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Original Article

Experts' Opinion on the Role of Synbiotic Interventions in Infertility Management

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Abstract

Background: Female reproductive tract (FRT) dysbiosis, especially vaginal dysbiosis, is one of the reasons for adverse pregnancy outcomes, including preterm birth and miscarriage. Probiotics are increasingly recognized as an effective approach for support and maintaining FRT health.

Methods: The current survey was conducted to evaluate expert insights into the potential of a synbiotic formulation comprising prebiotics and probiotics as a therapeutic intervention in infertility management, particularly for focusing on recurrent pregnancy loss (RPL), recurrent implantation failure (RIF), and preterm birth. An advisory meeting with experts across India was planned, where they deliberated on the influence of the FRT microbiome on adverse pregnancy outcomes and assessed the role of synbiotic interventions in its management. A 10-question survey was used to assess clinical opinions on the benefits of synbiotic formulations in improving pregnancy outcomes. Responses were analyzed quantitatively.

Results: Approximately half of the experts reported that vaginal infections occur in >20% of pregnant women. The majority of experts (66.6%) strongly agreed that vaginal infections increase the risk of RPL, RIF, and preterm birth. All experts suggested that probiotics and prebiotics exert multiple benefits on FRT dysbiosis, including inhibiting biofilm formation and *Candida* adhesion, increasing the production of lactic acid and H_2O_2, inhibiting Gram-negative bacterial growth and reducing the recurrence of vaginal infections. The majority of experts agreed that low *Lactobacillus* dominance increases the risk of infertility, miscarriage, and preterm birth. Around 83.3% of experts agreed that *Lactobacillus* administration during pregnancy improves vaginal pH, Nugent score, and angiogenesis. Similarly, 83.3% supported lactoferrin for reducing oxidative stress and microbial growth, and enhancing probiotic efficacy.

Conclusion: All experts suggested that synbiotics can be beneficial in reducing infection recurrence, improving pregnancy outcomes and supporting implantation. This survey indicated that synbiotic intervention in pregnant women may be beneficial in improving pregnancy outcomes and reducing the risk of vaginal infections.

Key words: Dysbiosis, Female reproductive tract, *Lactobacillus*, Preterm birth, Recurrent implantation failure, Recurrent pregnancy loss, Synbiotic formulations

INTRODUCTION

The female reproductive tract (FRT) microbiome plays a key role in the initiation of conception and impacts pregnancy outcomes, gynecological health, and fetal development.[1] A dominance of *Lactobacillus* species is typically observed in the vagina, which protects against pathogenic infections. Rising estrogen levels during the follicular phase promote *Lactobacillus* dominance, lower vaginal pH, and reduce microbial diversity, creating a favorable environment for conception [Figure 1].[1-3] FRT dysbiosis, especially vaginal dysbiosis, can lead to a sequence of changes, including a decrease in vaginal lactobacilli, reduction in hydrogen peroxide (H_2O_2) and lactic acid, a rise in pH and increased overgrowth of pathogens, leading to vaginal infections.[1] Vaginal infections are one of the reasons for adverse pregnancy outcomes, including preterm birth and miscarriages.[4]

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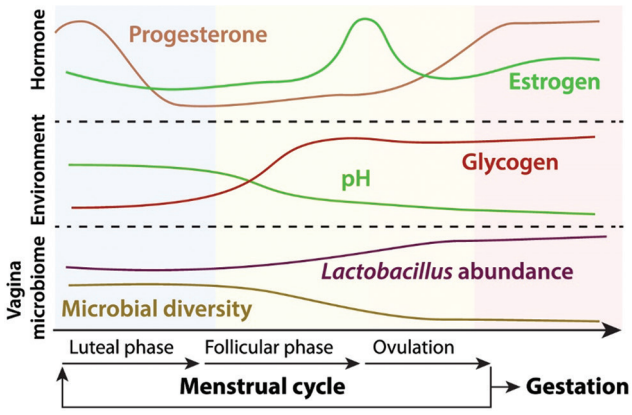

Figure 1: Changes in microbiome before and during pregnancy

Probiotics, once primarily regarded as a treatment for diarrhea, have seen significant expansion in their recognized applications due to increased scientific understanding. They are now reported to offer benefits in the management of metabolic and gastrointestinal disorders, atopic diseases, bacterial vaginosis (BV), urinary tract infections, respiratory conditions, and even anxiety and depressive disorders.[5] Notably, as research reveals the crucial role of the microbiome in reproductive health, probiotics are being increasingly acknowledged as an effective strategy for promoting and maintaining the overall health of the FRT.[6]

MATERIALS AND METHODS

An advisory meeting with seven gynecologists and infertility experts from across India was conducted on July 27, 2025, to deliberate on the emerging understanding of the role of the microbiota in the FRT – an often overlooked yet pivotal factor in reproductive health. The aim was to gain expert insights into how modulation of the FRT microbiome could offer a novel and supportive therapeutic strategy to improve implantation success, reduce recurrent pregnancy loss (RPL) and enhance fertility outcomes.

At the end of the meeting, a pre-designed comprehensive questionnaire was discussed among the panelists. The questionnaire consisted of 10 questions [Box 1] that assessed real-world clinical opinions from experts regarding the potential advantages of a synbiotic formulation combining clinically validated prebiotics and probiotics for managing RPL and recurrent implantation failure (RIF), and reducing the risk of preterm birth. Responses from the healthcare professionals (HCPs) were documented in Microsoft Excel. The average percentage of HCPs favoring each answer was calculated.

RESULTS AND DISCUSSION

Prevalence of Vaginal Infection among Pregnant Women

Approximately half of the experts reported that vaginal infections occur in more than 20% of pregnant women. Around 33.3% estimated the prevalence to be between 10% and 15%, whereas the remaining experts observed it in approximately 5–10% of cases. This expert opinion aligns with current evidence from published literature indicating that approximately 22.5% of pregnant women in India experience vaginal infections during pregnancy.[7]

Association between Vaginal Infections and Adverse Pregnancy Outcomes

A majority of experts (66.6%) strongly agreed that vaginal infections are associated with an increased risk of adverse pregnancy outcomes. The remaining HCPs agreed with this observation. Supporting this consensus, existing literature indicates that vaginal and endometrial dysbiosis are linked to a heightened risk of complications such as RPL, RIF, and preterm birth.[4,8-10]

Vaginal Pathogens and Resistance to Antibiotics

Half of the HCPs (50%) strongly agreed, one-third agreed, and the remainder somewhat agreed that vaginal pathogens are showing increasing resistance to antibiotics and antifungals, leading to higher recurrence rates of BV. Supporting this, current literature highlights that the standard treatment for BV – typically involving antibiotics such as metronidazole or clindamycin – is becoming less effective due to several challenges.[11]

Cure rates for these first-line therapies, once exceeding 90%, have now declined to approximately 50–80%. A key factor in treatment failure is the formation of biofilms by BV-associated bacteria, which act as physical and biochemical barriers hindering antibiotic penetration. Within these biofilms, pathogens employ various resistance mechanisms, including the activation of efflux pumps, the production of drug-neutralizing enzymes, and the secretion of protective extracellular matrices. These adaptations not only reduce antibiotic efficacy but also contribute to the persistence and recurrence of infection.[12]

Alarmingly, approximately 58% of women experience BV recurrence within 1 year, which may further drive the emergence and spread of antibiotic resistance genes.[13]

Role of Probiotics and Prebiotics in Managing Vaginal Infections

All experts agreed that probiotics and prebiotics play a role in managing vaginal infections. Specifically, they noted that:

- *Lactobacillus crispatus* and *Lactobacillus gasseri* inhibit biofilm formation, hyphal growth and *Candida* adhesion to the vaginal epithelium[14]

Box 1: Questionnaire

1.	**Based on your clinical practice, how common are vaginal infections among pregnant women?** A. 0–5%, B. 5–10%, C. 10–15%, D. >20%
2.	**An association is observed between vaginal infections in pregnant women and an increased risk of adverse pregnancy outcomes. What is your opinion?** A. Strongly agree, B. Agree, C. Somewhat agree, D. Disagree
3.	**Vaginal pathogens are showing increased resistance to antibiotics and antifungals, leading to higher recurrence rates of bacterial vaginosis. What is your opinion?** A. Strongly agree, B. Agree, C. Somewhat agree, D. Disagree
4.	**Based on your clinical experience, what role do probiotics and prebiotics play in managing vaginal infections?** A. *L. crispatus*, *L. gasseri,* and *L. jensenii* inhibit biofilm formation, hyphal growth, and Candida adhesion to the vaginal epithelium, B. *L. rhamnosus* and *L. gasseri* increase lactic acid production C. *L. jensenii* produces higher levels of hydrogen peroxide (H_2O_2), D. *L. crispatus* disrupts the cell wall of Gram-negative bacteria and inhibits their growth, E. Lactobacillus+lactoferrin combination helps relieve symptoms of vaginal infection and lowers the risk of recurrent vulvovaginal candidiasis (VVC), F. All of the above
5.	**Women with low *Lactobacillus* dominance in the vaginal microbiome may face increased risks of adverse reproductive outcomes such as reduced fecundity, poor pregnancy rates, early miscarriage, late pregnancy loss, preterm birth, and maternal infections. What is your opinion?** A. Strongly agree, B. Agree, C. Somewhat agree, D. Disagree
6.	**Evidence suggests that administering *Lactobacillus* during pregnancy may reduce the risk of miscarriage. Which of the following do you believe to be true?** A. Lactobacilli promote lactic acid production, lowering vaginal pH, B. They help reduce the Nugent score, C. They stimulate angiogenesis during early pregnancy, D. All of the above
7.	**Which of the following do you consider key factors contributing to embryo implantation failure?** A. Endometrial microbiota with low *Lactobacillus* abundance, B. Reduced vaginal Lactobacillus levels linked to pro-inflammatory cytokines and increased risk of reproductive failure, C. Both A and B, D. Other (please specify): _____
8.	**What is the role of lactoferrin supplementation in maintaining a healthy vaginal microbiome?** A. Antibacterial activity, B. Antifungal action, C. Enhances the effect of probiotics, D. Reduces inflammation, E. Limits oxidative stress and iron availability, thereby restricting microbial growth
9.	**In your clinical practice, would you consider prescribing a synbiotic formulation (a combination of probiotics and prebiotics) containing key *Lactobacillus* strains and lactoferrin to reduce vaginal infection risk and improve pregnancy outcomes?** A. Yes, B. No
10.	**Based on your experience, what benefits have you observed from using a synbiotic formulation in pregnant women?** *(Select all that apply)* A. Reduced risk of recurrent implantation failure and pregnancy loss, B. Prevention and treatment of vaginal infections, C. Lowered risk of preterm birth, D. Support in managing iron deficiency during pregnancy

- *Lactobacillus rhamnosus* and *L. gasseri* increase lactate production[14]
- *Lactobacillus jensenii* produces higher levels of H_2O_2[14]
- *Lactobacillus* + lactoferrin combination helps relieve symptoms of vaginal infection and lowers the risk of recurrent vulvovaginal candidiasis.[15]

These insights are supported by current literature [Table 1] and reflect an evolving approach to the non-antibiotic management of vaginal infections. Literature suggests that formulations including probiotics such as *L. rhamnosus, L. crispatus, L. gasseri, L. jensenii, L. reuteri, L. plantarum,* and *L. casei* are beneficial in the management of vaginal infections.[16-18]

Association between low *Lactobacillus* Dominance in the Reproductive Tract (Vagina and Endometrium) and Risk of RPL

The majority of experts (66.6%) strongly agreed, whereas the rest agreed, that women with low *Lactobacillus* dominance in the vaginal microbiome are at increased risk of adverse reproductive outcomes, including reduced fecundity, poor pregnancy rates, early miscarriage, late pregnancy loss, preterm birth, and maternal infections. Evidence suggests that reproductive tract dysbiosis leads to increased proinflammatory cytokines, resulting in increased uterine contractions, which in turn elevate the risk of miscarriage [Figure 2].[19]

Clinical evidence also suggests that diminished *Lactobacillus* presence in the vagina and endometriosis is associated with RPL. Evidence suggests that a low abundance of *Lactobacillus* species, specifically *L. crispatus*, *L. jensenii*, and *L. gasseri,* in the vagina is associated with an increased risk of pregnancy loss [Table 2].[20,21] Thus, maintaining a *Lactobacillus*-rich vaginal environment is regarded as essential for optimal reproductive health and favorable pregnancy outcomes.[20]

Administering *Lactobacillus* Probiotics during Pregnancy Lowers Risk of Miscarriages

A strong majority of experts (83.33%) opined that administering *Lactobacillus* during pregnancy has multiple benefits, including increasing lactic acid production, lowering vaginal pH, reducing the Nugent score, and stimulating angiogenesis by increasing the levels of vascular endothelial growth factor (VEGF) during early pregnancy. Experts opined that VEGF plays a critical role in vasculogenesis and angiogenesis, both essential for successful embryo implantation. Experts agreed

Table 1: Role of probiotics in the management of vaginal infections in Indian women

Author	Study group	Intervention	Outcome
Thekho *et al*. (2024)[16]	Indian women newly diagnosed with VVC (*n*=60)	Group A (*n*=30) was treated with oral fluconazole 150 mg single dose; Group B (*n*=30) was treated with oral fluconazole 150 mg single dose+oral probiotic capsules *(Lactobacillus rhamnosus, L. crispatus, L. gasseri, L. jensenii)* for 2 months	A higher number of patients in Group B (97%) achieved complete remission compared to Group A (90%). Both treatments were safe.
Faruqui *et al*. (2022)[17]	Indian women with BV (*n*=58)	1 capsule (*L. crispatus 1 bn, L. rhamnosus* 1 bn, *L. jensenii* 0.02 bn, and *L. gasseri* 0.03 bn CFU) daily for 4 weeks	At week 4: • Significant improvement in the symptoms* versus baseline • pH <4.5 in 96.4% of women • 71.4% of investigators rated the probiotic's efficacy as excellent; its safety was rated excellent by 60.3% and good by 39.7%
Sudha *et al.* (2012)[18]	Indian women diagnosed with BV (*n*=30)	Two probiotic capsules UB-01BV** per day for 7-days	All subjects showed a significant (*P*<0.001) reduction in vaginosis symptoms#

*Vaginal discharge, odor, itching, and painful urination. #increased discharge, odor, color of discharge and pruritus. VVC: Vulvovaginal Candidiasis; BV: Bacterial vaginosis; bn: Billion. **_Lactobacillus acidophilus_ strain UBLA-34, _Lactobacillus rhamnosus_ strain UBLR-58, _Lactobacillus reuteri_ strain UBL Ru-87, _Lactobacillus plantarum_ strain UBLP-40, _Lactobacillus casei_ strain UBLC-42, _Lactobacillus fermentum_ strain UBLF-31, _Bifidobacterium bifidum_ strain UBBB-55

Table 2: Low *Lactobacillus* dominance in the female reproductive tract (vagina and endometrium) and increased risk of miscarriage

Author	Study group	Specimen type	Composition: Phylum/Genus/ Species	Outcome
Low *Lactobacillus* dominance in the vagina and increased risk of miscarriages				
Caliskan *et al.* (2022)[20]	Women with recurrent miscarriages (*n*=25); healthy controls (*n*=25)	Vaginal swabs	Genus *Lactobacillus*↓*Enterobacterium* spp., *Eubacterium* spp. *Megasphaera* spp., and *Sneathia* spp. ↑	A decrease in *Lactobacillus spp*. and an increase in anaerobic microorganisms were found in the vaginal microbiota of women with RPL.
Jiao *et al.* (2022)[20]	History of recurrent miscarriages (*n*=16); healthy controls (*n*=20)	Vaginal swabs	Genus *Lactobacillus* ↓* *Gardnerella* ↓* *Atopobium* ↑*	A decrease in *Lactobacillus* and an increase in the abundance of *Atopobium* and *Prevotella* were found in the vaginal microbiota of women with RPL.
Ncib *et al.* (2022)[20]	Women with unexplained RPL (*n*=65); healthy controls with at least two live births and no miscarriages (*n*=50)	Vaginal swabs	Genus *Enterococcus, Staphylococcus, Streptococcus*↑	There was a high prevalence of aerobic vaginitis-causing bacteria in women with RPL (65%).
Sun *et al.* (2022)[21]	Cases of missed abortion (*n*=54); cases of normal pregnancy (*n*=50)	Vaginal swabs	*L. crispatus**, *L. jensenii**, and *L. gasseri** ↓	The relative abundance of *L. crispatus*, *L. jensenii*, and *L. gasseri* was lower in women with missed abortions versus those with normal pregnancies.
Low *Lactobacillus* dominance in endometrial tissue and increased risk of miscarriages				
Peuranpaa *et al.* (2022)[20]	Women with RPL (*n*=47); healthy controls (*n*=39)	Transcervical endometrial tissue	Species *L. crispatus*↓*Gardnerella vaginalis* ↑	*L. crispatus* was less abundant in women with RPL compared to controls (17.2% vs. 45.6%). *G. vaginalis* was more abundant in the RPL group.
Liu *et al.* (2022)[20]	Women with RPL (*n*=25, with 50% chronic endometritis); healthy controls (*n*=25, with 24% chronic endometritis)	Transcervical endometrial tissue	Phylum *Proteobacteria*↑*Genus Lactobacillus* (<10%) *Anaerobacillus* ↑* *Erysipelothrix* ↑* *Hydrogenophilus*↑*	A lower abundance of *Lactobacillus* spp. was found, and *Acinetobacter* spp. were predominant.

↑: Increased abundance of the bacteria, ↓: Decreased abundance of the bacteria, *: Significant difference between the study group and the control group

that administering *Lactobacillus* probiotics, including *Ligilactobacillus salivarius*, during pregnancy is beneficial in lowering the risk of adverse pregnancy outcomes, including pregnancy loss. These findings are supported by Fernández *et al.*, who recently demonstrated that the administration of *L. salivarius* in women with a previous history of reproductive problems modulates immunological and microbiological parameters in the vaginal ecosystem. Researchers report that the administration of *L. salivarius* improves vaginal pH, Nugent score, transforming growth factor beta-1 (TGFβ-1), TGFβ-2, VEGF expression, pregnancy effectiveness, and positive pregnancy outcomes in both women with repetitive abortion and those with unknown infertility [Table 3].[22,23]

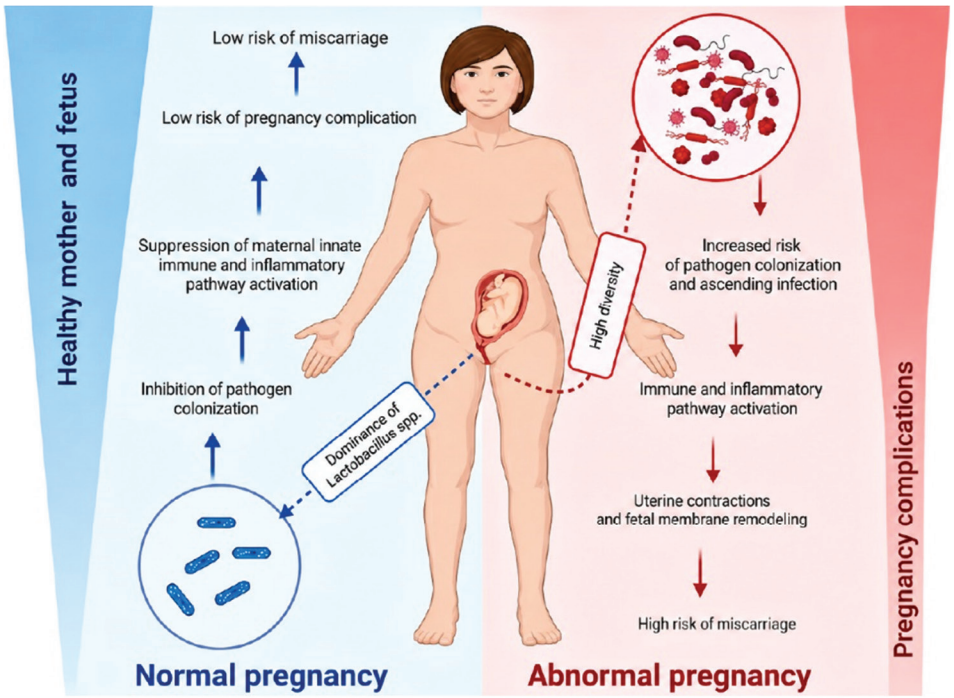

Figure 2: Role of vaginal microbiome in healthy pregnancy and in increasing the risk of miscarriages

Table 3: Role of probiotics in lowering the risk of miscarriages

Author	Study group	Intervention	Outcome
Fernández *et al.* (2023)[22]	Women (*n*=74; age 28–45 years) were classified into four groups: RA (*n*=20), infertility (*n*=20), healthy non-pregnant women (*n*=14), and women with natural pregnancies (*n*=20).	Oral *L. salivarius* CECT 30632 (~9 $\log_{10}$ CFU) daily for 6 months or until pregnancy	*L. salivarius* coaggregated with and inhibited the growth of vaginal pathogens. *L. salivarius* supplementation improved pregnancy effectiveness (conceived) (RA: 80%, infertile women: 55%) and successful pregnancy (full-term live births) (RA: 75%, infertile women: 50%). *L. salivarius* significantly improved vaginal pH, Nugent score, TGFβ-1, TGFβ-2 and VEGF expression and increased *Lactobacillus* and *L. salivarius* concentrations in RA women with full-term pregnancies versus women who did not achieve pregnancy. *L. salivarius* was well-tolerated and safe in pregnant women.
Fernández *et al.* (2021)[23]	Women (*n*=58; age 28–45 years) were classified into three groups: Women with a history of RA (*n*=21), women with infertility despite undergoing at least three rounds of ART (*n*=23), and fertile controls (*n*=14).	Oral administration of *L. salivarius* CECT5713 (~9 $\log_{10}$ CFU) daily for up to 6 months or until pregnancy.	*L. salivarius* showed strong adhesion to vaginal epithelial cells. *L. salivarius* supplementation improved pregnancy effectiveness (conceived) (RA: 81%, infertile women: 52%) and successful pregnancy (full-term live births) (RA: 71%, infertile women: 43%). *L. salivarius* significantly improved vaginal pH, Nugent score, TGFβ-1, TGFβ-2, VEGF expression, lactobacilli and *L. salivarius* count in RA women with full-term pregnancies vs. those who did not achieve pregnancy. Improvement in *L. salivarius* count was associated with a positive pregnancy outcome in both women with repetitive abortion and unknown infertility.

ART: Assisted reproductive technology, *L. salivarius: Ligilolactobacillus salivarius,* RA: Repetitive abortions, TGFβ: Transforming growth factor beta, VEGF: Vascular endothelial growth factor

Low Abundance of *Lactobacillus* in the Reproductive Tract (Vagina and Endometrium) Increases the Risk of Embryo Implantation Failure

The majority of experts (83.33%) opined that the primary factors contributing to embryo implantation failure include:

- Low abundance of *Lactobacillus* in the endometrial microbiota
- Reduced vaginal *Lactobacillus* levels.

Experts agreed that dysbiosis in the reproductive tract (vagina and endometrium) leads to inflammation, which alters the integrity of the endometrial mucosa and impairs embryo implantation [Figure 3].[20]

Experts also discussed that, beyond these microbial factors, various other physiological, immunological, and environmental influences contribute to the complex pathophysiology of embryo implantation failure.

Clinical evidence also supports reproductive tract dysbiosis-associated inflammation (in the vagina and endometrium) altering the integrity of the endometrial mucosa, in turn leading to impaired embryo implantation [Table 4].[16]

Experts agreed that *Lactobacillus* supplementation may help reduce the risk of implantation failure by restoring the balance of the reproductive tract microbiota balance. Reproductive tract dysbiosis has been associated with impaired implantation outcomes, as shown in Figure 2 and Table 4. Improving microbial balance by administering *Lactobacillus* may enhance implantation success rates. Clinical evidence supports the use of *L. rhamnosus* and *L. crispatus* in the management of reproductive tract dysbiosis [Table 5].[25-27]

Impact of Lactoferrin Administration on FRT Dysbiosis

The majority of experts (83.33%) agreed that lactoferrin supplementation helps limit oxidative stress and reduces free iron availability, thereby inhibiting microbial growth and promoting a healthy vaginal microbiome. In addition, one expert noted that lactoferrin may enhance the efficacy of probiotics. Supporting this expert consensus, existing literature indicates that lactoferrin exerts multiple beneficial effects on the FRT, including antimicrobial, anti-inflammatory, and immunomodulatory actions.[28]

Benefits of Synbiotic Formulation

All experts agreed on the value of prescribing a synbiotic formulation – comprising probiotics and lactoferrin – as

Table 4: Reproductive tract dysbiosis and risk of recurrent implantation failure

Author	Study group	Specimen type	Composition: Phylum/Genus/Species	Outcome
Ichiyama *et al*. (2021)[20]	Women with RIF (*n*=145); healthy controls (*n*=21)	Vaginal swabs	*Atopobium, Megasphaera, Gardnerella, Prevotella* ↑* *Lactobacillus* ↓*	The vaginal microbiota of the RIF group had lower levels of *Lactobacillus* than in the control group. The dysbiotic microbiota from the RIF group consisted of significantly higher levels of 4 other genera.
Ichiyama *et al*. (2021)[20]	Women with RIF (*n*=145); healthy controls (*n*=21)	Endometrial tissue with a pipette	*Atopobium, Megasphaera, Gardnerella, Prevotella, Schlegelella, Delftia, Burkholderia, Sphingobacterium, Dietzia, Enterococcus, Micrococcus, Ralstonia, Leucobacter, and Hydrogenophaga* ↑*	The dysbiotic microbiota from the RIF group consisted of significantly higher levels of 14 other genera.
Diaz-Martinez *et al*. (2021)[20]	Patients with a RIF history (*n*=23) and without a RIF history (*n*=25)	Transcervical endometrial tissue	Genus *Prevotella and Sneathia amnii* ↑* Species *L. helveticus* ↑*	The RIF group had significantly different compositions of the endometrial fluid microbiota. A higher abundance of *Prevotella* was detected in RIF patients.
Chen *et al*. (2022)[20]	Women with RIF (*n*=75); healthy controls (*n*=36)	Transcervical endometrial tissue	Phylum *Dominance of Firmicutes, Proteobacteria, Bacteroidetes, Cyanobacteria, and Actinobacteria* Genus *Sphingomonas, Brevundimonas, DMER64, Methylobacterium, Rhodoferax, Caulobacter* ↑* *Lactobacillus, Pseudomonas, Delftia* ↓*	There was a significant difference in community composition at the genus level in the RIF group compared to the control group. The dominance of *Sphingomonas* was found in the endometrial microbiota of the RIF group.
Lozano *et al*. (2023)[24]	Women with RIF (*n*=27); healthy controls (*n*=18)	Transcervical endometrial tissue	*Lactobacillus* ↑* *Prevotella* ↑* *Dialister* ↑* *Streptococcus* ↑*	An endometrial microbiota with a lower abundance of lactobacilli was associated with RIF.

↑: Increased abundance of the bacteria, ↓: Decreased abundance of the bacteria, *: Significant difference between the study group and the control group. RIF: Recurrent implantation failure

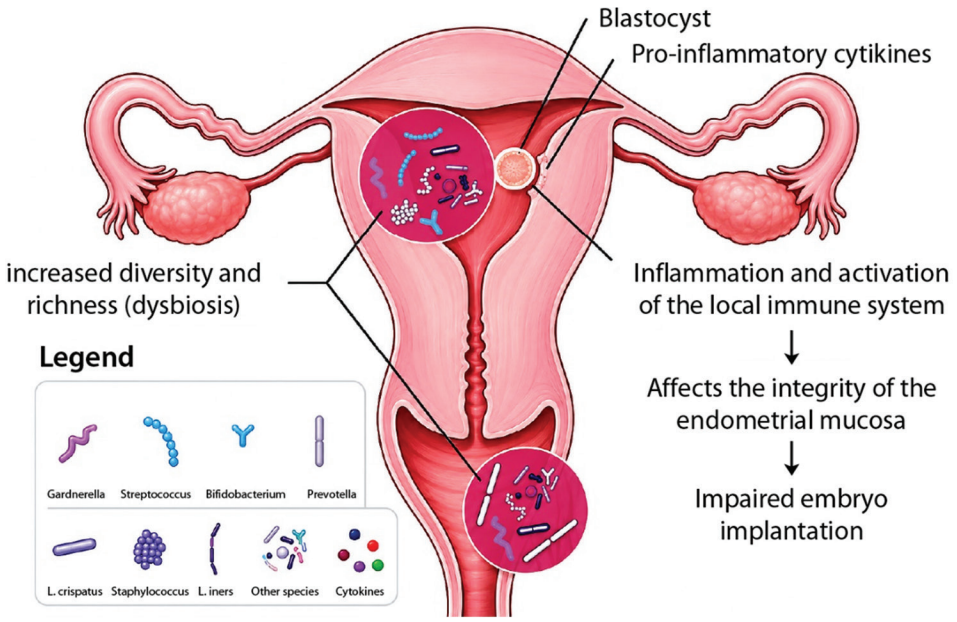

Figure 3: Pathophysiology of reproductive tract dysbiosis and embryo implantation failure

Table 5: Administration of *Lactobacillus* in improving reproductive tract dysbiosis

Author	Study group	Intervention	Outcome
Sakamoto *et al.* (2024)[25]	Women with repeated implantation failure with non-*Lactobacillus* dominance (*n*=27; age 35.5±1.2 years)	Treatment group A (*n*=17): Oral antibiotics (metronidazole or amoxicillin-clavulanic acid), butyric acid bacteria combination drug (3 g/day) as a probiotic for 30–60 days Treatment group B (*n*=10): Probiotic: *Lactobacillus rhamnosus HN001* (13.4 mg) and *Lactobacillus acidophilus* La-14® (45 mg)	Intrauterine flora was cured or improved in a significantly higher number of patients (90%) in treatment group B versus treatment group A (41.2%) (*P*=0.01). A significantly higher *Lactobacillus* occupancy was observed in treatment group B than in treatment group A (62.9% vs. 5.7%; *P*=0.0016).
Di Pierro F *et al.* (2023)[26]	Women undergoing assisted reproductive technology procedures (*n*=160; age 21–46 years)	The probiotic group (*n*=80) was administered *L. crispatus M247* (20 billion CFU/day) Control group (*n*=80) 90 days (started after vaginal swab test was negative for pathogens or after antibiotic treatment)	*L. crispatus* supplementation improved clinical pregnancies (40.54% vs. 21.62%) and live birth rate in patients receiving blastocysts versus controls (24.3% vs. 8.1%).
Kitaya *et al.* (2022)[27]	Women with a history of RIF and non-*Lactobacillus* dominant microbiota (NLDM) in vaginal secretions/endometrial fluid (*n*=172) (RIF group [*n*=117]; non-RIF group [*n*=55])	Eligible RIF patients with NLDM received oral enteric-coated lactoferrin (700 mg/day) for at least 28 days.	Lactoferrin supplementation improved NLDM in 43.2% of RIF women. Live birth rate was higher (57.1%) in RIF women with improved microbiota versus those with unimproved microbiota (11.1%).

RIF: Recurrent implantation failure, NLDM: Non-*Lactobacillus* dominant microbiota

part of a comprehensive strategy to reduce the vaginal infection risk and improve pregnancy outcomes.

One-third of the experts were of the opinion that synbiotic formulations play a valuable role in reducing the risk of RIF and pregnancy loss, supporting the prevention and treatment of vaginal infections, and lowering the risk of preterm birth. In addition, 16% of the experts believed that these formulations can help manage iron deficiency during pregnancy, whereas another 16% highlighted their specific benefits in the prevention and treatment of vaginal infections.

The experts' opinion, along with clinical evidence, suggests that the dominance of *Lactobacillus* species in the FRT plays a key role in a healthy pregnancy. Administering a synbiotic formulation containing clinically studied prebiotics + probiotics can be beneficial for the management of vaginal infections and associated complications, RPL, RIF, and iron deficiency anemia in pregnant women [Box 2].

Box 2: Synbiotic formulation

Lactobacillus rhamnosus: 2 billion CFU
Lactobacillus reuteri: 2 billion CFU
Lactobacillus crispatus: 2 billion CFU
Lactobacillus acidophilus: 2 billion CFU
Lactobacillus salivarius: 1 billion CFU
Lactobacillus casei: 1 billion CFU
Lactobacillus fermentum: 1 billion CFU
Lactobacillus plantarum: 1 billion CFU
Lactobacillus gasseri: 0.6 billion CFU
Lactobacillus jensenii: 0.4 billion CFU
Bifidobacterium bifidum: 1 billion CFU
Lactoferrin: 50 mg

CONCLUSION

This expert opinion supports the use of synbiotic formulations comprising probiotics and prebiotics as a comprehensive, non-antibiotic strategy to reduce the risk of vaginal infections, improve implantation success, and ultimately enhance pregnancy outcomes. These formulations may also address related complications such as iron deficiency during pregnancy.

In conclusion, integrating synbiotic formulations into infertility management represents a promising approach to overcoming antimicrobial resistance challenges and improving adverse pregnancy outcomes, including vaginal infections, RIF, RPL, and preterm birth.

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