from older animals administered probiotics exhibited healthy seminiferous tubules and Leydig cells, which typically exhibit atrophy in older mice. Aged mice given *Lactobacillus reuteri* probiotics showed a notable quantity of circulating testosterone. These unique findings, according to research, probiotics may be utilised as a natural treatment for male hypogonadism brought on by ageing.

Zeitoun et al. [32] assessed the synbiotic effects of probiotics and the medicinal plant dandelion (*Taraxacum officinale*) on the testicular histopathology and semen quality of male lambs. Traditional medicines have traditionally been made from dandelion roots and leaves. It is used to treat joint, kidney, liver, gallbladder, and constipation issues.

However, it was shown that dandelion plant had an anti-fertility effect *in vivo*, causing a significant decline in testosterone levels. Apoptosis was observed. Both localised and widespread oedema were blamed for these results. The testicular health was significantly improved according to histological findings. Tissue from lambs given probiotic treatment. Probiotics are said to have an anti-oxidative stress action that shields sperm from free radicals. The anti-fertility effects of dandelion on spermatogenesis and testosterone production are lessened by combining it with probiotics in a synbiotic cocktail.

The impact of two specific anti-oxidant probiotic strains (*Lactobacillus rhamnosus* CECT8361 and *Bifidobacterium longum* CECT7347) on sperm was examined in a recent study by Valcarce et al. [33]. Guys who meet the asthenozoospermic (low motility) requirements. Sperm motility, cellular viability, DNA fragmentation, and ROS level were the four factors that were assessed. While the other three evaluated metrics showed a considerable improvement following probiotic administration, viability was unaffected. These results demonstrate the significance of taking probiotics to increase male fertility in humans. Infertile men who received prebiotic/probiotic therapy significantly increased their testosterone levels and sperm quality, according to the first placebo-controlled trial by Maretti and Cavallini [34]. Data indicated a direct effects of prebiotic/probiotic therapy on pituitary gland activity in terms of raising FSH and LH serum levels. The GELDING hypothesis was put up by Tremellen [35]. Gut microbiota and testicular ability was found to be strongly correlated in the study (Gut Endotoxin Leading Decline in Gonadal function). According to Tremellen et al. [36], Sertoli and Leydig cell dysfunction is linked to compromised gut mucosa and the leakage of endotoxin-producing microorganisms into the systemic circulation. According to Tirandaz et al. [37], there is a significant connection between treating sexual dysfunction and gut microbiome. This theory is supported by a solid evidence that hormonal imbalances, stress, obesity, hypertension, and diabetes have a negative impact on sexual issues. Since prebiotics and probiotics are the main regulators of microbiota improvement, as many studies have demonstrated, they may have a significant therapeutic impact on the aforementioned disorders.

Intestinal health and female fertility

A healthy vaginal microbiome environment serves as a barrier between the female reproductive system and potentially ascending pathogens. Various gynaecological issues and damage to the upper reproductive tract. Approximately 7.5 million women of reproductive age are thought to exist (15–44 years) According to recent statistics from 2016 (National Center for Health Statistics) [38], are dealing with an infertility issue. Any illness in the female reproductive system is known to pose a substantial

risk to both fertility and pregnancy. Bacterial vaginalization (BV) hence has a negative impact on the implantation rate in assisted reproductive technologies, preterm birth of low-weight newborns, and postpartum problems.

Female genital tract normobiosis and dysbiosis

The vaginal microbiota is being colonised by more than 200 bacterial species [39]. The majority of the species are detected in 70% of women with a healthy vaginal microbiota and belongs to the species *Lactobacillus* [40]. According to reports, the four most common *Lactobacillus* species include among other bacterial strains, widespread. The most prevalent *Lactobacillus* species is *L. crispatus*, followed by *L. jensenii*, *L. iners*, and *L. gasseri* [41]. The less prevalent *Lactobacillus* spp. *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus vaginalis*, *Lactobacillus salivarius*, and *Lactobacillus coleohominis* have all been found [14]. About 20–30% of women with healthy VMB also have non-*Lactobacillus* dominating strains, including *Gardnerella*, *Corynebacterium*, *Atopobium*, *Anaerococcus*, *Prevotella*, and others [41]. As a result, it has been determined that *Lactobacillus* spp. presence is a significant biomarker for evaluation of a healthy vaginal

microbiome. The term "normalobiosis" refers to a microbiome in which *Lactobacillus* spp. and other obligatory anaerobic bacteria predominate. Contrarily, dysbiosis is a Such as a VMB imbalance and a predominance of pathogenic bacteria as *Candida*, *Mycoplasma*, and *Urea-plasma*. Sexually transmitted diseases (STDs), bacterial vaginosis (BV), adhesions, tubal mucosal damage, pelvic pain, ectopic pregnancy, pre-term labour, post-partum complications, cancers of the reproductive tract, and infertility are a few of the gynaecological pathogenic effects that may coexist with dysbiosis [42]

Variations in the vaginal microbiome

Several factors, including hormonal fluctuations, have a significant impact on the vaginal ecology during a woman's life cycle. Menstrual cycle, pregnancy, menopause, age, sexual behaviour, antibiotic use [43], hygiene practises, and ethnicity [14] are some more factors to consider. For instance, it has been discovered that the ratio of *L. crispatus* remains consistent throughout menstruation, whereas the ratio of *L. iners* substantially increases at this time and

thereafter returns to normal [43]. In contrast, a different study found that in women with healthy VMBs, the level of *L. iners* and many other *Lactobacillus* strains increased whereas the level of *L. crispatus* declined 100 times during the menstrual cycle [44].

Bovine vaginosis

Once the bacterial composition surpasses the "normal," the microbial vaginal ecology is regarded as harmful fluctuation amplitude. A vaginal condition known as bacterial vaginosis (BV) is characterised by the disruption of the vagina's commensal bacterial habitat and the colonisation of pathogenic microorganisms [45]. With a larger overgrowth of other pathogenic bacteria such as *Gardnerella* spp., *Atopobium* spp., *Prevotella* spp., and *Mobiluncus* spp. in BV, a considerable drop in *Lactobacillus* spp. has been seen [39]. While the hostile pathogens will drive the synthesis of mucin-degrading enzymes (e.g., sialidases and mucinases) that damage the mucus coating the vaginal epithelium, interfering with a healthy pH and lactic acid level is connected with an unbalanced microbiota in the vagina [18]. Significant infection-prevention barrier [46]. Additionally, Harwich [47] has demonstrated that those pathogenic strains can create a polymicrobial biofilm that permits other harmful species' prevalence. This dysbiotic condition is regarded as the most frequent cause of infertility, urinary tract infections (UTIs), and sexually transmitted diseases (STDs) [48]. According to estimates [49], bacterial vaginosis affects roughly 19% of women with reproductive issues.

Probiotics' uses as complementary treatments for menopause, pregnancy, and fertility preservation. Numerous research have led to the conclusion that exogenous *Lactobacillus* probiotic supplementation can enhance menopausal infection, fertility, and pregnancy outcomes by restoring the vaginal flora. Bhandari and his coworkers put in a lot of effort to check the effectiveness of *Lactobacillus plantarum* in the selective exclusion of *Escherichia coli* (*E. coli*) bacteria that agglutinate sperm. Their findings demonstrated that *L. plantarum* has a significant ability to replace *E. coli* colonisation determined by the quantity and presence of *E. coli* bacteria. This result highlights the important part *L. plantarum* plays in the treatment of infertility [21, 50]. The earlier another study by the same group that used the mouse model to evaluate the probiotics' efficacy as

a therapeutic approach to restore fertility supported our findings. They administered intravaginally to the therapeutic group *E. coli* for 10 days, followed by 10 days of *L. plantarum* treatment. In comparison to the control group, the therapy group's fertility was normal, which supports the hypothesis that utilising *Lactobacillus* probiotics as a therapeutic agent can reverse infertility brought on by sperm-agglutinating *E. coli*. Additionally, the potential for *L. plantarum*'s anti-inflammatory action in reducing LPS-mediated inflammation-induced infertility was investigated. Response of probiotics in upregulating anti-inflammatory cytokines to reduce LPS-induced inflammation. By histopathologically examining female reproductive organs and using mating tests to determine fertility potential, these findings were confirmed [51].

Reestablishing the vaginal microbiome

Anukam et al. [16] reported one of the first studies on the use of well-characterized probiotic strains in the treatment of BV. Forty Nigerian women who had bacterial vaginosis were investigated to see how taking capsules containing *Lactobacillus rhamnosus* and *Lactobacillus reuteri* affected them. 90% of the women with BV recovered after taking probiotics, according to the findings. This discovery could influence the use of probiotic capsules as over-the-shelf self-use therapy. Another investigation assessed *Lactobacillus* in treating bacterial BV and rebuilding the vaginal microbiome by using vaginal pills. Mastromarino and his coworkers conducted a double-blind, placebo-controlled clinical investigation in 2008 [52]. 39 BV-positive women signed up for the trial and were split into two groups at random. The test group was compared to the placebo group after receiving *Lactobacillus*-vaginal pills (*L. brevis*, *L. salivarius*, and *L. plantarum*) every day for seven days. The outcomes demonstrated a dramatic change in the vaginal microbiota, as 83% of the test group women were completely free of BV following the therapy period, while 17% displayed intermediate levels of BV flora in the vagina. An investigation carried out in 2010 by Ya and coworkers that demonstrated the efficacy of exogenous *Lactobacillus* probiotics are administered to treat BV and restore a healthy vaginal flora. Following these findings, numerous further research confirmed the importance of exogenous probiotics in treating bacterial vaginosis and restoring the

normal flora of the vagina. Ling and colleagues [53] shown that administering probiotics had a superior received antibiotic therapy, in preventing BV recurrence. These findings pointed to Lactobacillus' crucial function in reducing BV recurrence during antibiotic therapy [54].

Use of assisted reproduction techniques

As was previously said, BV is a key contributor to infertility around the world as it triggers a number of other illnesses such increased risk of STDs, endometriosis, pelvic inflammatory illness, and tubal obstruction [55]. As a result, the word "BV" is inaccurate because it affects the lower and upper female reproductive tracts as well, not just the vagina [56]. According to earlier studies, the makeup of the vaginal microbiota at the moment of embryo transfer has a strong correlation with the success of an in vitro fertilisation (IVF) cycle [57]. An ART study that discovered a greater pregnancy rate following IVF cycles strongly supported the idea that Lactobacillus species can improve fertility. Patients with a solely Lactobacillus sp.-dominated vaginal microbiota. Only 8% of the 84 women who underwent IVF cycles were found in the cohort research.

Compared to a clinical pregnancy rate of 40% in healthy women, women with bacterial vaginosis (*Gardnerella vaginalis* and/or *Atopobium vaginae*) were able to conceive.

In spite of this, a randomised controlled experiment was set up to examine the preventative effects of the antibiotic co-amoxiclav in IVF patients before embryo transfer. A total of 350 patients were included in the study, and the findings revealed a significant difference between the control group and the group that received antibiotics in the microbial contamination of catheter tips following embryo transfer [59]. However, no difference in clinical pregnancy was found between the two groups. This result can be explained by the antibacterials' capacity to reduce bacterial load but not to reduce bacterial residues that remain impair immunity device [60]. Additionally, several investigations revealed that by reducing the intrauterine growth factor, colonisation the embryo catheter tip with Lactobacillus sp. at the moment of embryo transfer may increase the rate of live birth and implant-rate of infection [61]. According to a different study, using Lactobacillus supplements

helped patients with polycystic ovarian syndrome (PCOS) reduce inflammation, which in turn increased their fertility. An excessive amount of the hormone testosterone is secreted, there is an increase in inflammation, there is ovarian malfunction, and as a result, there is infertility. PCOS is a common but treatable endocrine illness. The purpose of this current study was to investigate how probiotic supplementation may reduce inflammation associated with PCOS. The test group that received probiotic supplementation had lower levels of IL-6 and hs-CRP and significantly higher levels of IL-10 than the control group, according to the data. group cebo. On the other hand, there was no discernible change in the test group's TNF-level. Previous studies have shown that probiotics can reduce inflammation, which helps PCOS patients become more fertile [62].

Pregnancy with a preterm birth

An ecosystem dominated by Lacto-bacillus sp. is more stable and well-balanced in the vagina during a healthy pregnancy. An earlier investigation by Hillier and colleagues in 1995 [63] discovered a significant correlation between bacterial vaginosis and low birth weight preterm deliveries. A recent study with 593 participants a study on pregnant women was conducted to determine the incidence of imbalanced vaginal microbiota in the various trimesters of pregnancy and to look at the impact on delivery before term or miscarriage. In the second trimester before 28 weeks, they found a significant correlation between aberrant vaginal microbiota and preterm birth (PTB). The main causative agent of PTB before 28 weeks of gestation has been identified as *Klebsiella pneumoniae* [64]. Early post-partum endometritis may also be indicated by the presence of BV-associated bacteria like *Gardnerella vaginalis*, *Bacteroides* spp., *Peptococcus* spp., *Staphylococcus epidermidis*, *Streptococcus agalactiae*, and *Ureaplasma urealyticum* [65]. Approximately the cause of 40–50% of preterm deliveries is bacterial infection. Anaerobic pathogenic bacteria will proliferate in the absence of vaginal Lactobacilli sp. and cause change of the immune system and possible promotion of cervical barrier degeneration, which causes pathogenic invasion of the endometrium and amniotic fluid. After a while, myometrial contractions might be triggered and pre-term labour might be brought on [66]. The research of the vaginal and uterine microbiomes

using next-generation sequencing (NGS), a novel technology, revealed that microbial dysbiosis may pose a major risk to the embryo during the pre-implantation stage and in sustaining a healthy pregnancy [67]. 7847 women were identified as having bacterial vaginosis and received antibiotic treatment in a Cochrane evaluation. The analysis revealed that antibiotic medication is effective in lowering BV throughout pregnancy and lowering the risk of late miscarriage. However, it was unable to completely remove the risk of preterm birth before 37 weeks or the risk of premature membrane rupture [68]. Use of probiotics may reduce pregnancy problems like PTB and pre-eclampsia. Probiotics can be used as prophylaxis to prevent BV recurrence in healthy women with a history of BV incidence, according to a meta-analysis investigation. The outcomes demonstrated a gradual effect of probiotic therapy on BV improvement. In addition, using probiotics is preferred to using antibiotics because they may be used for a long time without experiencing any negative side effects, especially the damage of the natural immune system Microbiome of bacteria [69].

Infection of the vaginal menses

The ability of the gastrointestinal (GI) bacteria to metabolise oestrogen is closely related to how well the reproductive system works. For oestrogen to be processed, either by releasing it back into circulation or by excreting it through urine or faeces in a process known as enterohepatic circulation, their enzymatic activity is required. The bacteria responsible for this regulatory process are referred to as *estro-blome* [70]. The thickness and flexibility of vaginal tissues will decrease in women who are progesterone- and estrogen-deficient 47% or so of postmenopausal women [71].

According to a survey, 56% of women who are approaching menopause have an unbalanced vaginal flora with dominating species different than. The genus *Lactobacillus* [72]. In a Chinese study, 22 menopausal healthy women and 92 fertile women participated. It was discovered that 97% of fertile women contain 2 or 3 species of *Lactobacillus* spp., compared to 3% of fertile women who only have one *Lactobacillus* sp.

On the other hand, only one species of *Lactobacillus* was present in 91% of menopausal women, and 9% of them displayed two *Lactobacillus* species [73]. *L. crispatus* is the most

frequent invading species in healthy women with, according to a recent analysis from Korea, special antibacterial activity, which was proposed to be employed in Korean women as a probiotic therapeutic alternative to antibiotics [74].

II. Conclusions

Probiotics have a considerable impact on body health reinforcement in general and fertility improvement in particular, according to numerous evidence-based research. The effectiveness of probiotics in promoting fertility is addressed on two levels: the first level is the restoration of male fertility by counteracting the negative effects of oxidative stress brought on by a fatty diet and ageing, influencing negatively

testosterone level and sperm quality, with female fertility enhancement coming in second. Scientists have been motivated to discover and define the vaginal flora because of the crucial function of the vagina as a first-line defence against pathogens that may ascend to the upper reproductive system. For this, the most recent technologies, such as next-generation sequencing (NGS), have been used. It is now widely recognised that having a dominant *Lactobacillus* species is a sign of a healthy, symbiotic female vaginal tract. It has been discovered that pathogenic vaginal invasion and an imbalance in vaginal homeostasis alter the predominance of helpful *Lactobacillus* species, resulting in a number of gynaecological issues, including infertility, menopausal infection, bacterial vaginosis, and preterm birth in pregnancy.

The potential use of probiotics as all-natural anti-pathogenic supplements and fertility enhancers still requires further study. Furthermore, to increase male and female fertility potential, rigorous *in vivo* studies on Probiotics should be conducted to clarify their diverse mechanism of action, method of administration and synergistic interactions with antibiotics

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- studies on probiotics should be conducted to clarify their diverse mechanisms of action, methods of administration, and synergistic interactions with antibiotics. long-term therapeutic impact than the conventional antibiotic (metronidazole) in the treatment of BV. They discovered that probiotics gradually improve vaginal homeostasis by preventing the proliferation of harmful bacterial strains, resulting in a continuous restoration of the vaginal microbiota. In a recent study, the effectiveness of long-term *Lactobacillus* supplementation in rebuilding vaginal microbiota was examined. In the study, 250 non-pregnant over nine months, BV in women. The patients were split into two groups: group A received metronidazole as the typical antibiotic treatment, whereas group B received antibiotics followed by *Lactobacillus rhamnosus*. The findings demonstrated that group B was superior to group A, which only