INPLASY

Microbiome and Reproductive Outcomes: A Systematic Review and Meta-analysis (2015–2025)

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INTRODUCTION

Review question / Objective Does the presence of bacterial vaginosis affect live birth outcomes in women undergoing fertility treatment?2 Is Lactobacillus-dominated vaginal microbiota associated with improved clinical pregnancy rates?3 What is the impact of endometrial microbiome dysbiosis on implantation failure?4. How does antibiotic exposure influence microbial diversity in the reproductive tract, and what are the potential reproductive implications?

Rationale Given the emerging recognition of microbial influences on fertility and the ongoing debate about their clinical relevance, this systematic review and meta-analysis aims to evaluate the association between alterations in vaginal and endometrial microbiota and reproductive outcomes, including infertility, implantation failure, IVF pregnancy, spontaneous pregnancy, and spontaneous abortion.

Condition being studied By including only comparative studies from 2015 to 2025 with control groups and prevalence data, we aim to provide a clearer assessment of the diagnostic and therapeutic relevance of microbial evaluation in the infertility workup.

METHODS

Search strategy This systematic review and meta-analysis was conducted according to PRISMA 2020 guidelines24, focusing on the relationship between female reproductive outcomes and microbiome-related conditions. The outcomes of interest included infertility, implantation failure, spontaneous pregnancy, IVF pregnancy, and spontaneous abortion. The exposures considered were microbiome, endometriome, microbiota, vaginal microbiota, vaginal bacteriosis, and endometritis.

Participant or population Information Sources and Search Strategy We searched PubMed, Scopus, EMBASE, Web of Science, and Cochrane

Library using the following keywords and MeSH terms: "infertility," "implantation failure," "IVF outcomes," "spontaneous pregnancy," "abortion," "microbiome," "endometrial microbiota," "vaginal microbiota," "vaginal bacteriosis," and "endometritis." Boolean operators (AND/OR) were used to combine terms. The search was supplemented by hand-searching reference lists of included studies.

Intervention Study Selection and Data Extraction Two reviewers independently screened titles and abstracts and then assessed full texts for eligibility. Discrepancies were resolved by consensus or consultation with a third reviewer. Data extraction was performed using a standardized form that captured study characteristics, exposure definitions, sample size, reproductive outcomes, and statistical results.
Risk of Bias Assessment The ROBINS-I tool was used to assess the risk of bias in non-randomized studies across seven domains: confounding, selection, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each study received a rating of low, moderate, serious, or critical risk of bias25 .
Certainty of Evidence (GRADE) We used the GRADE approach to evaluate the certainty of evidence for each outcome, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence was graded as high, moderate, low, or very low26.

Comparator Anbormal verus normal microbiome.

Study designs to be included This systematic review and meta-analysis was conducted according to PRISMA 2020 guidelines24, focusing on the relationship between female reproductive outcomes and microbiome-related conditions.

Eligibility criteria Systemativ review with meta analysis.

Information sources We searched PubMed, Scopus, EMBASE, Web of Science, and Cochrane Library using the following keywords and MeSH terms: "infertility," "implantation failure," "IVF outcomes," "spontaneous pregnancy," "abortion," "microbiome," "endometrial microbiota," "vaginal microbiota," "vaginal bacteriosis," and "endometritis." Boolean operators (AND/OR) were used to combine terms. The search was supplemented by hand-searching reference lists of included studies.

Main outcome(s) Data extraction was performed using a standardized form that captured study characteristics, exposure definitions, sample size, reproductive outcomes, and statistical results.

Quality assessment / Risk of bias analysis Risk of Bias Assessment The ROBINS-I tool was used to assess the risk of bias in non-randomized studies across seven domains: confounding, selection, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each study received a rating of low, moderate, serious, or critical risk of bias25 .
Certainty of Evidence (GRADE) We used the GRADE approach to evaluate the certainty of evidence for each outcome, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence was graded as high, moderate, low, or very low26.

Strategy of data synthesis Where feasible, a meta-analysis was performed using a random-effects model. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Heterogeneity was assessed using the I² statistic, with thresholds of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Subgroup analyses were conducted based on microbiome type (vaginal vs. endometrial) and outcome type (e.g., IVF vs. spontaneous pregnancy).

Subgroup analysis
· Reported reproductive outcomes compared between exposed and unexposed/control groups.
· Focused on the vaginal or endometrial microbiome, endometriome, vaginal bacteriosis, or endometritis
· Spontaneous and IVF pregnancy and miscarriages.

Sensitivity analysis Where feasible, a meta-analysis was performed using a random-effects model. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Heterogeneity was assessed using the I² statistic, with thresholds of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Subgroup analyses were conducted based on microbiome type (vaginal vs. endometrial) and outcome type (e.g., IVF vs. spontaneous pregnancy).

Language restriction English.

Country(ies) involved Italy.

Dissemination plans Publication in scientific indexed journal.

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