Review Article

# Association Between Vaginal Microbiota and Infertility: A Systematic Review

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## ABSTRACT

The aim of this systematic review was to synthesize the available evidence on the relationship between vaginal microbiota and infertility, highlighting key microbial factors and their impact on reproductive outcomes. A comprehensive search of four databases identified 1,216 relevant publications. After duplicate removal using Rayyan QCRI and relevance screening, 605 full-text articles were reviewed, with nine studies ultimately meeting inclusion criteria. The included nine studies involving 1,768 women with vaginal infections. A significant microbial imbalance was observed in infertile women compared to non-infertile women, with a decrease in Lactobacillus and an increase in pathogenic bacteria such as Gardnerella and Mycoplasma. These findings support the inclusion of microbial assessments in infertility evaluations and highlight the potential benefits of managing bacterial imbalances to improve fertility outcomes. We conclude that vaginal microbial imbalance is associated with infertility, suggesting that targeted microbial interventions could benefit fertility treatments. Further researches are needed to explore these relationships in greater depth and apply them clinically.

**Keyword:** Vaginal Microbiota; Infertility; Reproductive Health; Dysbiosis; Bacterial Vaginosis; Systematic review.

## Introduction

Millions of people and couples suffer from the complicated illness known as infertility. Globally, infertility encompassing various biological, environmental, and lifestyle factors [1]. The relationship between vaginal microbiota and reproductive health is one new field of study that has attracted a lot of attention lately. A varied population of bacteria that live in the female genital tract, the vaginal microbiota is essential for preserving reproductive health, and new research indicates that it may be linked to infertility [2]. The vaginal microbial community is predominantly composed of bacteria, with Lactobacillus species being the most dominant in healthy individuals of reproductive age.

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By generating lactic acid, which contributes to the maintenance of an acidic environment that prevents the growth of harmful bacteria and yeast, Lactobacillus performs a critical role in preserving vaginal health. A balanced vaginal microbiota is essential not only for the prevention of infections but also for reproductive function [3]. Research has identified various types of vaginal microbiota profiles, which can be broadly classified into three categories based on the dominance of specific bacterial species: Lactobacillus-dominated, non-Lactobacillus-dominated, and mixed microbiota. Each of these profiles is associated with different reproductive outcomes and overall health [4]. While the primary function of vaginal microbiota is protective, it also has broader implications for reproductive health. The vaginal microbiota is believed to influence several reproductive processes, including the menstrual cycle, ovulation, and implantation [5]. Disruptions in the microbiota balance, known as dysbiosis, can occur due to various factors, including hormonal fluctuations, antibiotic use, and lifestyle choices. Disturbances in the vaginal microbiota can elevate the risk of infections, including bacterial vaginosis (BV) and pelvic inflammatory disease (PID), both of which are associated with fertility complications [2]. BV is a condition marked by a reduction in Lactobacillus species and an overgrowth of other bacterial species. Research indicates that BV is linked to adverse reproductive outcomes, which can include challenges in conceiving and higher instances of pregnancy complications. The inflammatory responses provoked by BV can disrupt sperm motility and function, as well as hinder the implantation process of an embryo [6]. PID is frequently triggered by sexually transmitted infections (STIs) such as chlamydia and gonorrhea, leading to inflammation of the reproductive organs. When PID becomes chronic, it can result in scarring and damage to the fallopian tubes, which can profoundly affect fertility. Furthermore, dysbiosis is frequently linked to the development of these disorders, emphasizing the need of preserving a healthy vaginal microbiome as a defense against STIs [7]. Infertility is inherently multifaceted, with both male and female factors influencing reproductive outcomes. While the focus here is on the female perspective, it is important to recognize the impact of male reproductive health on overall fertility. A balanced vaginal microbiota may also influence the male partner's sperm health. For instance, some studies indicate that the presence of certain bacterial species in the female genital tract can affect the motility and viability of sperm, potentially leading to reduced chances of conception [8]. Moreover, the inflammatory cytokines produced in response to an imbalanced microbiota can have systemic effects, influencing ovulatory function and hormonal balance necessary for successful conception and pregnancy [9]. The composition of vaginal microbiota is not static and can be influenced by various lifestyle and environmental factors. Diet, hygiene practices, stress, and sexuality can all impact the microbial balance [7]. For instance, a high-sugar or processed diet may contribute to increased levels of inflammatory markers, thus disrupting the microbiota. Similarly, stress has been shown to affect hormonal levels, leading to dysregulation in the menstrual cycle and potentially impacting fertility. Furthermore, environmental exposures, such as chemicals found in personal care products and the use of certain contraceptives, can influence the composition of the vaginal microbiota [10]. The phenomenon of infertility affects approximately 10-15% of couples globally, underscoring the urgent need for improved understanding of its etiological factors. Emerging evidence suggests that the vaginal microbiota plays a pivotal role in reproductive health, influencing not only local immunity but also systemic health. Traditional infertility assessments have predominantly focused on physiological factors, often neglecting the role of the microbiome. Recent studies have indicated that an imbalance in vaginal microbiota, characterized by dysbiosis, may adversely affect fertility by leading to conditions such as pelvic inflammatory disease and negatively impacting embryo implantation [8, 10]. This study aims to clarify the connection between infertility and the makeup of the vaginal microbiome.

## Methods

To guarantee an open and organized methodology, this systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards. To find pertinent English-language research, a thorough search of electronic databases was carried out, including PubMed, Web of Science, SCOPUS, and Science Direct. The search was narrowed down using specific terms associated with vaginal microbiome, infertility, and reproductive health outcomes. After screening the search results, two independent reviewers chose studies that satisfied the predetermined eligibility requirements, retrieved pertinent data, and used the proper instruments to evaluate the included studies' quality.

Eligibility Criteria

Inclusion criteria: Studies eligible for inclusion examined the relationship between vaginal microbiota composition and infertility outcomes. This included research focusing on microbial diversity, dysbiosis, and their impact on reproductive health, such as conception rates, pregnancy outcomes, and infertility treatments. Only peer-reviewed articles published in English within the last 15 years were considered to ensure the inclusion of recent and relevant findings. Cohort studies, case-control studies, cross-sectional studies, and randomized controlled trials were among the study types used to offer a thorough evaluation of the available data.

Exclusion criteria: Studies that did not directly address the association between vaginal microbiota and infertility were excluded. This included research focusing solely on general microbiome studies, non-reproductive health outcomes, or infertility causes unrelated to microbial factors. Additionally, studies involving animal models, in vitro experiments, non-peer-reviewed literature, or those lacking clear data on vaginal microbiota and infertility outcomes were excluded. Studies conducted in non-clinical settings or those without a clear methodological framework were also omitted to maintain the focus on human clinical data.

Data extraction: The screening and evaluation of search results were conducted using Rayyan (QCRI), a tool designed to enhance the reliability and efficiency of systematic reviews. The inclusion and exclusion criteria were used to assess abstracts and titles for relevancy. The study team analyzed full-text publications of possibly qualifying studies and used consensus talks to settle any disagreements. Key data, such as research title, authors, publication year, study design, sample size, participant demographics, microbiological analysis techniques, and infertility-related outcomes, were gathered using a standardized data extraction form. Furthermore, a different instrument? was used to evaluate the included studies' risk of bias.

Data Synthesis Strategy: To enable a qualitative interpretation of the results, the retrieved data were combined and displayed in summary tables. The literature's major topics, trends, and gaps were noted and examined. Once data collection was completed, the most appropriate methods for analyzing and presenting the results were determined, ensuring a clear and comprehensive overview of the association between vaginal microbiota and infertility.

Risk of Bias Assessment: Since bias resulting from missing factors is frequent in research in this field, we used the ROBINS-I approach to assess the likelihood of bias since it enables a thorough examination of confounding. The ROBINS-I tool may be used for cohort designs where individuals exposed to different staffing levels are tracked over time and is designed to assess non-randomized studies. Each paper's risk of bias was evaluated independently by two reviewers, and any differences were settled by group discussion [11].

## Results

The targeted search approach produced 1216 papers (Figure 1). Following the elimination of duplicates (n = 611), 605 trials were assessed using the abstract and title. 503 of these did not meet the qualifying requirements, therefore just 98 full-text papers were left for a thorough evaluation. 9 individuals met the criteria for eligibility with synthesized evidence for analysis. Sociodemographic and clinical outcomes: A total of 1768 women with vaginal infections from nine trials were included. Four of the research designs were cross-sectional [15, 17-19], three were prospective cohorts [14, 16, 20], one was a retrospective cohort [13], and one was a case-control study [21]. notable variations in microbial composition were observed between two infertile groups, highlighting an increased frequency of Gardnerella vaginalis and Faenyhessaea vaginae, with a predominance of Lactobacillus crispatus and Lactobacillus gasseri in women with primary infertility. This indicates a significant shift in the vaginal microbiome associated with infertility.

Research [14] suggests that bacterial vaginosis (BV) may adversely impact the time to live birth in fertility treatments, emphasizing the need for careful management of vaginal microbiota in such interventions. Another study [15] underlined the importance of considering Mycoplasma and Ureaplasma as potential causes of infertility and genital infections, particularly when the infertility etiology remains unidentified. This insight is based on sequence analyses of these bacteria in the genital tracts of both asymptomatic and infertile women, showing a significant association. An additional study [16] noted that infertility might be connected to specific changes in the vaginal microbiome. It was found that a lower abundance of Lactobacillus and a higher prevalence of Gardnerella, Prevotella, Atopobium, and Pseudomonas are commonly observed in infertile women. Another investigation [17] highlighted that infertile females often show signs and symptoms typical of reproductive tract infections or sexually transmitted infections (STIs), suggesting a close link

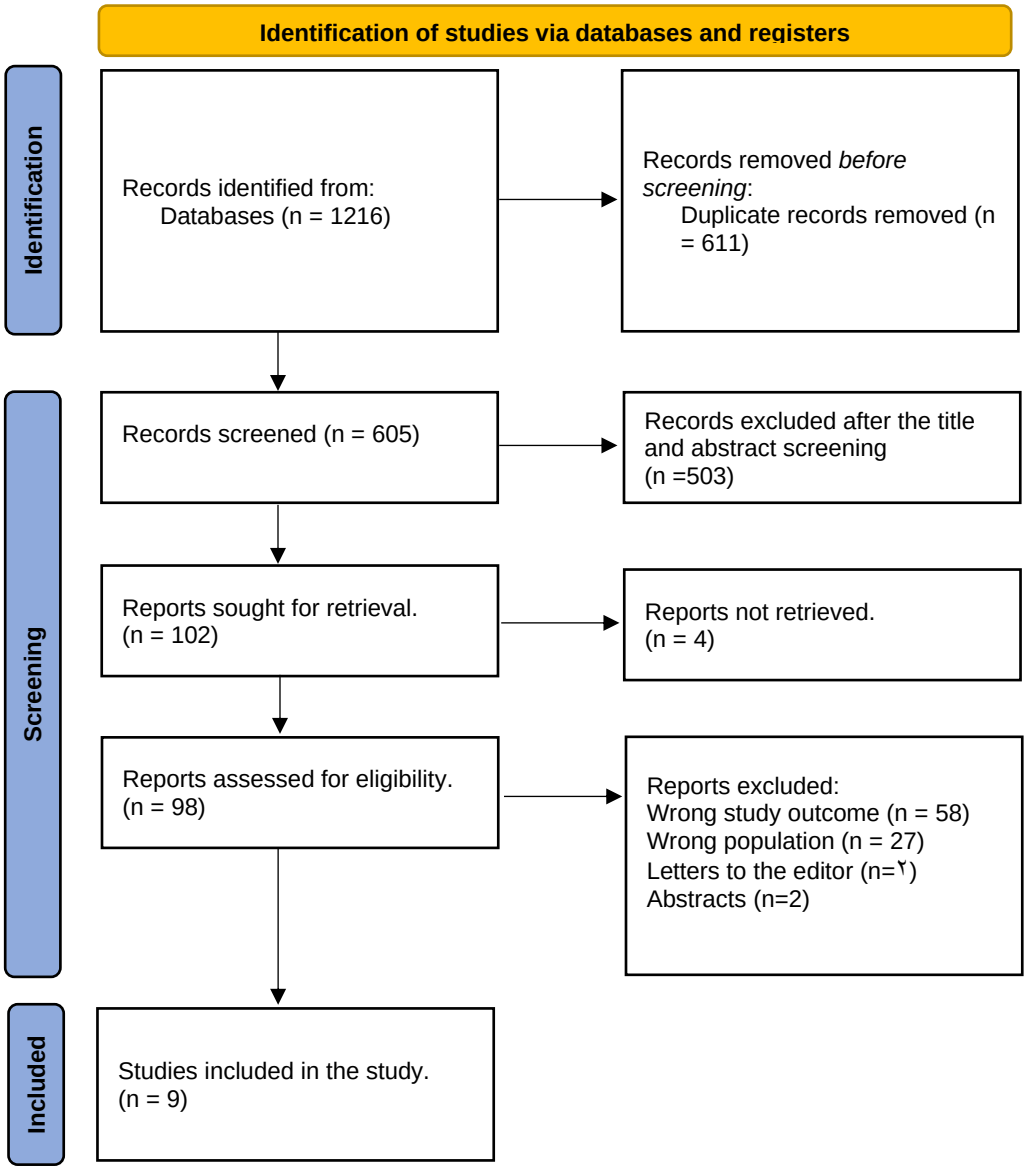


*Figure 1: PRISMA flowchart [12].*

**Table 1**: Outcome measures of the included studies.

| Study ID | Country | Study design | Sociodemo-graphic (age year) | Infection type | Infertility type | Key findings |
|---|---|---|---|---|---|---|
| **Cortés-Ortíz et al., 2025 [13]** | USA | Retrospective cohort | Participants: 136 Age range: 18-47 | Lactobacillus crispatus and Lactobacillus gasseri | Primary and secondary infertility | The two infertile groups also showed notable variations in microbial composition. Along with a high frequency of Gardnerella vaginalis and Fannyhessea vaginae, women with primary infertility had dominating Lactobacillus crispatus and Lactobacillus gasseri. |
| **van den Tweel et al., 2024 [14]** | The Netherlands | Prospective cohort | Participants: 163 Mean age: 33 | NM | NM | When a subfertile person is indicated for fertility treatment, BV may have a detrimental effect on the time to live birth of the pregnancy. |
| **Ezeanya-Bakpa et al., 2021 [15]** | Nigeria | Cross-sectional | Participants: 31 Mean age: 18-49 | *Mycoplasma* and *Ureaplasma* | Primary and secondary infertility | It is crucial to take into account Mycoplasma and Ureaplasma as potential etiologic agents of infertility and genital infection, particularly when the cause of infertility is unknown, as the sequence analysis of these two bacteria in the genital tracts of asymptomatic and infertile females revealed a significant association. |
| **Chopra et al., 2024 [16]** | India | Prospective cohort | Participants: 80 Mean age: 25.3 | Gardnerella, Prevotella, Atopobium, and Enterococcus | NM | It has been noted that infertility may be related to specific microbial compositions seen in the vaginal microbiome. In particular, infertility has been linked to lower abundance of Lactobacillus and higher prevalence of Gardnerella, Prevotella, Atopobium, and Pseudomonas. |
| **Kataria et al., 2023 [17]** | India | Cross-sectional | Participants: 444 Age range: 18-49 | STIs and reproductive tract infection | Primary and secondary infertility | Infertile females exhibited nearly all of the signs and symptoms of a reproductive tract infection or STI. |
| **Nazarzadeh et al., 2022 [18]** | Iran | Cross-sectional | Participants: 160 Age range: 20-49 | M.Hominis | NM | M. hominis infections were found in a sizable portion of infertile women. |
| **Abdo et al., 2023 [19]** | UAE | Cross-sectional | Participants: 308 Age range: 19-54 | *C. trachomatis* | Primary and secondary infertility | The significant seroprevalence of C. trachomatis that has been identified, especially in individuals who have experienced a loss of pregnancy in the past, may suggest that the disease is contributing to the rising risk of infertility in the United Arab Emirates. |
| **Zhou et al., 2024 [20]** | China | Prospective cohort | Participants: 309 | *C. trachomatis* | NM | These findings showed that among infertile women, C. trachomatis was highly prevalent, especially seroprevalence. |
| **Mongane et al., 2024 [21]** | Congo | Case-control | Participants: 137 Age range: 23-45 | *C. trachomatis* | Primary and secondary infertility | Infertility caused by tubal factors is closely linked to BV and C. trachomatis infections. The risk of tubal factor infertility should be decreased by screening and prevention. |

Not mentioned (Not Mentioned), sexually transmitted infections (STIs).

**Table 2**: Risk of bias assessment using ROBINS-I.

| Study ID | Bias due to confounding | Bias in the selection of participants into | Bias in the classification of interventions | Bias due to deviations from the intended interval | Bias due to missing data | Bias in the measurement of outcomes | Bias in the selection of reported result | Overall bias |
|---|---|---|---|---|---|---|---|---|
| **Cortés-Ortíz et al., 2025 [13]** | Low | Low | Mod | Low | Low | Low | Mod | Low |
| **van den Tweel et al., 2024 [14]** | Mod | Low | Low | Low | Low | Low | Low | Low |
| **Ezeanya-Bakpa et al., 2021 [15]** | Low | Low | Mod | Low | Low | Low | Low | Low |
| **Chopra et al., 2024 [16]** | Low | Low | Mod | Low | Low | Low | Mod | Low |
| **Kataria et al., 2023 [17]** | Mod | Mod | Mod | Low | Low | Mod | Low | Moderate |
| **Nazarzadeh et al., 2022 [18]** | Mod | Mod | Mod | Low | Mod | Mod | Low | Moderate |
| **Abdo et al., 2023 [19]** | Mod | Mod | Low | Low | Low | Mod | Mod | Moderate |
| **Zhou et al., 2024 [20]** | Mod | Low | Mod | Low | Low | Mod | Low | Moderate |
| **Mongane et al., 2024 [21]** | Mod | Crit | Low | Low | Low | Mod | Low | Critical |

between these health issues and infertility. In another context [18], a significant prevalence of M. hominis infections was found among infertile women, suggesting that microbial factors might play a more pronounced role in infertility than previously recognized. Lastly, findings [20, 21] indicate a high prevalence and potential impact of C. trachomatis infections on infertility, particularly linked to tubal factor infertility. This underscores the importance of screening and preventive measures to mitigate this risk.

## Discussion

The studies reviewed collectively highlight the critical impact of vaginal microbiota on infertility, emphasizing the need for a deeper understanding of microbial dysbiosis in reproductive health. Variations in microbial composition, such as the increased presence of Gardnerella vaginalis and Fannyhessea vaginae (formerly Atopobium vaginae) alongside a reduced predominance of Lactobacillus species in women with primary infertility [13], suggest a significant microbial imbalance linked to reproductive dysfunction. Bacterial vaginosis (BV), characterized by a depletion of Lactobacillus and an overgrowth of anaerobic bacteria, has been shown to adversely affect the time to live birth during fertility treatments, necessitating careful management of vaginal microbiota to optimize conception success [14]. A systematic review by de Souza et al. [22] further elucidated these differences, demonstrating that whereas the vaginal microbiomes of fertile women were predominantly colonized by Lactobacillus species (particularly L. crispatus, L. gasseri, L. jensenii, and L. iners), those of infertile women exhibited greater microbial diversity with a lower abundance of protective Lactobacillus strains. This dysbiosis was associated with negative reproductive outcomes, including reduced implantation rates and increased pregnancy loss [22]. Conversely, a Lactobacillus-dominant microbiome was correlated with improved fertility treatment success, reinforcing the importance of microbial equilibrium in reproductive health [22]. Vitale et al. [23] expanded on these findings, emphasizing that the stability of the vaginal microbiota relies on complex interactions between different Lactobacillus species. Specifically, Lactobacillus crispatus was identified as a key protective factor against asymptomatic bacterial vaginosis (BV) and was positively associated with fertility [23]. In contrast, the presence of Gram-negative bacteria such as Gardnerella vaginalis and Chlamydia trachomatis in the cervical flora, particularly in conjunction with a diminished Lactobacillus population, was strongly linked to infertility [23]. These findings suggest that microbial screening could serve as a predictive tool for infertility risk. Beyond BV-associated bacteria, the role of Mycoplasma and Ureaplasma species in infertility has been increasingly recognized. Multiple studies have identified these microorganisms as significant contributors to unexplained infertility, with their presence strongly correlated with tubal factor infertility and impaired embryo implantation [15]. A meta-analysis by Tantengco et al. [24] confirmed that infections with M. genitalium, M. hominis, and U. urealyticum are significantly associated with female infertility, particularly in cases of chronic endometritis and tubal occlusion. However, despite their clinical relevance, routine screening for genital mycoplasma infections remains inconsistent due to diagnostic challenges [25]. The detection of these pathogens requires specialized culture media and molecular techniques (e.g., PCR), which are not routinely available in many clinical settings [25]. Additionally, a substantial proportion of women with genital mycoplasma infections remain asymptomatic, leading to underdiagnosis and prolonged exposure to microbial-induced reproductive harm [25]. This underscores the need for improved diagnostic protocols, particularly for women undergoing fertility treatments, as untreated infections may contribute to long-term infertility and adverse pregnancy outcomes [25]. The growing body of evidence supports a paradigm shift in infertility management, advocating for the integration of microbiome analysis into standard diagnostic workups. Proactive screening and treatment of bacterial vaginosis, C. trachomatis, and genital mycoplasmas could mitigate microbial-related infertility and enhance assisted reproductive technology (ART) success rates [14, 25]. Furthermore, the use of probiotics to restore Lactobacillus-dominant microbiota has shown promise in preliminary studies, though further research is needed to establish standardized therapeutic protocols [22, 23].

Study Strengths: The strengths of this review include the diverse study designs and populations analyzed, providing a comprehensive overview of the

association between vaginal microbiota and infertility. The use of advanced microbial sequencing techniques across studies has allowed for a detailed characterization of microbial communities and their functional implications on fertility.

Study Limitations: However, the studies reviewed have limitations, including their observational nature, which limits causality inference. The variability in sample sizes and methodologies across studies may also affect the generalizability of the findings. Furthermore, most studies focus on correlations rather than mechanisms, highlighting a gap in understanding how microbial changes physically impact fertility.

## Conclusion

The vaginal microbiota plays a significant role in reproductive health, influencing both the occurrence of infertility and the outcomes of fertility treatments. In order to determine causal linkages and investigate therapies that may alter the vaginal microbiota to improve fertility, future research should concentrate on longitudinal studies.

## Conflict of Interest

None

## Funding

None

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