International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	THE VAGINAL AND ENDOMETRIAL MICROBIOME IN ASSISTED REPRODUCTIVE TECHNOLOGY (ART)
DOI	https://doi.org/10.31435/ijitss.1(49).2026.5262
RECEIVED	14 February 2026
ACCEPTED	27 March 2026
PUBLISHED	30 March 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

THE VAGINAL AND ENDOMETRIAL MICROBIOME IN ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

Agnieszka Krajewska *(Corresponding Author, Email: agnieszkakrajewska767@gmail.com)*
Maria Skłodowska-Curie Voivodeship Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0003-2961-7565

Adrianna Kowalik
Independent Public Healthcare Complex in Płońsk, Płońsk, Poland
ORCID ID: 0009-0001-4092-5839

Agnieszka Korzeniewska
Military Medical Institute – National Research Institute, Warsaw, Poland
ORCID ID: 0009-0006-0337-961X

Julia Dębczak
Military Medical Institute – National Research Institute, Warsaw, Poland
ORCID ID: 0009-0004-4574-8466

Karolina Łuczak
Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0000-5952-8457

Katarzyna Tłustochowicz
Independent Public Healthcare Centre of the Ministry of the Interior and Administration, Kielce, Poland
ORCID ID: 0009-0006-4209-2558

Magdalena Korba
St. Anne's Hospital in Miechów, Miechów, Poland
ORCID ID: 0009-0002-5577-9923

Natalia Malicka
Independent Public Healthcare Centre of the Ministry of the Interior and Administration, Kielce, Poland
ORCID ID: 0009-0002-3045-2908

Wiktoria Polkowska
Central Clinical Hospital of the Medical University of Łódź, Łódź, Poland
ORCID ID: 0009-0006-3812-9573

ABSTRACT

Background: Infertility affects a substantial proportion of the global population, and assisted reproductive technologies (ART) do not guarantee success. Increasing evidence suggests that the vaginal and endometrial microbiomes play a critical role in female reproductive health, influencing implantation, pregnancy maintenance, and ART outcomes.
Objective: This narrative review aims to synthesize current evidence on the composition of the vaginal and endometrial microbiota and to explore biological mechanisms linking microbial profiles with reproductive success in ART.
Materials and Methods: A comprehensive narrative review of published literature was conducted, focusing on studies evaluating vaginal and endometrial microbiota composition, associated immunological and metabolic mechanisms, and reproductive outcomes in natural conception and ART cycles.
Results: In healthy reproductive-age women, a Lactobacillus-dominant vaginal and endometrial microbiome is associated with enhanced immune tolerance, epithelial barrier integrity, and metabolic activity supporting endometrial receptivity. Lactobacilli regulate local immune responses via anti-inflammatory cytokine signaling, modulation of pattern recognition receptor pathways, and production of metabolites involved in prostaglandin synthesis, angiogenesis, and uterine contractility. In contrast, dysbiotic communities enriched in non-Lactobacillus taxa are linked to increased pro-inflammatory signaling, impaired decidualization, mucosal barrier disruption, and altered immune cell balance. Clinical studies consistently report higher implantation, clinical pregnancy, and live birth rates in women with Lactobacillus-dominant microbiota; however, methodological heterogeneity limits causal interpretation. Emerging microbiome-modulating interventions, including probiotics, antibiotics, and vaginal microbiota transplantation, show potential but remain experimental.
Conclusions: A Lactobacillus-dominant reproductive tract microbiome appears strongly associated with improved ART outcomes. Standardized prospective and interventional studies are needed to establish clinically relevant microbial biomarkers and develop effective microbiome-targeted therapies.

KEYWORDS

Infertility, Vaginal Microbiome, Endometrial Microbiome, Assisted Reproductive Technologies, Immune Modulation

CITATION

Agnieszka Krajewska, Adrianna Kowalik, Agnieszka Korzeniewska, Julia Dębczak, Karolina Łuczak, Katarzyna Tłustochowicz, Magdalena Korba, Natalia Malicka, Wiktoria Polkowska. (2026) The Vaginal and Endometrial Microbiome in Assisted Reproductive Technology (ART). *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.5262

1. Introduction

Infertility is a prevalent global health issue, defined as the inability to conceive after 12 months of regular, unprotected sexual intercourse [1]. Infertility prevalence varies across regions and populations, influenced by socioeconomic factors, access to healthcare, and cultural practices. According to the World Health Organization, approximately 1 in 6 couples worldwide experience infertility during their reproductive years, with relatively higher prevalence rates observed in some regions such as the Americas, Western Pacific, African, and European regions, although underlying causes and contributing factors vary across populations [2]. These epidemiological patterns highlight the global public health significance of infertility and underscore the need for research into modifiable biological factors, including the reproductive tract microbiome, that may improve outcomes in assisted reproductive technologies. It is estimated that 50–80 million individuals worldwide are affected by infertility, with female factors accounting for nearly 50% of cases and male factors contributing to 20–30% [3,4]. Among female-related causes, ovulatory disorders (including polycystic ovary syndrome), tubal factor infertility, uterine abnormalities, and endometriosis are most common, while approximately 15–20% of cases remain unexplained despite comprehensive diagnostic evaluation [5]. Lifestyle and environmental factors, such as advanced maternal age, obesity, smoking, and psychological stress, further adversely affect reproductive potential. Despite significant advances in reproductive medicine and assisted reproductive technologies (ART), a substantial proportion of infertility cases still lack a clearly identifiable etiology. Growing evidence suggests that the microbiome of the female reproductive tract plays a critical role in reproductive health, influencing immune tolerance, endometrial receptivity, implantation, pregnancy maintenance, and ART outcomes. The aim of this narrative review is to synthesize current knowledge on the role of the vaginal and endometrial microbiomes in ART outcomes, with particular emphasis on immunological and metabolic mechanisms that influence implantation success, pregnancy rates, and live birth outcomes.

2. Vaginal microbiome

In healthy women of reproductive age, the vaginal microbiota is often dominated by Lactobacillus species, including L. crispatus, L. jensenii, L. gasseri, and L. iners. These bacteria help maintain an acidic vaginal environment ($pH < 4.5$) by producing lactic acid and hydrogen peroxide, supporting mucosal health and reproductive function. Such a balanced and relatively uniform microbial composition, referred to as eubiosis, is considered essential for female reproductive health [6]. In contrast, imbalances in the microbial ecosystem, commonly referred to as dysbiosis, are characterized by a depletion of protective Lactobacillus species and an increased abundance and diversity of potentially pathogenic microorganisms (e.g., Gardnerella vaginalis, Prevotella spp.). In many studies this altered microbial environment has been associated with impaired fertility, reduced implantation success, poor ART success rates and adverse pregnancy outcomes, including miscarriage and preterm birth [7,8].

The vaginal microbiome can be further classified into community state types (CSTs), a framework that describes common microbial patterns observed in reproductive-age women. According to Ravel et al. (2011), there are five primary CSTs:

- **CST I** — dominated by Lactobacillus crispatus;
- **CST II** — dominated by Lactobacillus gasseri;
- **CST III** — dominated by Lactobacillus iners;
- **CST IV** — low abundance of Lactobacillus and high diversity of anaerobic bacteria, including Gardnerella, Atopobium, Prevotella, Megasphaera, and Sneathia;
- **CST V** — dominated by Lactobacillus jensenii.

CST I, II, III, and V are generally associated with a stable, protective vaginal microbiota, whereas CST IV is linked to dysbiosis and has been associated with higher prevalence of adverse reproductive outcomes. This classification highlights that not only the presence of Lactobacillus, but also the overall composition and diversity of the vaginal microbial community, can influence female reproductive health.

Vaginal microbiome is influenced by host and environmental factors, including hormonal fluctuations, age, ethnicity, sexual activity, antibiotic exposure, contraceptive use, and lifestyle factors such as diet and hygiene practice all of which can modulate microbial diversity and dominance patterns with potential implications for reproductive outcomes [9].

Additionaly, Estrogen plays a key role by promoting proliferation of the vaginal epithelium and glycogen deposition, creating a favorable environment for glucose-fermenting Lactobacillus species. Therefore, natural fluctuations in estrogen levels throughout a woman’s life—from puberty, through the menstrual cycle, to menopause—can substantially influence the composition of the vaginal microbiota [10].

3. Endometrial microbiome

Although the endometrial cavity was long thought to be sterile, emerging evidence demonstrates that it harbors a resident microbiome. However, there is currently no consensus on a core endometrial microbiota, largely due to the low microbial biomass and challenges associated with sampling the uterine cavity without risk of contamination [11]. Several studies have classified the endometrial bacterial community into Lactobacillus-dominant (LD; >90% Lactobacillus spp.) and non-Lactobacillus-dominant (NLD; <90% Lactobacillus spp.) profiles. LD profiles are generally associated with favorable reproductive outcomes, including higher implantation rates and improved chances of clinical pregnancy, whereas endometrial dysbiosis, characterized by increased abundance of genera such as Gardnerella, Streptococcus, and Bifidobacterium, has been linked to reduced implantation success and lower pregnancy rates in infertile patients undergoing assisted reproductive technologies (ART) [12,13]. Despite substantial interest, debate remains regarding the existence of a definitive “core” endometrial microbiome, the thresholds defining eubiosis versus dysbiosis, and the relative clinical impact of specific taxa on reproductive outcomes. Endometrial bacterial communities, similar to those in the vagina are shaped by multiple factors, including age, hormonal fluctuations, ethnicity, sexual activity, and the use of intrauterine devices [14]. Notably, women with a history of multiple pregnancies or miscarriages may show reduced distinctions between vaginal and endometrial microbiota, likely due to disruptions in the uterine environment caused by cervical insufficiency. Under certain conditions, alterations in the vaginal microbiome may influence the bacterial communities of the endometrium. This is supported by observations that women with a non–Lactobacillus-dominant (NLD) endometrium often also exhibit NLD or dysbiotic vaginal microbiota [15,16].

4. Vaginal microbiome - impact on ART outcomes

A growing body of clinical evidence indicates that the composition of the vaginal microbiome is closely associated with reproductive outcomes in women undergoing assisted reproductive technologies (ART). In a large propensity score–matched cohort study including 2,285 women undergoing their first fresh IVF/ICSI cycle, NLD vaginal microbiota were associated with significantly inferior reproductive outcomes compared with Lactobacillus-dominant profiles. Specifically, women in the non-dominant group exhibited lower rates of biochemical pregnancy (50.1% vs. 57.6%, $p = 0.03$), clinical pregnancy (41.0% vs. 50.8%, $p < 0.01$), and live birth (31.8% vs. 41.2%, $p < 0.01$). In the same cohort, non–Lactobacillus dominance was further associated with a higher rate of preclinical pregnancy loss (18.2% vs. 11.8%, $p = 0.05$) as well as an increased incidence of preterm birth (33.1% vs. 21.6%, $p = 0.02$), while rates of miscarriage and ectopic pregnancy [17]. In a study of approximately 1,411 women (1,255 undergoing embryo transfer), moderate Lactobacillus abundance (~80%) was associated with pregnancy rates of ~54–58%, compared with ~45–51% in women with very high (>90%) Lactobacillus dominance, suggesting that not only the presence but also the relative abundance and specific species composition of Lactobacillus influence reproductive outcomes. The study sample was stratified according to vaginal community states [18].

A recent systematic review and meta-analysis including 6,835 IVF patients across 25 studies reported that vaginal dysbiosis—used as an approximation of community state type IV (CST IV), a Lactobacillus-deficient, diverse microbial profile—was associated with lower clinical pregnancy rates and higher risk of early pregnancy loss, although no significant effect was observed on live birth or biochemical pregnancy rates. The authors emphasize that these findings are difficult to interpret due to heterogeneity in dysbiosis definitions, microbiome assessment methods, and study populations, highlighting the complex and still poorly understood relationship between vaginal microbiota and ART outcomes [19].

Taken together, these clinical data indicate that a vaginal microbiome dominated by Lactobacillus spp. is generally associated with higher implantation success, increased clinical pregnancy rates, and a greater likelihood of live birth in ART settings. Conversely, dysbiotic profiles—particularly those enriched in anaerobic bacteria—are linked to poorer reproductive outcomes. While causality cannot yet be definitively established due to the predominantly observational nature of available studies, these findings underscore the potential value of vaginal microbiome profiling as a prognostic tool in ART. Nonetheless, routine clinical implementation will require further validation in well-designed, standardized studies.

5. Endometrial microbiome- impact on ART outcomes

Clinical evidence suggests that the composition of the endometrial microbiome may influence ART outcomes, particularly implantation, clinical pregnancy, and live birth rates, although most available data are derived from observational studies. Kyono et al. analyzed the endometrial microbiome of 342 infertile women undergoing ART using 16S rRNA sequencing. Women with a Lactobacillus-enriched endometrial microbiota exhibited a significantly higher live birth rate (32.7%) compared with women with dysbiotic, non–Lactobacillus-dominant profiles (18.1%, $p < 0.05$). Dysbiosis was characterized by increased abundance of genera such as Gardnerella, Atopobium, Streptococcus, Bifidobacterium, and Klebsiella, and was more frequently observed in women experiencing implantation failure or early pregnancy loss [20]. These findings are supported by a recent systematic review and meta-analysis which evaluated studies published between 2015 and 2024. In pooled analyses focusing specifically on endometrial microbiota, Lactobacillus dominance was associated with a markedly increased likelihood of achieving clinical pregnancy (pooled odds ratio 9.88; 95% CI: 4.40–22.19) compared with non-Lactobacillus-dominant profiles. Due to heterogeneity in outcome definitions and reporting, implantation and live birth rates could not be quantitatively pooled; however, the direction of effect was consistent across included studies [21].

In another study Bui et al. investigated endometrial microbiome composition in 141 women with previous IVF failure and correlated microbial profiles with subsequent reproductive outcomes. Women who achieved live birth showed a significantly higher relative abundance of Lactobacillus crispatus. Notably, 70.4% of women who did not achieve live birth had ≤10% L. crispatus, compared with 42.1% in the live birth group ($p = 0.015$), suggesting a species-specific association between endometrial Lactobacillus composition and

ART success [22]. Overall, evidence from prospective studies, large observational cohorts, and meta-analytic data consistently indicates that a Lactobacillus-dominant endometrial microbiome is associated with higher clinical pregnancy and live birth rates in ART, whereas dysbiotic profiles enriched in non-Lactobacillus taxa are linked to poorer reproductive outcomes, including implantation failure, biochemical pregnancies, and early miscarriage. Nevertheless, methodological heterogeneity, differences in sampling techniques, and the lack of randomized interventional trials limit causal interpretation and the routine clinical application of endometrial microbiome profiling as a predictive tool.

6. Biological mechanisms linking vaginal and endometrial microbiota to ART outcomes.

The female reproductive tract microbiome may influence assisted reproductive technology (ART) outcomes through complex and interrelated immunological, metabolic, and barrier-related mechanisms that shape endometrial receptivity and early pregnancy establishment. Although the precise pathways remain incompletely elucidated, growing evidence indicates that microbial composition critically modulates local immune tolerance, inflammatory balance, and tissue integrity. Under eubiotic conditions, commensal bacteria—particularly Lactobacillus species—promote a tolerogenic endometrial immune environment by limiting excessive inflammatory signaling and supporting regulatory immune pathways essential for implantation. Lactobacillus enhances the secretion of anti-inflammatory mediators, including interleukin-10 (IL-10) and interleukin-1 receptor antagonist (IL-1RA), while stimulating the production of antimicrobial peptides, including bacteriocins (e.g., lactocin, gassericin), which inhibit the growth of potentially pathogenic bacteria and help maintain vaginal microbial balance, thereby strengthening epithelial barrier function. This immunomodulatory profile maintains a delicate balance between immune tolerance and controlled defense, which is critical for successful embryo implantation [16].

Lactobacillus also contributes to reproductive success through metabolic activity. The production of lactic acid lowers local pH, inhibiting pathogen overgrowth and modulating immune responses to bacterial lipopolysaccharides. Additionally, bacterial metabolites such as glycerophospholipids and benzopyran derivatives act as modulators of prostaglandin synthesis, which regulates uterine contractility critical for embryo transport, and support angiogenesis by promoting the formation of new blood vessels in the endometrium, creating a receptive environment for implantation. While these metabolites do not directly move the blastocyst, by modulating uterine contractions and optimizing endometrial vascularization, they indirectly facilitate blastocyst transport and successful implantation [13].

In contrast, dysbiotic microbial profiles, characterized by overgrowth of non-commensal or anaerobic bacteria, are associated with elevated levels of pro-inflammatory cytokines, including IL-1β, IL-6, and tumor necrosis factor-α (TNF-α). These inflammatory signals can impair decidualization, reduce trophoblast invasion, and recruit neutrophils and macrophages, creating a hostile endometrial environment that compromises implantation. Pattern recognition receptors, particularly Toll-like receptors (TLRs), link microbiome alterations to immune activation. Endometrial epithelial cells express TLRs that recognize pathogen-associated molecular patterns, such as lipopolysaccharides from Gram-negative bacteria, and activation of TLR4 triggers nuclear factor-κB (NF-κB) signaling, amplifying inflammatory responses that may reduce endometrial receptivity [8]. Dysbiosis can also disrupt the balance of critical immune cell populations, including regulatory T cells (Tregs), Th17 cells, and uterine natural killer (uNK) cells, shifting toward a Th17-dominant pro-inflammatory milieu that diminishes maternal immune tolerance. Furthermore, dysbiotic bacteria may compromise the mucosal barrier by degrading epithelial tight junctions and mucins, increasing epithelial permeability and promoting aberrant immune activation within the endometrium [23].

Additional mechanisms by which dysbiosis may impair implantation include impaired angiogenesis, potentially through reduced expression of vascular endothelial growth factor (VEGF) and other pro-angiogenic mediators, leading to suboptimal tissue perfusion and a non-receptive endometrium [24] oxidative stress, via increased production of reactive oxygen species (ROS), which can damage endometrial epithelial and stromal cells and interfere with decidualization [25] and alterations in steroid metabolism, as certain bacteria express enzymes such as β-glucuronidase and sulfatase that deconjugate estrogen metabolites, potentially disrupting local estrogen and progesterone availability [26]. Moreover, dysbiotic taxa such as Gardnerella vaginalis and Prevotella spp. may form biofilms, which protect pathogenic communities from host defenses and antimicrobial factors, contributing to persistent inflammation and barrier disruption [27]. Collectively, these mechanisms highlight the multifactorial impact of vaginal and endometrial dysbiosis on the endometrial environment and its potential to compromise ART outcomes.

7. Discussion

The expanding field of reproductive microbiome research has significantly improved our understanding of the potential role of microbial communities in female fertility and assisted reproductive technology (ART) outcomes. Evidence summarized in this review suggests that both vaginal and endometrial microbiota may represent previously underappreciated determinants of reproductive success. While many studies demonstrate associations between microbial composition and ART outcomes, the interpretation of these findings requires careful consideration of methodological variability, biological complexity, and unresolved questions regarding causality.

One of the most consistent observations across clinical studies is the association between Lactobacillus-dominant microbiota and improved reproductive outcomes. Both vaginal and endometrial microbial profiles enriched in Lactobacillus species have been linked with higher implantation rates, increased clinical pregnancy rates, and improved live birth outcomes in women undergoing ART. These findings have been reproduced across multiple observational cohorts and meta-analyses, suggesting that microbial composition may represent an important factor influencing the reproductive environment. At the same time, several studies indicate that reproductive outcomes may not depend solely on the presence of Lactobacillus, but also on the relative abundance of specific species and the overall structure of the microbial community.

An important aspect emerging from recent research is the heterogeneity of microbial profiles observed among women undergoing fertility treatment. Even among patients classified as having Lactobacillus-dominant microbiota, considerable variation exists in the composition and stability of microbial communities. Differences between species such as Lactobacillus crispatus, Lactobacillus iners, or Lactobacillus gasseri may have distinct biological implications, as these bacteria differ in metabolic activity, stability, and interactions with other microorganisms. This variability suggests that simple binary classifications of Lactobacillus-dominant versus non-dominant microbiota may not fully capture the complexity of microbial ecosystems within the reproductive tract.

Another important issue concerns the relationship between the vaginal and endometrial microbiota. Although these microbial niches are anatomically separated, several studies suggest that microbial communities within the female reproductive tract may form a partially interconnected system. Observations indicating that women with dysbiotic endometrial microbiota often present with similar vaginal microbial profiles support the hypothesis that microbial alterations may extend across different compartments of the reproductive tract. Understanding these relationships may be particularly important for developing clinically applicable diagnostic strategies, as vaginal sampling represents a considerably less invasive method than endometrial biopsy.

Despite the increasing number of studies investigating reproductive microbiota, several methodological challenges continue to limit the interpretation and comparability of results. One of the major issues is the lack of standardized protocols for sample collection, DNA extraction, sequencing techniques, and bioinformatic analysis. These methodological differences can substantially influence the detection and classification of microbial taxa, making direct comparisons between studies difficult. In addition, studies of the endometrial microbiome face the challenge of extremely low microbial biomass, which increases the risk of contamination from the lower genital tract or the laboratory environment. As a result, distinguishing genuine uterine microbial communities from background contamination remains an ongoing scientific challenge.

Another limitation of the current literature is the predominance of observational study designs. Although observational studies are valuable for identifying potential associations between microbiome composition and reproductive outcomes, they do not allow for definitive conclusions regarding causality. It therefore remains unclear whether microbial dysbiosis directly contributes to implantation failure and infertility, or whether it represents a secondary consequence of underlying reproductive disorders. Addressing this question will require well-designed prospective studies and randomized controlled trials evaluating microbiome-targeted interventions.

In addition to methodological considerations, patient-related factors may further influence reproductive microbiome composition and its clinical significance. Age, hormonal fluctuations, ethnicity, sexual behavior, antibiotic exposure, and lifestyle factors may all contribute to interindividual variability in microbial communities. These variables are rarely controlled uniformly across studies, which may partly explain discrepancies in reported findings. Future research should therefore aim to incorporate these factors into study design in order to better understand how host characteristics interact with microbial ecosystems. From a clinical perspective, the possibility of incorporating microbiome assessment into fertility diagnostics is an area of growing interest. If reliable microbial biomarkers associated with ART success can be identified, microbiome profiling could potentially become a useful adjunct to existing reproductive evaluations. However, before such approaches can be implemented in routine clinical practice, substantial gaps in knowledge must be addressed, including the establishment of standardized diagnostic thresholds and validation of microbiome-based predictive models in large prospective cohorts. Overall, current evidence suggests that the vaginal and endometrial microbiota may represent important modulators of the reproductive environment in women undergoing ART. Nevertheless, significant uncertainties remain regarding the mechanisms, clinical relevance, and potential therapeutic implications of these microbial communities. Continued research integrating microbiology, immunology, and reproductive medicine will be essential to clarify the role of the reproductive microbiome and determine whether targeted microbiome interventions can ultimately improve fertility treatment outcomes.

8. Potential modulation of the reproductive microbiome: therapeutic perspectives

Considering increasing evidence linking vaginal and endometrial dysbiosis to adverse ART outcomes, studies are exploring strategies to modulate the reproductive microbiome with the aim of improving implantation, pregnancy, and live birth rates. These strategies range from conventional interventions such as antibiotics and probiotics to emerging approaches like combined therapies and vaginal microbiota transplantation (VMT). However, there are currently no standardized clinical protocols for routine microbiome modulation aimed at improving ART outcomes, and available evidence remains largely preliminary. Antibiotic therapy is used selectively in cases of confirmed infection or chronic endometritis, guided by clinical indications rather than microbiome-based protocols.

Probiotics are hypothesized to promote a Lactobacillus-dominant vaginal or endometrial microbiota by lowering pH, suppressing pathogenic bacteria, and producing metabolites such as lactic acid and short-chain fatty acids with immunomodulatory properties. In a randomized clinical trial involving women with recurrent implantation failure and thin endometrium, the combined use of vaginal probiotics and vitamin D supplementation was associated with significantly higher pregnancy rates and favorable modulation of immune markers compared with probiotics alone, vitamin D alone, or control, suggesting a potential benefit of adjunctive probiotic therapy in this selected population [28]. In contrast, a large randomized controlled trial evaluating intravaginal Lactobacillus supplementation prior to frozen embryo transfer found no improvement in biochemical or clinical pregnancy rates in the overall study population. Nevertheless, probiotic use was associated with a significantly lower miscarriage rate and a higher live birth rate among women undergoing blastocyst transfer, and with improved live birth outcomes in a subgroup of patients with bacterial vaginosis, indicating that potential benefits may be limited to specific clinical contexts [29].

Conversely, another randomized, double-blinded, placebo-controlled trial demonstrated that vaginal probiotics containing Lactobacillus gasseri and L. rhamnosus failed to improve an unfavorable vaginal microbiota prior to fertility treatment, underscoring the heterogeneity of probiotic effects and the lack of consistent efficacy across strains and patient populations [30]. Nevertheless, clinical data in the ART setting are inconsistent, and no consensus exists regarding optimal strains, dosing, or timing of administration. Vaginal microbiota transplantation represents an emerging but still experimental concept. Inspired by the success of fecal microbiota transplantation in gastrointestinal disease, VMT involves transferring vaginal microbial communities from healthy donors into recipients with dysbiosis. Small exploratory studies and case reports indicate that VMT may restore a Lactobacillus-dominant microbiota in women with refractory vaginal dysbiosis and may reduce symptoms in some cases [31]. However, this approach remains limited to pilot research. Key challenges include donor selection, procedural standardization, safety, and long-term outcomes. In conclusion, although some studies suggest potential benefits, the majority of reproductive microbiome interventions remain experimental in ART, and their efficacy and safety must be established through rigorous, well-controlled clinical trials.

9. Clinical implications and research gaps

Despite growing evidence linking the female reproductive tract microbiome to gynecological and obstetric outcomes, no definitive microbial biomarkers or consensus on the precise composition of a “healthy” vaginal or endometrial microbiome have been established. The lack of standardized assessment protocols and validated biomarkers limits the routine use of microbiome screening in clinical practice. Larger, well-designed studies are needed to enable comparative analyses, clarify physiological microbial profiles, and better understand how dysbiosis impacts ART outcomes. Such research is essential to refine diagnostic tools and develop personalized microbiome-targeted strategies aimed at improving fertility and pregnancy outcomes.

10. Conclusion

Current evidence underscores the pivotal role of the vaginal and endometrial microbiome in determining ART outcomes. A Lactobacillus-dominant microbial profile is consistently associated with higher rates of implantation, clinical pregnancy, and live birth, whereas non-Lactobacillus-dominant or dysbiotic communities are linked to reduced reproductive success, likely through mechanisms involving immune modulation and mucosal barrier function. Although these findings are promising, most studies remain observational, often with small sample sizes, heterogeneous methodologies, and a lack of standardized microbiome assessment. Interventions such as probiotics, antibiotics, combination therapies, and vaginal microbiota transplantation have demonstrated potential, but robust randomized controlled trials are needed to confirm their efficacy and safety in ART populations. Future research should focus on identifying reliable microbial biomarkers and developing standardized, targeted microbiome interventions to optimize ART outcomes.

Author Contributions:

Conceptualization, A.Kr.; Literature search, A.Kr., K.T., A.Kow.; Analysis and interpretation of the literature, A.Kr., K.T., A.Kow.; Writing—original draft preparation, A.Kr., A.Kow., A.Kor.; Writing—review and editing, J.D., K.Ł., M.K., N.M., W.P., K.T.; Supervision, K.T. All authors have read and agreed to the published version of the manuscript.

Funding: The article did not receive any funding.

Data Availability Statement: No new data were created or analyzed in this study.

Conflicts of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Vander Borght, M., & Wyns, C. (2018). Fertility and infertility: Definition and epidemiology. *Clinical Biochemistry, 62*, 2–10. https://doi.org/10.1016/j.clinbiochem.2018.03.012
2. Njagi, P., Groot, W., Arsenijevic, J., Dyer, S., Mburu, G., & Kiarie, J. (2023). Financial costs of assisted reproductive technology for patients in low- and middle-income countries: A systematic review. *Human Reproduction Open, 2023*(2), hoad007. https://doi.org/10.1093/hropen/hoad007
3. Andone, B. A., Handrea-Dragan, I. M., Botiz, I., & Boca, S. (2023). State-of-the-art and future perspectives in infertility diagnosis: Conventional versus nanotechnology-based assays. *Nanomedicine, 54*, Article 102709. https://doi.org/10.1016/j.nano.2023.102709
4. Babakhanzadeh, E., Nazari, M., Ghasemifar, S., & Khodadadian, A. (2020). Some of the factors involved in male infertility: A prospective review. *International Journal of General Medicine, 13*, 29–41. https://doi.org/10.2147/IJGM.S241099
5. Carson, S. A., & Kallen, A. N. (2021). Diagnosis and management of infertility. *JAMA, 326*(1), 65. https://doi.org/10.1001/jama.2021.4788
6. Ravel, J., et al. (2011). Vaginal microbiome of reproductive-age women. *Proceedings of the National Academy of Sciences of the United States of America, 108*(Suppl. 1), 4680–4687. https://doi.org/10.1073/PNAS.1002611107/-/DCSUPPLEMENTAL
7. de Souza, S. V., et al. (2023). Vaginal microbioma and the presence of *Lactobacillus* spp. as interferences in female fertility: A review system. *JBRA Assisted Reproduction, 27*(3), 496–506. https://doi.org/10.5935/1518-0557.20230006
8. Xiao, L., Zuo, Z., & Zhao, F. (2024). Microbiome in female reproductive health: Implications for fertility and assisted reproductive technologies. *Genomics, Proteomics & Bioinformatics, 22*(1). https://doi.org/10.1093/GPBJNL/QZAD005
9. Günther, V., et al. (2022). Vaginal microbiome in reproductive medicine. *Diagnostics, 12*(8). https://doi.org/10.3390/DIAGNOSTICS12081948
10. Zhao, C., et al. (2020). Characterization of the vaginal microbiome in women with infertility and its potential correlation with hormone stimulation during in vitro fertilization surgery. *mSystems, 5*(4). https://doi.org/10.1128/MSYSTEMS.00450-20
11. Reschini, M., et al. (2022). Endometrial microbiome: Sampling, assessment, and possible impact on embryo implantation. *Scientific Reports, 12*(1). https://doi.org/10.1038/S41598-022-12095-7
12. Moreno, I., et al. (2022). Endometrial microbiota composition is associated with reproductive outcome in infertile patients. *Microbiome, 10*(1). https://doi.org/10.1186/S40168-021-01184-W

13. Gao, X., Louwers, Y. V., Laven, J. S. E., & Schoenmakers, S. (2024). Clinical relevance of vaginal and endometrial microbiome investigation in women with repeated implantation failure and recurrent pregnancy loss. *International Journal of Molecular Sciences, 25*(1). https://doi.org/10.3390/IJMS25010622
14. Medina-Bastidas, D., Camacho-Arroyo, I., & García-Gómez, E. (2022). Current findings in endometrial microbiome: Impact on uterine diseases. *Reproduction, 163*(5), R81–R96. https://doi.org/10.1530/REP-21-0120
15. Wang, J., et al. (2021). Translocation of vaginal microbiota is involved in impairment and protection of uterine health. *Nature Communications, 12*(1). https://doi.org/10.1038/S41467-021-24516-8
16. Balla, B., et al. (2024). The role of the vaginal and endometrial microbiomes in infertility and their impact on pregnancy outcomes in light of recent literature. *International Journal of Molecular Sciences, 25*(23), 13227. https://doi.org/10.3390/IJMS252313227
17. Zeng, H., et al. (2022). Non-*Lactobacillus* dominance of the vagina is associated with reduced live birth rate following IVF/ICSI: A propensity score-matched cohort study. *Archives of Gynecology and Obstetrics, 305*(2), 519–528. https://doi.org/10.1007/S00404-021-06171-Y
18. Wang, T., et al. (2024). Vaginal microbiota are associated with in vitro fertilization during female infertility. *iMeta, 3*(3). https://doi.org/10.1002/IMT2.185
19. Maksimovic Celicanin, M., Haahr, T., Humaidan, P., & Skafte-Holm, A. (2024). Vaginal dysbiosis - the association with reproductive outcomes in IVF patients: A systematic review and meta-analysis. *Current Opinion in Obstetrics and Gynecology, 36*(3), 155–164. https://doi.org/10.1097/GCO.0000000000000953
20. Kyono, K., Hashimoto, T., Kikuchi, S., Nagai, Y., & Sakuraba, Y. (2018). A pilot study and case reports on endometrial microbiota and pregnancy outcome: An analysis using 16S rRNA gene sequencing among IVF patients, and trial therapeutic intervention for dysbiotic endometrium. *Reproductive Medicine and Biology, 18*(1), 72–82. https://doi.org/10.1002/RMB2.12250
21. Foteinidou, P., Exindari, M., Chatzidimitriou, D., & Gioula, G. (2024). Endometrial microbiome and its correlation to female infertility: A systematic review and meta-analysis. *Acta Microbiologica Hellenica, 69*(1), 14–28. https://doi.org/10.3390/AMH69010004
22. Bui, B. N., et al. (2023). The endometrial microbiota of women with or without a live birth within 12 months after a first failed IVF/ICSI cycle. *Scientific Reports, 13*(1), 3444. https://doi.org/10.1038/S41598-023-30591-2
23. Gao, H., et al. (2024). Deciphering the role of female reproductive tract microbiome in reproductive health: A review. *Frontiers in Cellular and Infection Microbiology, 14*. https://doi.org/10.3389/FCIMB.2024.1351540
24. Salmasi, S., Sharifi, M., & Rashidi, B. (2021). Ovarian stimulation and exogenous progesterone affect the endometrial miR-16-5p, VEGF protein expression, and angiogenesis. *Microvascular Research, 133*, Article 104074. https://doi.org/10.1016/j.mvr.2020.104074
25. Stoyancheva, G., Mihaylova, N., Gerginova, M., & Krumova, E. (2025). Endometrial microbiome and reproductive receptivity: Diverse perspectives. *International Journal of Molecular Sciences, 26*(21). https://doi.org/10.3390/ijms262110796
26. Li, Z. F., Yin, Z. F., Chen, W. Q., & Wang, Z. H. (2025). Impact of gut and reproductive tract microbiota on estrogen metabolism in endometriosis. *American Journal of Reproductive Immunology, 93*(6). https://doi.org/10.1111/aji.70109
27. Swidsinski, S., Moll, W. M., & Swidsinski, A. (2023). Bacterial vaginosis-vaginal polymicrobial biofilms and dysbiosis. *Deutsches Ärzteblatt International, 120*(20), 347–354. https://doi.org/10.3238/arztebl.m2023.0090
28. Badihi, E., et al. (2025). The effect of vitamin D supplementation and vaginal probiotics on fertility in women with recurrent implantation failure: A randomized clinical trial. *Human Immunology, 86*(3). https://doi.org/10.1016/j.humimm.2025.111259
29. Thanaboonyawat, I., Pothisan, S., Petyim, S., & Laokirkkiat, P. (2023). Pregnancy outcomes after vaginal probiotic supplementation before frozen embryo transfer: A randomized controlled study. *Scientific Reports, 13*(1). https://doi.org/10.1038/S41598-023-39078-6
30. Jepsen, I. E., et al. (2022). Probiotic treatment with specific lactobacilli does not improve an unfavorable vaginal microbiota prior to fertility treatment—A randomized, double-blinded, placebo-controlled trial. *Frontiers in Endocrinology, 13*, 1057022. https://doi.org/10.3389/FENDO.2022.1057022
31. Luo, H., Zhou, C., Zhou, L., He, Y., & Xie, R. H. (2024). The effectiveness of vaginal microbiota transplantation for vaginal dysbiosis and bacterial vaginosis: A scoping review. *Archives of Gynecology and Obstetrics, 310*(2), 643–653. https://doi.org/10.1007/S00404-024-07611-1