

Decoding the Enigma: Vaginal Microbiome's Influence on Recurrent Pregnancy Loss - A Short Review

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Recurrent pregnancy Loss

Recurrent pregnancy loss (RPL) is a significant reproductive health issue, particularly in India, where the prevalence and risk factors associated with RPL are of particular interest Patki & Chauhan (2015). RPL is defined as the spontaneous loss of two or more consecutive pregnancies before 20 weeks of gestation (Kashyap et al., 2023). Research has explored chromosomal abnormalities among cases of recurrent spontaneous abortions in India, indicating the importance of cytogenetic analysis in investigating the causes of RPL (Janani et al., 2016). Furthermore, the association between diminished ovarian reserve and RPL has been studied, emphasizing the need for a comprehensive understanding of the factors contributing to RPL in the Indian population (Abohashim et al., 2022). Understanding the prevalence and etiology of RPL is crucial for developing targeted interventions and improving reproductive outcomes for couples affected by this condition. Recent research has focused on understanding the relationship between the vaginal microbiome and RPL.

Vaginal Microbiome and RPL

The vaginal microbiome plays a crucial role in women's reproductive health, particularly during pregnancy and the postpartum period. Research has shown that substantial changes occur in the composition of the vaginal microbiome following the end of pregnancy Nunn et al. (2021). These changes are associated with hormonal fluctuations, menstrual flow, cervical and vaginal secretions, and sexual activity (Walther-Antonio et al., 2014). Disruption of the vaginal microbiome has been linked to various pregnancy complications, including recurrent miscarriages, preterm birth, intra-uterine infection, and stillbirth. Moreover, the maintenance of vaginal microbiota has been highlighted as an important factor in achieving ideal pregnancy outcomes (Celik et al., 2022). Furthermore, the vaginal microbiome has been studied in the context of premature ovarian insufficiency, recurrent implantation failure, and unexplained infertility, highlighting its potential role in RPL (Rezende et al., 2023; Patel et al., 2022; Lk et al., 2019). The vaginal microbiome undergoes significant changes during pregnancy, characterized by reduced diversity and increased stability, with a dominance of *Lactobacillus* species (MacIntyre et al., 2015; Serrano et al., 2019; Freitas et al., 2017; Walther-Antonio et al., 2014; Morselli et al., 2022; Nunn et al., 2021). Studies have identified specific microbial species that are commonly found in the vaginal microbiome, including *Lactobacillus crispatus*, *Lactobacillus iners*, *Lactobacillus gasseri*, and *Lactobacillus jensenii*, which are known to dominate the vaginal

microbiome in healthy individuals (Doyle et al., 2018; Chang et al., 2020). The presence of other microbial species, such as *Gardnerella vaginalis*, *Prevotella*, and *Megasphaera*, has been associated with alterations in the vaginal microbiome and gynecological conditions (Putonti et al., 2021; Mu et al., 2019). Additionally, Grewal et al. (2022) reported low co-occurrence of *L. crispatus*, a species associated with vaginal bacterial stability, with other microbial species in RPL cases. Moreover, the association between gut dysbiosis and an imbalanced cytokine network in women with unexplained miscarriage has been identified, highlighting the potential role of gut microbiome dysbiosis in adverse pregnancy outcomes, including RPL (Liu et al., 2020). The microbiome in the female reproductive tract, including the endometrial and vaginal microbiota, has been associated with RPL, suggesting that microbiota composition may play a role in the etiology of RPL (Peuranpää, 2021; Peuranpää, 2022).

Need for studies in RPL and vaginal microbiome

Conducting studies on the relationship between the vaginal microbiome and recurrent pregnancy loss (RPL) is crucial for several reasons. Firstly, for investigating the vaginal microbiome in individuals experiencing recurrent pregnancy loss can help identify specific microbial factors or dysbiosis patterns associated with increased risk. This knowledge is essential for understanding the root causes of RPL. Secondly, these studies can lead to discovery of novel microbial biomarkers associated with recurrent pregnancy loss. Establishing such biomarkers could facilitate the development of diagnostic tools that help identify individuals at risk of RPL, enabling early intervention and personalized care. In addition, it can also contribute to the development of targeted therapeutic interventions based on the modulation of the vaginal microbiome. Understanding how specific microbial profiles influence pregnancy outcomes may lead to novel treatments or preventive measures. Studies can help in categorizing individuals into risk groups based on their vaginal microbiome composition. This risk stratification can guide healthcare providers in tailoring interventions and monitoring strategies for those at higher risk of recurrent pregnancy loss. Insights into the role of the vaginal microbiome in recurrent pregnancy loss can enhance the success rates of assisted reproductive technologies. Optimizing the microbiome environment may improve outcomes for individuals undergoing procedures like in vitro fertilization (IVF). Understanding the interplay between individual variations in the vaginal microbiome and recurrent pregnancy loss allows for personalized medical approaches. Tailoring interventions based on a person's unique microbial profile can enhance treatment effectiveness. As recurrent pregnancy loss has significant emotional and economic implications, studies on the vaginal microbiome can have a broader public health impact. Insights gained may lead to interventions that reduce the overall burden of RPL on individuals and healthcare systems. In summary, studies on the vaginal microbiome and recurrent pregnancy loss are essential for advancing our understanding of the underlying mechanisms, improving diagnostic capabilities, and developing targeted interventions to enhance reproductive outcomes for individuals experiencing RPL.