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Commentary

Influence of Endometrial Microbiota Diversity on Implantation Outcome in Assisted Reproduction

Sofia Lindgren*

Department of Obstetrics and Molecular Fertility, Northern Arc University, Stockholm, Sweden

DESCRIPTION

Successful implantation depends on synchronized communication between the embryo and endometrium during a limited receptive period of the menstrual cycle. Hormonal preparation, vascular remodeling, cytokine activity, and immune cell regulation all contribute to this process. During recent years, another factor has gained substantial scientific attention within reproductive medicine: the endometrial microbiota. Earlier assumptions described the uterine cavity as a sterile environment, though advanced sequencing technologies have demonstrated the presence of microbial populations within the upper reproductive tract. Investigation into these microbial communities has introduced new perspectives regarding implantation failure, recurrent pregnancy loss, and variability in assisted reproductive treatment outcomes.

The human reproductive tract contains multiple microbial ecosystems that differ according to anatomical location, hormonal state, age, and health condition. The vaginal microbiota has been extensively studied and is often dominated by *Lactobacillus* species that produce lactic acid and maintain an acidic environment unfavorable to pathogenic organisms. In contrast, the endometrial cavity contains a lower microbial biomass and displays greater variability among individuals. Some women exhibit *Lactobacillus*-dominant uterine profiles, whereas others present mixed bacterial populations including *Gardnerella*, *Streptococcus*, *Atopobium*, *Bifidobacterium*, and *Prevotella* species.

Interest in uterine microbiota intensified after reports suggesting that non-*Lactobacillus* dominant microbial patterns might correlate with reduced implantation and pregnancy rates during *In Vitro* Fertilization (IVF) treatment. Molecular sequencing methods such as 16S ribosomal Ribonucleic Acid (RNA) analysis allowed researchers to detect bacterial Deoxyribonucleic Acid (DNA) from endometrial samples collected during hysteroscopy or embryo transfer preparation. Several early studies proposed that women with *ssss* levels above ninety percent demonstrated improved reproductive outcomes compared with women showing more diverse bacterial compositions. These observations encouraged discussion regarding microbial balance as a possible contributor to implantation competence.

Interpretation of endometrial microbiota findings remains difficult because sample collection methods are vulnerable to contamination from the lower reproductive tract. The uterine cavity contains relatively low bacterial concentrations, making accurate detection technically challenging. Even minimal contamination during catheter insertion may alter sequencing results substantially. Laboratory processing, DNA extraction methods, and sequencing platforms also vary among studies, contributing to inconsistent observations across reproductive centers.

Despite these limitations, multiple investigations suggest that abnormal microbial populations may influence inflammatory signaling within the endometrium. Bacterial metabolites can affect cytokine production, epithelial barrier integrity, and local immune activity. Implantation requires balanced immune tolerance because the embryo contains paternal genetic material. Excess inflammatory activation within the endometrium may interfere with trophoblast attachment and vascular remodeling during early pregnancy. Some bacterial species associated with chronic endometritis appear capable of stimulating prolonged inflammatory responses that reduce receptivity.

Chronic endometritis has emerged as an important clinical topic in reproductive medicine. This condition involves persistent low-grade inflammation of the endometrial lining, often associated with plasma cell infiltration and microbial imbalance. Many affected women remain asymptomatic, though some experience abnormal bleeding, pelvic discomfort, or recurrent implantation failure. Histological examination combined with immunohistochemical staining for plasma cells can assist diagnosis. Several studies report improved implantation rates after antibiotic treatment in selected patients diagnosed with chronic endometritis before embryo transfer.

The relationship between microbial diversity and immune regulation remains highly complex. Certain bacterial species may support endometrial stability through production of anti-inflammatory metabolites, while others stimulate cytokine

Correspondence to: Sofia Lindgren, Department of Obstetrics and Molecular Fertility, Northern Arc University, Stockholm, Sweden, E-mail: sofia.lindgren.nau@evolutionmail.net

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release and leukocyte recruitment. Natural killer cells, macrophages, dendritic cells, and regulatory T lymphocytes all participate in implantation physiology. Disturbance in microbial composition may alter communication between these immune populations and the endometrial epithelium. Researchers continue to examine whether microbial signals influence expression of implantation-related genes including leukemia inhibitory factor, integrins, and homeobox proteins.

Hormonal changes during the menstrual cycle also affect microbial composition. Estrogen promotes glycogen accumulation within epithelial tissue, indirectly influencing bacterial growth patterns. Progesterone modifies immune activity and vascular permeability during the secretory phase. Controlled ovarian stimulation used in IVF treatment produces supraphysiologic hormone concentrations that may alter both vaginal and endometrial microbial environments. Some investigators have observed temporary shifts in bacterial diversity during stimulation cycles, though long-term consequences remain uncertain.

Antibiotic exposure before fertility treatment represents another area of discussion. Empirical antibiotic use is common in some reproductive centers during embryo transfer or oocyte retrieval procedures. However, indiscriminate antibiotic administration may disturb beneficial microbial populations and contribute to antimicrobial resistance. Researchers increasingly emphasize the importance of selective treatment based on confirmed infection or inflammatory diagnosis rather than routine prophylactic use in all patients.

CONCLUSION

Current knowledge indicates that the uterine cavity contains dynamic microbial populations that may influence implantation through inflammatory and immune-related pathways. Although research findings remain inconsistent, the relationship between endometrial microbiota diversity and reproductive outcome continues to attract substantial scientific interest. Improved sequencing techniques, standardized sampling protocols, and carefully designed clinical trials will likely clarify the biological significance of microbial variation in assisted reproduction. Continued investigation may contribute to more precise understanding of implantation physiology and support development of targeted therapies for selected infertility patients.