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Reproductive tract microbiota and anatomical integrity: implications for fertility, pregnancy, and neonatal outcomes: a narrative review

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Abstract

Background The microbiota of the reproductive system is a vital factor in fertility, pregnancy and neonatal health. Microbiota composition may control implantation, gestational preservation and neonatal colonization. The vaginal, cervical and uterine/endometrial niches exhibit varying levels of consistency with evidence based on sampling techniques and analysis.

Methods We searched PubMed, Google Scholar, Scopus and Web of Science for articles published between January 2015 and September 2025. The inclusion criteria were human studies that have assessed microbiota of the reproductive tract in the vaginal, cervical, endometrial, placental or amniotic compartments against fertility, pregnancy or neonatal outcome. We excluded male-only, non-reproductive microbiomes or outcomes not aligned to fertility, pregnancy complications or neonatal health. Screening was done independently by two reviewers while a third reviewer assisted with conflict resolution.

Due to heterogeneity, a structured meta-analysis was not possible. We synthesized evidence narratively following screening for eligibility.

Results The most consistent evidence links vaginal dysbiosis particularly depletion of stable Lactobacillus-dominant communities and enrichment of anaerobic taxa with inflammatory disruption of cervicovaginal barrier function and increased risk of preterm birth related outcomes. By contrast, associations involving cervical especially endometrial microbiota with implantation failure, recurrent pregnancy loss and IVF outcomes remain suggestive but less consistent across studies. Evidence for a resident placental microbiota remains controversial with several recent low-biomass analysis favoring contamination interpretations over proof of viable colonization. Across sites, Lactobacillus dominance was not uniformly protective because species and strain level differences especially between *Lactobacillus crispatus* and *Lactobacillus iners* appeared clinically relevant. Maternal dysbiosis occurring pre-conception or early in pregnancy seem to have the greatest impact on adverse outcomes such as preterm birth. Modulation of local immune responses, inflammatory signaling and cervicovaginal barrier integrity were major highlighted mechanistic pathways. Emerging translational strategies include strain targeted probiotics/live biotherapeutics and vaginal

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microbiota transplantation although safety and standardized endpoints remain key constraint. Interventional and translational studies suggests that microbiome modulation can shift cervicovaginal community structure toward Lactobacillus enrichment.

Conclusion There are significant relations between the reproductive tract microbial conditions, anatomical/immune health and reproductive outcomes but they are species/strain and context specific. There is a need to make early risk stratification, mechanistic validation and carefully controlled intervention studies priorities in future work before broad clinical implementation.

Keywords Microbiota, Lactobacillus, Dysbiosis, Pregnancy, Preterm, Vaginosis, Infertility, Endometrium

Introduction

The Microbial community is present in all areas of the female reproductive tract, including the vulva and vagina, up to the cervix, and even in the uterine cavity [1]. The increased attention to the reproductive tract microbiome over the years has helped to shed light on its central role in reproductive pathology and physiology. Recent narrative syntheses have highlighted the role of reproductive tract microbiota in gynecologic pathology, particularly in inflammatory and neoplastic processes, through shared host–microbial mechanisms [2]. Microbial homeostasis (eubiosis) has been shown to promote mucosal barrier activity and immune homeostasis [3] whereas a dysbiotic microbiota can trigger inflammation or cause direct tissue damage to reproductive organs [4, 5]. Gao et al. 2024 [6] presented evidence that suggests that microbial ecosystems residing in the vagina, cervix and endometrium play a dynamic role in regulating fertility, successful implantation, and pregnancy outcomes through immune signaling, epithelial integrity and metabolic pathways. The implications of these interactions amongst hosts and microbes are far-ranging. They may affect the ability of a couple to conceive, the progression and the result of a pregnancy and the well-being of a newborn during the first days of life and later. Anatomical integrity in this review, is the structural and functional ability of reproductive tract barrier systems which restrain microbial ascent and excess inflammation and facilitate implantation and pregnancy maintenance. This concept involves operationally epithelial barrier continuity, tight-junction integrity, cervical mucus barrier activity and extracellular matrix stability. It also involves controlled local immune signaling and in pregnancy, maintenance of the fetal membranes and placental interface. This framework links microbial community structure to reproductive outcomes via three interconnected mechanistic domains: mucus and epithelial barrier maintenance, inflammatory and immunologic regulation, and matrix remodeling linked to tissue weakening or microbial ascendancy.

Global significance

Pregnancy complications and infertility are of significant public health concern throughout the world [7, 8], and in most cases, they have complicated etiologies. Current adverse outcomes are at least partially explained by classical risk factors (e.g., age, genetics, and underlying health conditions). Researchers are trying to determine the role of the maternal microbiome as a contributing factor. The vaginal microbiota has been identified as a gatekeeper that may prevent or predispose to such diseases as bacterial vaginosis (BV), pelvic inflammatory disease, preterm labor, and neonatal infection [9]. The study of these microbial ecosystems offers a more holistic view of reproductive health, a combination of microbiology with the field of gynecology and obstetrics.

Aim

The aim of this review is to synthesize current findings linking reproductive tract microbiota with fertility (natural conception and assisted reproductive technology outcomes), pregnancy outcomes (including miscarriage and preterm birth), and neonatal health. We examine proposed biological mechanisms that may underlie these associations. Emerging microbiome targeted interventions, their translational limitations and future research priorities will also be evaluated.

Although the main scope of this review is the female reproductive tract microbiota, only those gut-mediated and systemic pathways with direct mechanistic significance in reproductive tract immune regulation, pregnancy complications or maternal-to-neonatal microbial transmission are discussed.

Anatomical integrity is used in this review to refer to the structural and functional competency of host barriers that restrict microbial ascent and dysregulated inflammation. In pregnancy, these are the vaginal/cervical epithelium, cervical mucus layer and gestation barriers which are the fetal membranes (chorion-amnion) and placental interface.

Methods

Literature search and study selection

This review was conducted as a narrative review with structured literature identification and transparent study selection procedures. We searched PubMed, Scopus, Web of Science, and Google Scholar for literature

published from January 2015 to September 2025. A representative full Boolean search strategy was developed for PubMed and adapted for syntax and indexing differences in Scopus, Web of Science, and Google Scholar. The PubMed search string was as follows: ((vaginal OR cervicovaginal OR cervical OR endometrial OR uterine OR placental OR amniotic fluid) AND (microbiota OR microbiome OR '16S rRNA' OR '16S rDNA' OR metagenomic OR sequencing) AND (fertility OR infertility OR subfertility OR IVF OR ART OR implantation OR miscarriage OR pregnancy OR preterm birth OR PPROM OR neonatal outcome OR neonatal colonization)). Relevant human studies were selected for narrative synthesis. Where necessary, seminal pre-2015 references were retained only to provide foundational biological or conceptual context. Due to the fact that endometrial, placental, and amniotic samples are usually prone to contamination related bias, we interpreted these studies with special care. Greater attention was given to studies that reported negative controls, sequencing platform transparency and clear distinction between microbial DNA detection and evidence of viable colonization.

Microbiota sampling methods

The sampling methods in the included literature used varied across anatomical site. High vaginal or mid-vaginal swabs were often used to obtain vaginal microbiota. Endocervical swabs or cytobrush-based sampling were usually used to gather cervical microbiota during speculum examination. Endometrial microbiota was often investigated using transcervical catheter aspirates and endometrial biopsy although these approaches were recognized as vulnerable to contamination from the lower genital tract. Placental and intrauterine microbiota studies analyzed placental tissue biopsies, membrane samples or amniotic fluid using either culture-based methods or sequencing-based approaches such as 16S rRNA gene sequencing.

Inclusion and exclusion criteria

We included human observational and interventional studies of the female reproductive tract microbiota (vaginal, cervical, endometrial, placental, or amniotic fluid) in relation to fertility, pregnancy or neonatal outcome. Studies focusing solely on male factor infertility, non-reproductive microbiota, animal models, or lacking relevant clinical outcomes were excluded. Only articles published in English Language were included. Grey literature and conference abstracts were not included. The PECO framework was structured as follows: Population—women of reproductive age or pregnant women and neonates where maternal reproductive tract microbiota was clinically relevant. Exposure -reproductive tract microbiota composition or dysbiosis in vaginal, cervical, endometrial, placental, or amniotic compartments. Comparator- eubiotic vs dysbiotic states, Lactobacillus-dominant vs non-Lactobacillus-dominant communities, or clinically stratified outcome groups where available. Outcomes- fertility, implantation, IVF/ART outcomes, miscarriage, preterm birth, PPROM, pregnancy complications, and neonatal microbial or clinical outcomes.

Screening and selection

Titles and abstracts were screened by two independent reviewers, followed by full-text assessment of potentially relevant articles. Conflicts were resolved by discussion and consensus by a third reviewer. The study selection process is summarized in the PRISMA flow diagram (Fig. 1) showing records identified, screened, excluded and included.

Assessment of study quality

Due to the heterogeneity of study designs and the narrative nature of this review, a formal risk of bias tool was not uniformly applicable. However, evidence quality was appraised using a structured qualitative approach based on study design, methodological transparency, sampling and contamination control (particularly for low-biomass studies), clarity of outcome definitions, and consistency across studies. Based on these criteria, evidence was categorized as strong, moderate, or preliminary.

Data extraction and synthesis

In each of the included sources, we synthesized the following data: microbiota composition (which taxa were predominant or altered), a measure of anatomical or immunological integrity (e.g. inflammatory marker, barrier functioning assays), and the effect on fertility/pregnancy/neonatal outcomes. A qualitative synthesis was done because of the heterogeneity of the design of the studies. We classified results into thematic groups based on key phases of the reproductive process and anatomical locations. This helped in providing a logical story of the relationship between microbial patterns and clinical endpoints.

Findings

Site-specific reproductive tract microbiota

Vaginal microbiota

Vaginal microbiota is one of the most studied microbial ecologies of the female body [10]. The vaginal microbiota of healthy reproductive-age women is generally of low diversity and dominated by the genus Lactobacillus [11, 12]. The reproductive-age vaginal microbiota typically shows low diversity with dominance of lactic acid producing Lactobacillus spp. (e.g., *L. crispatus, L. jensenii, L. gasseri*) in an acidic environment (pH ~ 3.5–4.5) [13, 14] The comparative microbial composition across different

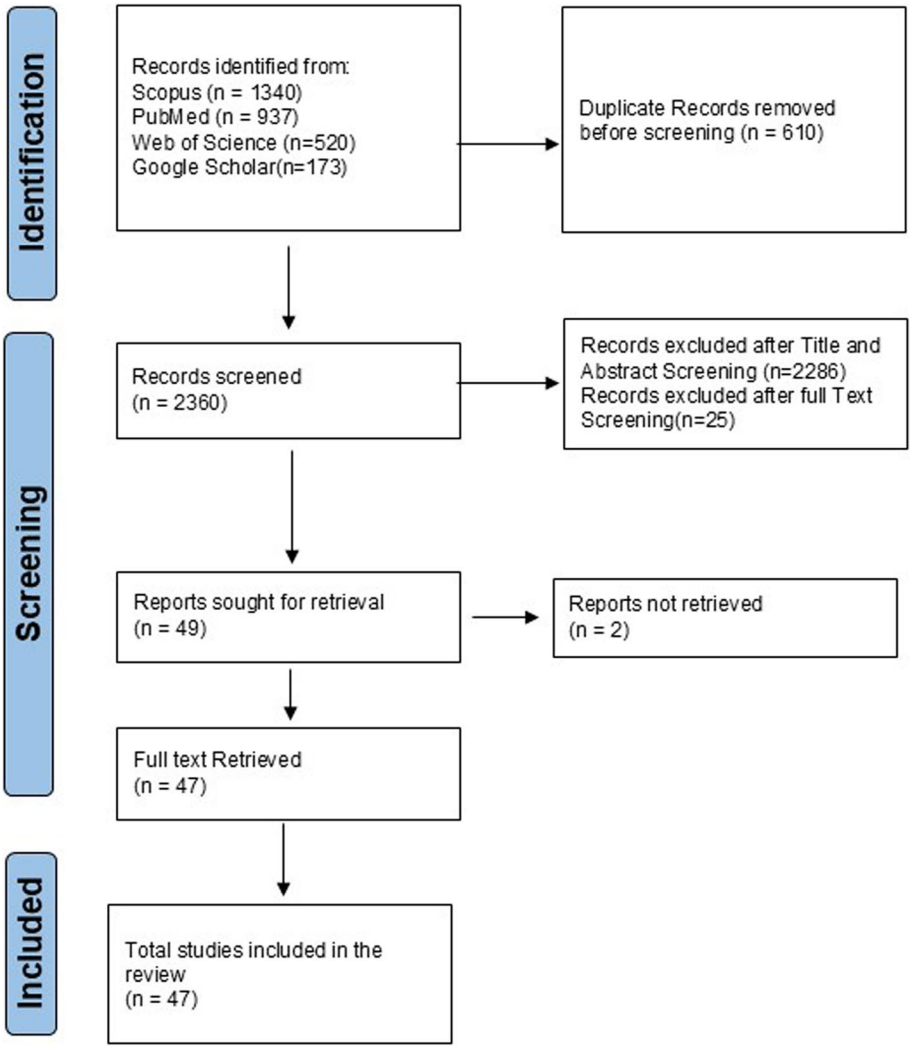


Fig. 1 PRISMA diagram. Figure 1 is a PRISMA 2020 flow diagram of study selection which shows the Identification, screening and final inclusion of studies retrieved from Scopus, PubMed, Web of Science, and Google Scholar

reproductive tract sites under eubiotic and dysbiotic conditions is summarized in Table 1. Lactobacilli are the keystone defenders inhibiting the growth and adhesion of potentially harmful microbes producing lactic acid, hydrogen peroxide, bacteriocins, and biosurfactants [15, 51]. It is believed that this acidic and antimicrobial environment keeps the vaginal epithelium and upper genital tract infections at bay. Furthermore, commensal Lactobacillus species may co-aggregate with pathogens and prevent their adherence on the epithelial surface, thus further protecting the integrity of the mucosa [17].

Even though Lactobacillus numerically dominates the vaginal flora of most women, vaginal microbial ecology is not homogenous. In this respect, vaginal communities are usually sorted into Community State Types (CSTs) according to the primary taxa and/or total diversity: CST I, II, III, and V are typically dominated by Lactobacillus species (*L. crispatus*, *L. gasseri*, *L. iners* and *L. jensenii*, respectively). CST IV is characterized by low Lactobacillus abundance and enrichment of strict anaerobes, including Gardnerella, Atopobium, Prevotella, and Sneathia [52].

Discussion

Although Lactobacillus-dominant vaginal communities are commonly associated with reduced risks of BV and sexually transmitted infections (STIs), growing evidence suggests that Lactobacillus dominance should be interpreted as a species, strain, and ecological context-dependent state rather than as a uniformly protective marker. In clinical and metabolomic studies in females with repeated BV. Zhu et al. [53] showed that antibiotic treatment often results in post treatment dominance by *Lactobacillus iners* rather than *Lactobacillus crispatus*. They observed that *L. iners* dominated states are associated with higher BV recurrence and reduced stability.

Table 1 Comparison of microbial composition in different reproductive tract sites (Eubiotic vs Dysbiotic)

Site	Condition	Dominant Taxa	Microbial Load	pH (Vagina)	Example CST	Anatomical Barriers/Notes	Reference(s)
Vagina	Eubiotic	Lactobacillus spp. (*L. crispatus, L. iners, L. jensenii, L. gasseri*)	High; Lactobacillus-dominant	~3.5–4.5	CST I (*L. crispatus*)	Acidic, Lactobacillus-dominated mucosa; squamous epithelium and mucus limit pathogen ascent	[2, 10, 13, 15, 16]
Vagina	Dysbiotic	BV-associated anaerobes: Gardnerella, Atopobium, Prevotella, Sneathia (± Ureaplasma/Mycoplasma)	Higher diversity; Lactobacillus depleted	> 4.5	CST IV (low-Lactobacillus)	Weakened barrier; ↑BV/STIs/sPTB risk; mucin degradation (↑sialidase) and inflammation	[17–26]
Cervix	Eubiotic	Lactobacillus-dominant (continuum of vaginal microbiota)	Moderate; protected by mucus	N/A	Shares vaginal CSTs I–III	Endocervical mucus plug and local immunity; samples easily contaminated from vagina	[13, 17, 27–31]
Cervix	Dysbiotic	Lactobacillus-depleted; anaerobes (e.g., Gardnerella, Sneathia); often L. iners present	Higher diversity/pathobionts	N/A	CST IV-like	Lactobacillus depletion + BV-associated taxa; linked to inflammation and slower HPV clearance/↑epithelial abnormalities	[13, 17, 27–31]
Endometrium	Eubiotic	Low-biomass; often Lactobacillus if any	Very low (orders of magnitude below vagina)	N/A	LD (Lactobacillus-dominant) vs NLD	Near-sterile/low-biomass cavity; transcervical sampling vulnerable to vaginal/kit contamination; interpret with controls	[32–40]
Endometrium	Dysbiotic	Non-Lactobacillus anaerobes (e.g., Gardnerella, Prevotella, Anaerococcus)	Increased burden; Increased microbial signal and/or inflammation	N/A	NLD (non-Lactobacillus-dominant)	Chronic endometritis with inflammation; associated with reduced implantation and IVF success	[32–40]
Placenta (Term)	Eubiotic	No stable resident microbiota; signals often reflect	Extremely low/undetectable in health	N/A	N/A	Placenta and membranes form a largely sterile fetal barrier; most positive signals reflect contamination	[41–46]
Placenta (Infected)	Dysbiotic (Chorioamnionitis)	Pathogens: Ureaplasma, Fusobacterium, *E. coli*, GBS, Mycoplasma	Detectable load by culture/16S	N/A	N/A	Barrier failure with maternal–fetal inflammation; associated with PTB, PPROM and neonatal sepsis via ascending or hematogenous spread	[47–50]

Table 1 compares the microbial composition in different reproductive tract sites under eubiotic and dysbiotic conditions. The table outlines the dominant taxa, microbial load, pH, and example Community State Types (CST) for each site. It also describes anatomical barriers and notes the potential clinical implications of each condition

Evidence level: Evidence summarized in this table is derived from a qualitative synthesis of human observational, molecular, and translational studies. It varies by anatomical site. Evidence is strongest for the vaginal microbiota and dysbiosis-associated states such as BV. It is moderate for cervicovaginal continuity and endometrial low-biomass patterns and more limited for placental microbial signals in uncomplicated pregnancy

Abbreviations: BV bacterial vaginosis, *CST* community state type, *GBS* Group B Streptococcus, *HPV* human papillomavirus, *IVF* in vitro fertilization, *LD* Lactobacillus-dominant, *NLD* non-Lactobacillus-dominant, *PPROM* preterm premature rupture of membranes, *PTB* preterm birth, *STI* sexually transmitted infection

This is consistent with the opinion that a Lactobacillus dominant community may not be universally protective. In line with these clinical findings, Nori et al. [16] revealed that vaginal *L. crispatus* and *L. iners* showed significant strain and subspecies level genomic heterogeneity, which included variations in those genes associated with host interaction and colonization capabilities. On the mechanistic level, a recent study by Xu et al. [27] points out the differences in the mechanisms of adhesion and colonization, the production of antimicrobial factors including bacteriocins and lactic acid. There are also interactions with pathogens and biofilms, and immunomodulatory effect of vaginal lactobacilli. These further underlines that host and environmental factors such as hormonal cycling, pregnancy, and other physiological states are of critical importance to vaginal microbial balance. Together, these studies have provided a subtle ecological explanation in that *L. iners* preeminence could indicate transitional or unsteady community conditions and that *L. crispatus*-dominant communities are more simply related to resilience. It highlights the fact that context of community and host considerations are necessary in defining eubiosis as opposed to solely Lactobacillus dominance. The contrasting states of cervicovaginal eubiosis and dysbiosis are illustrated in Fig. 2.

Cervical microbiota

Cervix is an important anatomical transition zone between the vagina and the sterile upper tract. The role of the cervix in microbiology has traditionally been viewed primarily as a barrier. The cervical mucus plug in pregnancy keeps ascending microbes out. Studies have indicated that a unique microbial niche is possibly harbored in the cervix. Cervicovaginal microbiota generally appear similar to the vaginal communities [28], although some reports suggest that some of these taxa including

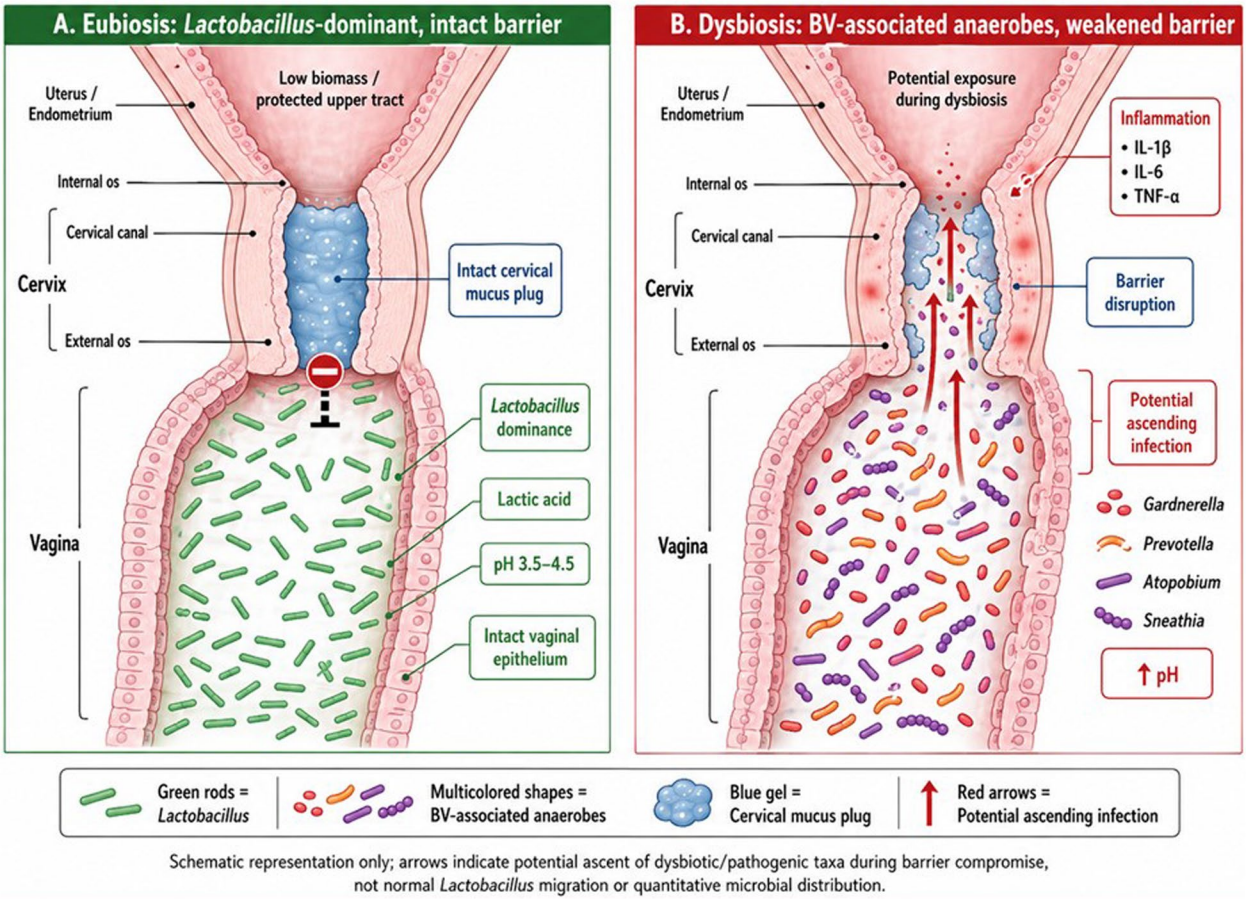


Fig. 2 Cervicovaginal eubiosis and dysbiosis: barrier integrity and potential ascending infection. Figure 2. Panel **A** shows a Lactobacillus-dominant cervicovaginal environment with lactic acid production, acidic pH, intact vaginal epithelium and a preserved cervical mucus plug. *Lactobacillus* spp. shown mainly in the vaginal/lower cervicovaginal compartment, while the uterus/endometrium is represented as a low-biomass protected upper tract. Panel **B** shows dysbiosis, with BV-associated anaerobes such as Gardnerella, Prevotella, Atopobium, and Sneathia, increased pH, inflammation, epithelial disruption, mucus plug weakening and potential ascending infection. Arrows indicate possible ascent of dysbiotic/pathogenic taxa after barrier compromise not normal Lactobacillus migration or quantitative microbial distribution. Figure generated using ChatGPT (OpenAI, DALL·E) and edited by the authors for scientific accuracy and clarity

Mycoplasmataceae (Mycoplasma and Ureaplasma species), are more commonly found in the cervical canal than around the vaginal introitus [14, 29]. Mycoplasma and Ureaplasma may be either asymptomatic commensals or opportunistic pathogens associated with pelvic inflammatory disease and preterm birth [30]. Human Papillomavirus (HPV) infection also takes place in the cervix. There is recent evidence that the resident microbiota at the site can be involved in HPV persistence or clearance, and consequently cervical dysplasia [28]. An example of this is that a cervicovaginal microbiota high in Lactobacillus (particularly *L. crispatus*) is linked to accelerated HPV clearance, and a microbiota high in BV-associated bacteria is linked to slower clearance and increased risk of cervical epithelial abnormalities [52].

In some reports, sampling of the cervix has been defined as a continuum with the vagina. However, microbial ascension can be altered by the anatomical integrity of the cervix (e.g. closed versus dilated, mucus versus absent, inflammatory state) [31, 32].

Endometrial microbiota

Historically, the upper uterus (endometrium) was considered sterile in healthy individuals, and the presence of bacteria was generally interpreted as evidence of infection [33]. Modern molecular methods have been able to detect microbial DNA signals in some upper-tract samples. Whether these represent viable resident communities remains argued, particularly because of low-biomass contamination risk [34, 35]. The endometrial microbiota of healthy, non-pregnant women also seems to contain a much smaller number of microbes than the vagina [36]. It is frequently dominated by a small number of genera such as Lactobacillus (Firmicutes phylum) and Bacteroides or other Flavobacterium (Bacteroidetes phylum). In one study they found that the endometrial tissue of asymptomatic women typically contained Lactobacillus species and a small amount of Gardnerella, but with a total bacterial burden far less than vaginal swabs of the same women [37]. These low microbial biomass values should be interpreted with care because vaginal or lab contamination can easily cause the presence of an endometrial microbiome to be overstated. Paired sampling methods that is sampling vagina, cervix, and endometrium in the same patient are encouraged to identify the difference between the bacteria that are really present in the uterus and the ones that were introduced during transcervical sampling. Recent studies indicate that when a Lactobacillus-dominated microbiota spreads into the uterus it could be either harmless or potentially useful in promoting endometrial receptivity [38, 39]. Conversely, non-Lactobacillus anaerobes such as Gardnerella, Atopobium, Sneathia and Streptococcus spp. have been detected in the endometrium and linked to chronic endometritis and implantation failures [14]. Chronic endometritis is a severe, asymptomatic inflammation of the uterine lining that is typically identified by histological detection of the presence of plasma cells in the endometrium and is commonly associated with bacterial presence. The implicated organisms include Enterococcus, Streptococcus, *E. coli* or Mycoplasma [35]. This low-grade inflammation may cause disruption of the finely tuned environment required to implant an embryo.

Placental and intrauterine low-biomass debate

The question of whether the placenta and amniotic fluid have their own microbiota remains controversial. A preliminary study of placental tissues of term pregnancies revealed the presence of bacterial DNA and community profile that is more suggestive of the oral microbiome than of the vaginal microbiome [14]. Panzer et al. [40] re-analyzed 15 publicly available placental 16S datasets with a harmonized pipeline and found that environmental DNA and mode of delivery exert a strong influence on the apparent signal. This prompted them to conclude that the existing evidence of the DNA-based data does not strongly support a uniform placental microbiota. Within a larger fetal microbiome synthesis, Kennedy et al. [41] argue that placenta results represent a cautionary example of sequence based low biomass microbiome pitfalls. They emphasized that DNA detection alone is not proof of a live, replicating ecosystem of microorganism. They therefore called for transdisciplinary standard which goes beyond contamination controls to biological/ecological credibility and mechanistic/functional evidence. In line with this, a study of term pregnancies through sequencing and bacterial culture by Sterpu et al. [42] found no evidence of a placental microbiome. They interpreted the rare signals as more likely evidence of contamination or exposure to microbes in the postpartum period, than colonization. By 2025, many have tended to take the position that the placenta and by extension the fetus is mostly sterile in normal pregnancies, and that the positive results of previous studies could have been due to contamination [40, 43].

It has been established clinically that pathological intrauterine infections are possible and dangerous. An example of this is chorioamnionitis, infection of the placenta and fetal membranes—a known cause of preterm labor and neonatal sepsis [44, 45]. The commonly occurring bacteria in such cases are *Ureaplasma urealyticum*, Fusobacterium, Gardnerella, Group B Streptococcus, and many others [46]. These infections are commonly preceded by an ascending vaginal infection. Oral bacteria such as *Fusobacterium nucleatum* have also been detected in the amniotic fluid or fetal tissues of women with stillbirth or preterm labor who had periodontal disease indicating a potential hematogenous pathway where

bacteria in the mouth infects the placenta through bloodstream [47]. Therefore, though a healthy commensal placental microbiome is uncertain, anatomical integrity violations via the cervix or blood have devastating consequences when they expose the fetus to bacteria. Preservation of the integrity of the fetal membranes and placental barrier is therefore in part dependent on the condition of the lower genital tract microbiota. A healthy microbiome helps to avoid ascending infection whereas dysbiosis can lead to the production of enzymes and inflammations that weaken the barriers.

Host defense mechanisms and microbiota

Lactobacillus-dominated microbiota throughout the female reproductive tract have been persistently associated with maintenance of epithelial integrity by synergistic action on junctional integrity, mucus homeostasis and mucosal immune control. Delgado-Diaz et al. [48],using Lactobacillus-derived lactic acid have shown an immediate effect on cervicovaginal epithelial barrier integrity by increased tight-junction proteins (claudins and occludins) and strengthening junctional stability and epithelial homeostasis. Similarly, Schwecht et al. [49] demonstrated that lactic acid synthesized by vaginal lactobacilli maintains epithelial barrier functions in addition to preventing dysbiotic metabolite induced inflammation. This has a dual effect on junctional maintenance and immunological regulation. On the level of mucus and barrier immunoprotective crosstalk, Dong et al. [50] provide evidence that Lactobacillus-dominant microflora can facilitate the cervical mucus organization and functionality and prevent pathogenic invasions and overactive immune stimulation. Within the immunoregulatory aspect, Glick et al. [54] reported the presence of bioactive b-carboline compounds produced by vaginal lactobacilli that has anti-inflammatory effects on the host mucosal tissues. This contributes to the understanding of the mechanism of how the dominance of Lactobacillus maintains mucosal tissues. Also, the synthesized emerging evidence in Cheng et al. [55] demonstrates that Lactobacillus driven microbial ecosystems are essential in maintaining region level physiology of reproductive tracts. This is through the coordination of epithelial homeostasis, mucus stability, and immune responsiveness both locally and systemically. Collectively, all of these results help to reinforce the idea that Lactobacillus dominant communities play a pivotal role in maintaining the integrity of the reproductive tract by an extremely well-coordinated set of structural and immunological responses. Key host factors contributing to anatomical integrity and their interactions with microbiota are outlined in Table 2.

Microbiota and host anatomical defenses clearly depend on each other. The vaginal and cervical epithelium secretes both mucus and antimicrobial peptides (AMPs), and contains immune cells to monitor pathogens [62, 63]. Some of these defensive factors are induced by commensal microbes such as the lactic acid produced in response to estrogen stimulated Lactobacillus proliferation which activates host immunity and keeps epithelial junctions tight [57]. The host environment (pH, nutrient availability, antibodies) in its turn selects those Lactobacilli that are beneficial forming a positive feedback loop. Disruption of this balance through antibiotic use or hormonal effects may alter the composition of the microbiota thus modulating tissue integrity through changes in immune signaling or direct microbial influence.

Reproductive and obstetric outcome

Fertilization and implantation are the first steps towards a successful pregnancy, and both of these processes can be affected by the microbial ecosystem of the reproductive system. The composition of the vaginal and endometrial microbiota has also been found to be associated with both natural fertility and the results of assisted reproductive techniques (ART) [58, 59].

Bacterial vaginosis-associated dysbiosis and infertility

Bacterial vaginosis (BV)-associated dysbiosis may impair fertility by disrupting the cervicovaginal conditions required for sperm survival, sperm transport and conception. Lactobacillus depletion, enrichment of anaerobes such as Gardnerella, Prevotella, Atopobium and Sneathia can create a hostile biochemical environment and alter cervical mucus properties required for sperm passage [64]. BV-associated inflammation and increased susceptibility to sexually transmitted infections may further compromise fertility through cervicitis, pelvic inflammatory disease, endometrial involvement and tubal damage. Thus, BV-associated dysbiosis may represent a modifiable contributor to infertility, particularly in women with recurrent reproductive failure, chronic cervicitis, or coexisting genital tract infections.

Inflammatory signaling and enzyme-mediated degradation of mucin- and matrix-rich barriers are also some of the mechanisms through which fertility may be impaired. Pelayo et al. demonstrated that Prevotella spp. are a significant contributor to vaginal sialidases with such enzymes being common and transcriptionally expressed in vaginal metagenomes. This supports the concept that BV-associated consortia have the capacity to promote high levels of neuraminidase/sialidase activity [65] This can target host glycans, including mucin-associated substrates. Agarwal et al. [66] have given direct biochemical and mechanistic evidence that *Gardnerella vaginalis* degrades cervicovaginal mucus sialoglycans. They described a pathway where *G. vaginalis* cleaves sialic acid residues of mucus sialoglycoproteins with sialidase followed by capturing and degrading the released

Table 2 Host factors contributing to anatomical integrity and their interaction with microbiota

Component	Location/role	Microbiota interaction (beneficial vs harmful)	Key mechanisms/ mediators	Impact on integrity/ pregnancy	Reference(s)
Cervical mucus & cervical mucus plug (CMP)	Endocervix; gel barrier in pregnancy; gates ascending microbes; mucus architecture supports cervical closure	Beneficial: Lactobacillus-dominant cervicovaginal communities are associated with a more protective mucus barrier Harmful: BV-associated taxa (e.g., Gardnerella/Prevotella) produce sialidases/glycosidases that erode mucus glycans and reduce barrier function	Gel-forming mucins (e.g., MUC5B/MUC5AC); lactic acid–supported mucus organization; bacterial sialidases/mucinases; glycan foraging	Weakened mucus → easier ascent of microbes, heightened local inflammation, ↑ risk of intrauterine infection and downstream PTB/PPROM	[18, 19, 30, 56]
Epithelial tight junctions & mucosal barrier (vagina/cervix)	Vaginal/cervical epithelium; physical barrier limiting microbial translocation and dampening inflammation	Beneficial: Lactobacillus-derived lactic acid supports epithelial homeostasis and tight-junction integrity Harmful: Dysbiotic metabolites/inflammation loosen junctional integrity, increasing permeability	Tight-junction proteins (claudins/occludins); lactic acid; TLR-linked inflammatory signaling (IL-1β/IL-6/TNF-α)	Barrier disruption is associated with increased susceptibility to ascending infection, cervicovaginal inflammation, and membrane/placental interface stress	[54, 55, 57]
Antimicrobial peptides (AMPs) & innate antimicrobials	Secreted by vaginal/cervical epithelium and leukocytes; contribute to antimicrobial tone and immune calibration	Beneficial: Eubiosis supports AMP expression and pathogen control Harmful: Dysbiosis/inflammation associates with reduced protective factors (e.g., β-defensin-2 reported lower in PTB-linked profiles)	β-defensins; secretory leukocyte protease inhibitor (SLPI); lactoferrin; epithelial sensing of commensals	Reduced AMP activity → increased pathogen persistence, inflammatory amplification, and higher risk of adverse pregnancy outcomes	[20, 58, 59]
Innate immune surveillance (macrophages, neutrophils) & cytokine tone	Immune cells embedded in FRT mucosa; balance defense vs tolerance (sperm/embryo)	Beneficial: Lactobacillus-dominant states correlate with restrained immune activation (homeostasis) Harmful: Pathobionts/dysbiosis activate TLR pathways → excess cytokines/chemokines and tissue-damaging inflammation	TLR signaling; IL-1β, IL-6, TNF-α; chemokines (e.g., MIP-1β)	Excess inflammation compromises tissue integrity (cervix/membranes), facilitates microbial ascent, and contributes to PTB pathways	[20, 31]
Fetal membranes ECM (chorioamnion) & protease/MMP balance	Chorioamniotic membranes provide tensile strength and barrier around fetus; resist stretch and infection	Beneficial: Intact ECM resists biomechanical stress and microbial invasion Harmful: Ascending infection/dysbiosis drives collagenase/protease activity and inflammatory up-regulation of degradative pathways	Collagen-rich ECM; microbial collagenases/proteases (BV-linked); inflammation-driven degradative enzymes	ECM weakening → PROM/PPROM, chorioamnionitis risk, fetal exposure to microbes → neonatal morbidity/sepsis risk	[60, 61]

Table 2 summarizes key host structural and immunological factors that maintain female reproductive tract integrity. It highlights their anatomical roles, interactions with the microbiota (protective vs dysbiotic), underlying molecular mechanisms and implications for infection risk and adverse pregnancy outcomes

Evidence level: Evidence summarized in this table is based on a qualitative synthesis of mechanistic, observational, and translational studies. It therefore varies in strength across anatomical sites and pathways. Evidence is strongest for cervicovaginal barrier dysfunction, microbiota-associated inflammation and links to preterm birth and PPROM. Evidence for upper reproductive tract and low-biomass microbial environments remains more limited

Abbreviations: AMP antimicrobial peptide, *BV* bacterial vaginosis, *CMP* cervical mucus plug, *ECM* extracellular matrix, *FRT* female reproductive tract, *MMP* matrix metalloproteinase, *PROM* premature rupture of membranes, *PPROM* preterm premature rupture of membranes, *PTB* preterm birth, *TLR* Toll-like receptor

monosaccharide. They therefore contribute to mucosal sialic acid depletion and pathogenic erosion of the mucus barrier in BV. Lithgow et al. [18] published evidence of collagenase activity by the microbes in the vagina of preterm labour in which collagen rich structures like cervix and chorioamniotic membranes are proposed as biomechanical barriers. These barriers can be broken by the proteolytic activity of microbes. This is consistent with a plausible pathway by which BV-linked protease and collagenase activity could contribute to ECM remodeling and membrane weakening aligning clinically with PROM/PPROM and infection susceptibility.

Original research has demonstrated that women who have untreated bacterial vaginosis (BV) or a disturbed vaginal flora can be sub fertile [64]. BV-associated organisms are also capable of providing a hostile environment to sperm by increasing vaginal pH and releasing enzymes that destroy sperm or the cervical mucus [56]. Augmented sialidase enzyme action evident in BV as earlier mentioned are capable of breaking down the mucus glycoproteins [60]. This degeneration not only compromises a protective mucus shield but may also slow down sperm motility since spermatozoa depend on their ability to navigate healthy mucus. Increased vaginal sialidase activity in early pregnancy has been associated with an increased risk of spontaneous and early preterm birth in BV positive women. Recent clinical validation studies continue to highlight this association noting that high sialidase levels in early gestation are predictive of early spontaneous preterm birth and late miscarriage [67]. This finding supports the notion that high sialidase is not merely a BV characteristic but rather a risk stratifying factor of pregnancy loss. Agarwal and Lewis [68] have reviewed evidence that BV-associated taxa (particularly Gardnerella) use sialidases to liberate sialic acids from cervicovaginal mucus sialoglycans which helps sialoglycan foraging and mucus glycan depletion. They also discuss how this enzymatic erosion of mucus may restructure the local environment in a pattern that is consistent with impaired barrier function and altered host-microbe interactions. In summary, a high level of vaginal sialidase during pregnancy in the early years indicates the increased risk of miscarriage or early birth of an infant. Although the fertilization process has taken place, the embryo might have less chance of surviving in this environment.

Upstream disruptors of the cervicovaginal microbiome in infertility: STIs and PCOS

In a microbiota-pregnancy-outcomes model, STIs are also examples of upstream disturbances, which can cause a shift in the cervicovaginal microbial ecosystem. *C. trachomatis* and *N. gonorrhoeae* may ascend the genital tract, causing PID via upper tract and endometrial involvement and long-term consequences such as tubal damage and infertility [19].

Emerging evidence suggests that systemic infertility-associated endocrine conditions including polycystic ovary syndrome (PCOS) may be accompanied by alterations in the cervicovaginal microbiome [69, 70]. This relationship should be interpreted as potentially bidirectional rather than strictly one-way. On one hand, the hormonal and metabolic features of PCOS may alter the vaginal microenvironment through changes in estrogen signaling, glycogen availability, epithelial maturation, immune tone and local nutrient conditions, thereby favoring reduced Lactobacillus abundance and enrichment of taxa such as Mycoplasma, Prevotella and Streptococcus [69, 70]. On the other hand, microbiota-related metabolic and inflammatory pathways may influence endocrine signaling, including follicle-stimulating hormone (FSH)-related pathways, although current evidence remains mainly associative and should not be interpreted as proof of direct causation [71]. Therefore, reproductive tract dysbiosis may accompany and potentially exacerbate infertility-related endocrine disorders, while endocrine dysfunction itself may also predispose to microbial imbalance.

Endometrial microbiota and implantation

The endometrium is a very important location in defining a pregnancy when implantation of the embryo occurs. Even in case of conception the embryo should implant itself into a receptive endometrial lining. Some recent research has narrowed on the endometrial microbiome to determine the role it plays in implantation success or failure. In one of the studies, the investigators discovered that women with > 90% Lactobacillus DNA in their endometrial fluid had much higher rates of implantation and live birth following IVF, than women whose endometrium was colonized by non-Lactobacillus microbes. The latter group reported higher rates of implantation failure and miscarriage [72, 73]. Therefore, these findings suggest that a pathogen-depleted Lactobacillus-enriched endometrial environment favors embryo attachment and maternal–fetal immune tolerance.

In line with this, one of the studies found that endometrial dysbiosis is linked to impaired implantation of the embryo, which is probably mediated by inflammatory mechanisms [74]. An endometrium harboring *Gardnerella vaginalis* or *Escherichia coli* may initiate a local innate immune response through Toll-like receptors that renders the uterine lining unreceptive [14]. Endometrial dysbiosis is associated with a pro-inflammatory milieu (elevated IL-1β, IL-6, TNF-α) that is antagonistic to implantation [14]. Similarly, in our included sources, Fasoulakis et al. [14] also posit that endometrial epithelial integrity may be disrupted by pathogenic microbes

and contribute to inflammation thus reducing endometrial receptivity. It is particularly interesting to note that chronic endometritis has been identified in a high percentage of women who experience recurring implantation failure (RIF) or recurring pregnancy loss. When these women are given antibiotics to clear the infection, some of them have a better fertility outcome, which is indicative of causation.

Implantation outcomes may also be reflected or influenced by cervical microbiota. Recent studies have characterized the cervical microbiome of IVF patients. They discovered that a dysfunctional cervical microbiota (such as Streptococcus, Staphylococcus or Gardnerella rather than lactobacilli) could be used to predict reduced success in pregnancy [14, 75, 76]. Wu et al. suggested an embryo implantation failure predictive model depending on cervical bacterial genera presence that performed well in high-risk patient identification [77]. This highlights the fact that the cervical environment which is more readily sampled than the endometrium may be used as a proxy of upper tract microbial health in infertility workups.

Non-invasive markers of endometrial microbiome status in ART

Since collection of an endometrial sample involves an invasive biopsy or aspirate, other researchers have sought alternative that are less invasive. Menstrual blood and vaginal swabs are under investigation as peep holes into the uterine environment. Menstrual blood in particular was demonstrated to be associated with microbial DNA that signals endometrial microbiome health and can be utilized to estimate health in the endometria [78, 79]. This points out that menstrual effluent could potentially be used as a non-invasive biomarker of endometrial receptivity that could provide microbiological and immunological data.

Mechanisms underlying microbiota-driven hostility to fertility

In mechanistic support of inflammation and barrier mediated infertility, Zhang et al. [80] developed patient derived endometrial epithelial gland organoids and demonstrated that *E. coli* infection produces a robust pro-inflammatory response, with critical rises in TNF-a, IL-8 and IFN-g following infection. They also discuss an LPS-TLR4/NF-kB axis driving cytokines (e.g. IL-1, IL-6, TNF-a) that may shape implant. In addition to this, Weckel et al. [81] utilized an ex vivo human decidua (maternal–fetal interface) infection model and established that Group A Streptococcus (*S. pyogenes*) invades tissues rapidly and kills approximately half of the host cells in 2 h and at the same time blocks the host innate immune response. Through competitive interference, an endometrial bacterial biofilm may hinder embryo adhesion by occupying epithelial surface area and affecting local receptivity [82]. Consistent with the bidirectional model, emerging evidence suggests that reproductive tract and gut–genital microbiota may interact with endocrine signaling through microbial metabolites, inflammatory mediators, and modulation of local hormone receptor activity [83]. However, these associations remain context-dependent, and the current evidence does not yet establish whether microbiota changes are a cause, consequence, or amplifier of altered reproductive hormone signaling. This bidirectional hormone–microbiome interaction is also relevant in pregnancy, where endocrine changes are among the major drivers of cervicovaginal microbial stability. In a normal pregnancy, the vaginal microbiome tends to stabilize and even become more dominated by Lactobacillus than before pregnancy. It has been suggested that the increased estrogen and glycogen pools in vaginal epithelial cells during pregnancy nourish Lactobacilli making them dominant [84]. This leads to reduced diversity microbiome dominated by *Lactobacillus crispatus* and other related species in many women as pregnancy advances which is thought to be beneficial. However, not all women experience this protective shift [85]. A longitudinal study mentioned in a 2025 systematic review by Ferrante et al. concluded that there was indeed a significant change between the first and second trimesters: *L. crispatus, L. gasseri*, and *L. jensenii* populations either decreased or increased [85]. *L. iners* was found to be a moderately ambiguous Lactobacillus. It is commonly found in transitional conditions and is not so evidently protective as *L. crispatus*. With the increase of *L. iners,* there was a relative increase of Gardnerella, Ureaplasma, and Mycoplasma in women who gave birth to preterm babies [85]. This implies that changes in microbiota in early pregnancy may be predictive. Women who fail to sustain a *L. crispatus* dominant low diversity vaginal microbiome seem susceptible to complications. The proposed mechanistic pathways linking cervicovaginal dysbiosis to preterm birth are shown in Fig. 3.

Spontaneous preterm birth (sPTB)

Preterm birth (birth before 37 weeks) is associated with one of the highest rates of neonatal morbidity and mortality. The contribution of the vaginal microbiome to sPTB has been highly researched. Studies revealed that women with a low-Lactobacillus vaginal microbiome (similar to CST-IV, high diversity) during pregnancy are at a much greater risk of preterm delivery compared to women with high-Lactobacillus communities [86, 87]. *Gardnerella*, *Atopobium*, or *Sneathia* are associated with increased rates of PTB. It was also observed that women with recurrent PTB tended to harbor microbiota dominated by *L. iners* early in pregnancy [88]. Ferrante et al. also observed that the existence of Ureaplasma, Mycoplasma, and

Gardnerella during pregnancy is linked to the high-rate of PTBs [85]. These bacteria are able to climb up beyond a compromised cervix or penetrate microlesions. They are hard to identify in normal practice since they often do not result in obvious symptoms until the inflammation they precipitate leads to labour. Premature Rupture of Membranes (PROM) and its earlier variant PPROM (Preterm Premature Rupture of Membranes) are closely related to subclinical infection. A common observation when membranes rupture without labour is that amniotic fluid culture or sequencing reveals the presence of bacteria. In the study by Yang et al., the particular focus was on PPROM cases that resulted in neonatal sepsis. They also discovered that PPROM and neonatal sepsis were closely linked to pathogenic microbiomes in the vagina [89].The diversity of vaginal microbiota was significantly greater in PPROM patients than in the controls and *Gardnerella vaginalis* and *Streptococcus gallolyticus* were found in both the vaginal secretions and the placental tissues of PPROM cases. This clearly points to an upwards infection resulting in membrane rupture and fetal infection. It underscores how a breach in anatomical integrity can be both caused by and a conduit for vaginal microbes.

Microbial factors are also a suspected cause in first trimester losses. Some studies have associated the presence of BV or aerobic Vaginitis with an increased risk of miscarriage. To illustrate this, women undergoing IVF who had a normal microbiota had a lower rate of early pregnancy loss than women with abnormal endometrial microbiome (low Lactobacillus, presence of

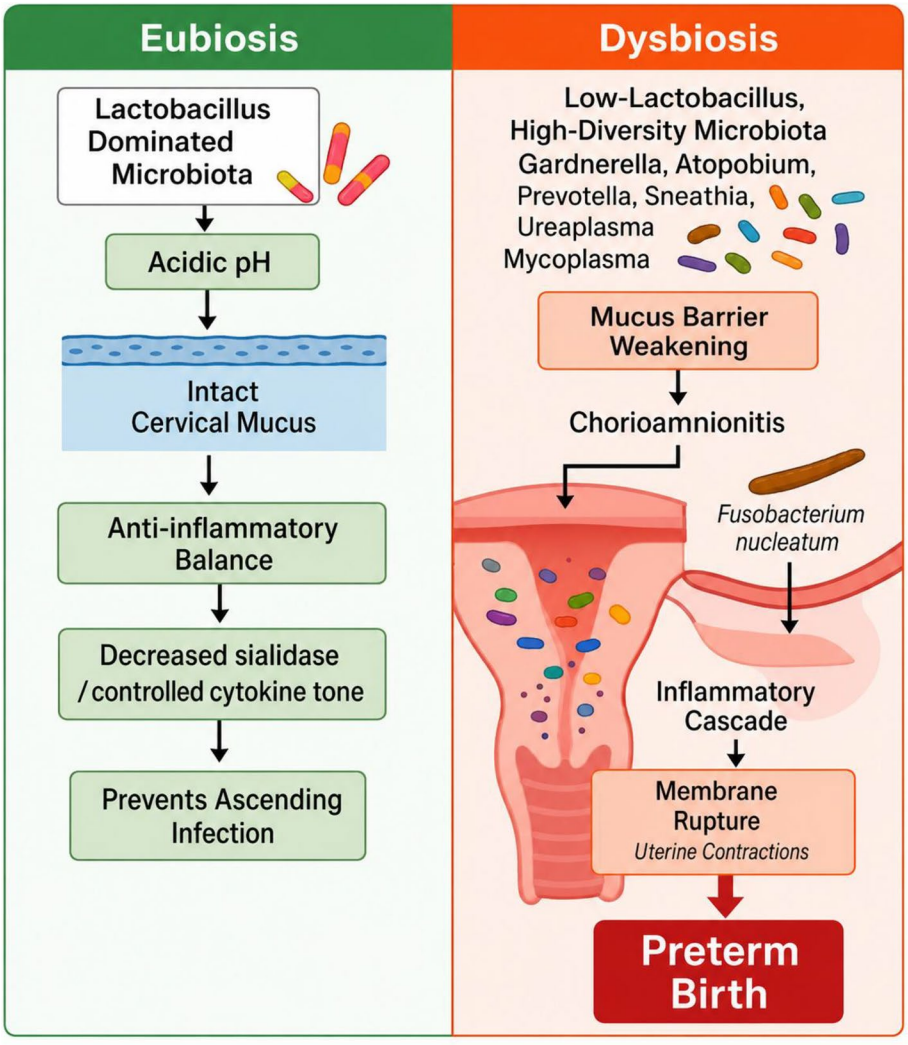


Fig. 3 Conceptual pathways linking cervicovaginal eubiosis and dysbiosis to preterm birth. Figure 3 is a conceptual pathway linking cervicovaginal eubiosis and dysbiosis to preterm birth Lactobacillus-dominant eubiosis is associated with acidic pH, preserved cervical mucus integrity and immune homeostasis. Dysbiosis is associated with barrier weakening, inflammation, ascending infection and pathways that may contribute to membrane rupture, uterine contractions, and preterm birth. This figure is schematic and intended for conceptual illustration only, not quantitative comparison. Figure generated using ChatGPT (OpenAI, DALL·E) and edited by the authors for scientific accuracy and clarity

Streptococcus or *E. coli*) [14]. In addition, the role of chronic endometritis is being increasingly acknowledged in recurrent pregnancy loss. Some studies have found that antibiotic treatment of chronic endometritis can increase the subsequent rates of pregnancy success [90].

Other pregnancy complications

Researchers are examining relationships of microbiota with other conditions in pregnancy:

Preeclampsia: Although the association between the vaginal microbiome and preeclampsia is less obvious, some studies have reported differences in the gut microbiome of women who develop preeclampsia [91]. It has been postulated that a factor when considering systemic inflammation may be gut dysbiosis.

Gestational Diabetes Mellitus (GDM): Surprisingly, an altered microbiota of the vagina has been reported in GDM. It was observed in one study that some Lactobacillus strains (such as *L. lucteri, L. amylovorus*) had been linked to cases of GDM and that *L. iners* was reduced in GDM [52]. Perhaps the microbiome is changed by metabolic changes in diabetes (e.g. increased glucose in vaginal fluids).

Neonatal microbiome development and early-life interventions

In addition to infections, the maternal microbiota affects the development of the neonatal microbiome which has long-term health consequences. Some studies reported that the vaginal microbiota of the mother bore minimal similarity with the meconium microbiota of the baby and that although mothers were Lactobacillus-dominant, the first stool of the baby did not necessarily include Lactobacillus [20, 21]. Others claim that the main source of colonization of the neonatal gut comes through maternal gut bacteria reaching the baby either by translocation into amniotic fluid during pregnancy or by exposure to feces during delivery [22]. In a vaginal delivery, the infant is exposed to the vaginal and fecal microbes of the mother which settle on the skin, eyes, mouth, and gut of the infant. This priming inoculation is essential in the development of the microbiome in the newborn [23]. Therefore, the baby microbiome is likely a pool of the microbiome of a mother in all its locations -gut, vagina, skin and breast.

Bogaert et al. [24] profiled six maternal body sites and four infant body sites during the first 30 days of life. They found that mother-to-infant microbial transfer occurs and that on average, 58.5 per cent of infant microbiota composition could be compartmentalized to maternal source communities. They observed that in C-section born babies, the reduced seeding of the infant microbiota by maternal microbes may be partially replaced by alternative pathways. Similarly, Dube-Zinatelli et al. [25] in their review highlight that the impacts of maternal microbes on the development of immune systems in the earliest phases of life provide critical sources of microbial and immune training in the earliest phases of development. This has subsequent effects on baby wellbeing. Infants born by Cesarean section (C-section) avoiding the vaginal canal have been found to develop microbiome differently and to be slightly more susceptible to a number of conditions including allergies and asthma [26]. C-section newborns do not receive such an early Lactobacillus and Bifidobacterium of the mother but rather receive more of a skin bacterium or hospital and environmental bacterium as their initial colonizers. Some of these differences even out over time, especially with breastfeeding, but early life differences in microbiota have been correlated with immune differences [61, 92]

One of the studies of maternal microbiota and neonatal immunity showed that Cesarean section is associated with 1.5- to twofold increased odds of childhood allergy, purportedly due to varying degrees of exposure to microbes [93]. As a result, there is interest in interventions such as vaginal seeding (swabbing C-section infants with vaginal fluids of the mother) to determine whether it can to some extent re-establish some of the microbial benefits. Mueller et al. [94] observed that vaginal seeding of C-section infants partially colonized the baby with maternal vaginal and gut microbes resulting in a microbiome that was more similar to vaginally delivered babies. Safety is being debated especially if the mother's vaginal microbiome is not optimal. But it underscores how important maternal vaginal flora is for initial colonization. Potential maternal–neonatal microbiota transmission routes are depicted in Fig. 4.

Therapeutic and preventative interventions

Antibiotic therapies

In recent translational research, antibiotics have been shown to be helpful where they eliminate a specific intrauterine inflammatory situation but less predictable where they are used to establish long-term vaginal eubiosis following BV therapy. This encourages interest in post antibiotic restoration programs. Liu et al. [95] reported that women with chronic endometritis (CE) who were cured had more ongoing pregnancy/live birth and clinical pregnancy rates but more prospective studies are required to establish the reproductive effects. Conversely, in their BV recurrence review, Vodstrcil et al. [96] highlighted that first-line antimicrobials (metronidazole or clindamycin) are usually adequate (70–85%). They noted that although the BV-associated bacteria are expected to be cured within one month, over half of women do recur within six months. The authors believe that multimodal personalized interventions will probably be required. Expanding this concept of restoration, Armstrong et al. [97]

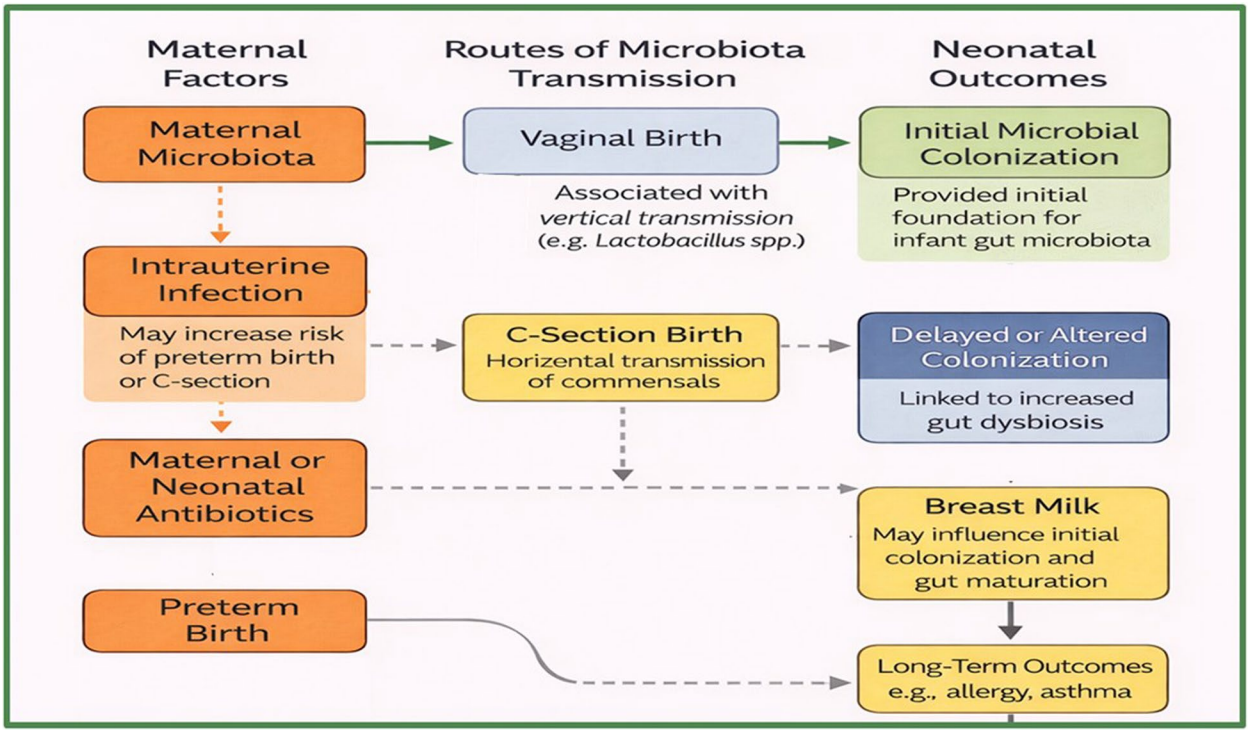


Fig. 4 Maternal neonatal microbiota transmission pathways. Figure 4 is a schematic representation of vertical and perinatal microbial transmission routes from the maternal reproductive tract to the neonate including intrauterine, intrapartum, and postnatal exposures that shape early-life microbial colonization. Figure generated using ChatGPT (OpenAI, DALL·E) and edited by the authors for scientific accuracy and clarity

reported that *L. crispatus* CTV-05 live biotherapeutic LACTIN-V decreased BV recurrence and vaginal inflammation following treatment with BV. They noted that colonization phenotypes were linked to baseline vaginal diversity and markers of epithelial disruption. This supports the idea that post antibiotic outcomes depend on ecological context and that microbiome directed therapies may require stratified and targeted implementation. Since systemic antibiotics may occasionally backfire by destroying Lactobacilli and allowing resistant bacteria or fungi to proliferate, focused interventions are preferred to avoid collateral damage to the microbiome.

Oral probiotics

This may have an indirect effect on vaginal flora through gut-vaginal axis. In expectant mothers receiving Lacticaseibacillus rhamnosus GR-1 and Limosilactobacillus reuteri RC-14, the vaginal microbiota improved and the postpartum rates of BV and candidiasis were minimized. Some fertility clinics recommend that women consume probiotics prior to IVF [98–101].

Vaginal microbiota transplant (VMT)

Based on the use of fecal transplants to treat *Clostridioides difficile* infection, researchers have suggested transplanting a whole vaginal community to a patient with unresponsive dysbiosis. A human VMT pilot reported that women with intractable recurrent BV achieved durable Lactobacillus-dominant vaginal communities and symptom resolution following VMT from screened healthy donors [102]. Grewal et al. address vaginal microbiota transplant as a future perspective of repopulation of a healthy microbiome in women who fail to respond to other treatment options [103]. This could potentially be a game changer in cases of recurrent BV or even before IVF to retain a good microbiota.

Lifestyle and adjunct interventions

Microbiota may also be affected by some lifestyle changes. One such example is the avoidance of behaviors that interfere with vaginal pH (e.g., douching or washing with rough detergent) to preserve Lactobacilli. Diet may also be a factor; a low-glycemic, fiber rich diet may promote a desirable gut flora which may then affect vaginal flora through immune regulation or co-metabolism. In one of such studies, it was determined that high-fat, low-fiber diets were associated with persistent GBS colonization and a modified vaginal microbiota structure [104]. In another study, the incidence of BV was lower in women who increased their dairy and fruit consumption [105], though it is difficult to attribute causality.

Immunomodulators

Since inflammation is part of the problem of dysbiosis, it has been proposed that anti-inflammatory drugs may be used to safeguard pregnancy despite the microbes not being completely eliminated. Indicatively, progesterone supplementation trials in women with a history of PTB have demonstrated lower rates of PTB [106]. In addition to the associations discussed above, a hypothetical link has also been proposed between disturbances in the maternal uterine microbiota and postpartum hemorrhage. Uterine dysbiosis has been proposed as a factor that could disrupt local inflammatory balance and postpartum uterine homeostasis, thereby potentially contributing to hemorrhagic complications [107].

Implementation challenges and safety considerations for pregnancy microbiome interventions

The use of pregnancy microbiome interventions is constrained by (i) absence of rapid, low-cost point-of-care diagnostics (ii) Need for very early detection (iii) stringent maternal–fetal safety in requirements of probiotics and VMT and (iv) increasing resistance to antibiotics.

Limitations

This review has limitations. First, the literature was judged to be diverse in study design, population, site of sampling, technology used for sequencing, and definition of clinical outcome, making it difficult to comprehensively compare studies. Second, many microbiome studies are observational and causality is hard to establish. Third, low-biomass niches, including the endometrium, placenta, and amniotic fluid, are highly susceptible to contamination, batch variability, and overinterpretation of microbial DNA. Fourth, antibiotic use, hormonal, sexual, and obstetric risk factors were poorly reported and could have confounding effects.

Conclusion and future prospects

A large body of research conducted in recent years has strongly associated female reproductive tract microbiota to reproductive success. Microbial communities in the vagina, cervix, and uterus actively communicate with the body of the mother modulating inflammation, tissue integrity, and the environment within which conception and gestation are taking place. Microbiota homeostasis is needed to maintain fertility and healthy pregnancy.

Microbiome-informed assessment of unexplained infertility or IVF failure is an emerging research direction, but its routine clinical use will require standardized sampling, prospective validation, and outcome-linked diagnostic thresholds. In the same way we maximize hormonal concentrations and uterine anatomy, we could potentially maximize the microbial environment of embryos.

In obstetrics we anticipate more prenatal care with stratification of patients by microbiome status. People who have had a history of PTB or are known to have BV (high risk) may receive increased scrutiny or prophylaxis to avoid future relapse. Non-invasive microbiome-based tests, including vaginal swab sequencing and metabolite profiling, are promising investigational tools, but their predictive value and clinical utility require further prospective validation.

In the case of neonatal health, and with growing interest in the developmental origins of health and pathology, the optimization of the maternal–fetal transfer of microbes is a promising direction. This includes enabling vaginal birth where safe, promoting breastfeeding, and potentially supplementing infants who have missed out on maternal microbes (e.g. C-section babies) in ways that are safe.

Research Gaps: More longitudinal research is required to prove causality. There is need to establish if there are particular keystone species that can be added or removed to radically alter the results. In addition, most research has been on bacteria but the reproductive tract also contains a virome and a mycobiome.

There is need to integrate microbiome informed diagnostics and targeted modulation into reproductive care pathways with rigorous evidence, safety oversight and equitable access. The potential beneficial impact of this microbiome-based solution is that the future of obstetric and neonatal practice can transform radically and become more prophylactic and precise. Therefore future studies should prioritize prospective cohorts and randomized controlled trials, particularly in underrepresented populations to strengthen causal inference and clinical applicability.

This review demonstrates an important shift in the paradigm of reproductive medicine and the need to include microbiome as a key determinant of fertility, pregnancy, and neonatal outcomes.

Abbreviations

ACOG	American College of Obstetricians and Gynecologists
AMP	Antimicrobial peptide
AMPs	Antimicrobial peptides
ART	Assisted reproductive technology/techniques
BPD	Bronchopulmonary dysplasia
CST	Community state type
CDC	Centers for Disease Control and Prevention
CST-I	Community state type I (Lactobacillus crispatus–dominant)
CST-IV	Community state type IV (low-Lactobacillus, anaerobe-dominant)
DNA	Deoxyribonucleic acid
ECM	Extracellular matrix
FSH	Follicle-stimulating hormone
GDM	Gestational diabetes mellitus
GBS	Group B Streptococcus (Streptococcus agalactiae)
HIV	Human immunodeficiency virus
HPV	Human Papillomavirus
IL-1	Interleukin-1
IL-6	Interleukin-6
IVF	In vitro fertilization
MIP-1β	Macrophage inflammatory protein-1β

NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
PID	Pelvic inflammatory disease
PCOS	Polycystic ovary syndrome
PROM	Premature rupture of membranes
PPROM	Preterm premature rupture of membranes
PTB	Preterm birth
RCT	Randomized controlled trial
RIF	Recurrent implantation failure
SNP	Single-nucleotide polymorphism
STI	Sexually transmitted infection
TNF	Tumor necrosis factor
USPSTF	U.S. Preventive Services Task Force
UTI	Urinary tract infection
VMT	Vaginal microbiota transplantation

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Authors' contributions
The study was conceptualized and designed by A.C.N. who wrote the manuscript and revised it for intellectual content. U.O.P.C. conducted the literature review, contributed to data analysis, and provided critical revisions. S.D.T. carried out data extraction and helped in the drafting of the manuscript. O.M.B. contributed in data extraction and critical feedback. R.M. was involved in editing the manuscripts. A.E.G. helped in structuring the manuscripts, giving comments on the general content and helped in revision. All authors read and approved the final manuscript.

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Consent for publication
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References

1. Liptáková A, Čurová K, Záhumenský J, Visnyaiová K, Varga I (2022) Microbiota of female genital tract - functional overview of microbial flora from vagina to uterine tubes and placenta. Physiol Res 71:S21. https://doi.org/10.33549/physiolres.934960
2. Aquino CI, Nicosia A, Ligori A, Volpicelli AI, Surico D (2024) Microbiota Status and Endometrial Cancer: A Narrative Review About Possible Correlations in Affected Versus Healthy Patients. https://doi.org/10.3390/sci6040075
3. Gholiof M, Adamson-De Luca E, Wessels JM (2022) The female reproductive tract microbiotas, inflammation, and gynecological conditions. Front Reprod Health 4:963752. https://doi.org/10.3389/frph.2022.963752
4. Ughade PA, Shrivastava D, Chaudhari K (2024) Navigating the Microbial Landscape: Understanding Dysbiosis in Human Genital Tracts and Its Impact on Fertility. Cureus 16(8). https://doi.org/10.7759/cureus.67040
5. Li H, Han M, Xu J, Li N, Cui H (2024) The vaginal microbial signatures of preterm birth woman. BMC Pregnancy Childbirth 24(1):1–12. https://doi.org/10.1186/s12884-024-06573-1
6. Gao H et al (2024) Deciphering the role of female reproductive tract microbiome in reproductive health: a review. Front Cell Infect Microbiol 14:1351540. https://doi.org/10.3389/fcimb.2024.1351540
7. Feng J, Wu Q, Liang Y, Liang Y, Bin Q (2025) Epidemiological characteristics of infertility, 1990-2021, and 15-year forecasts: an analysis based on the global burden of disease study 2021. Reprod Health 22(1):1–17. https://doi.org/10.1186/s12978-025-01966-7
8. World Health Organization (2023) 1 in 6 people globally affected by infertility. Geneva: World Health Organization. Available from:https://www.who.int/news/item/04-04-2023-1-in-6-people-globally-affected-byinfertility. Cited 2025 Jan 10
9. Chen X, Lu Y, Chen T, Li R (2021) The female vaginal microbiome in health and bacterial vaginosis. Front Cell Infect Microbiol 11:631972. https://doi.org/10.3389/fcimb.2021.631972
10. Ottinger S, Robertson CM, Branthoover H, Patras KA (2024) The human vaginal microbiota: from clinical medicine to models to mechanisms. Curr Opin Microbiol 77. https://doi.org/10.1016/j.mib.2023.102422
11. Juliana NCA, Peters RPH, Al-Nasiry S, Budding AE, Morré SA, Ambrosino E (2021) Composition of the vaginal microbiota during pregnancy in women living in sub-Saharan Africa: a PRISMA-compliant review. BMC Pregnancy Childbirth 21(1):1–15. https://doi.org/10.1186/s12884-021-04072-1
12. Zhai Q et al (2025) Characterization of vaginal microbiota across female reproductive phases. Front Microbiol 16:1599965. https://doi.org/10.3389/fmicb.2025.1599965
13. Vaneechoutte M (2017) The human vaginal microbial community. Res Microbiol 168(9–10):811–825. https://doi.org/10.1016/j.resmic.2017.08.001
14. Fasoulakis Z et al (2025) Impact of the female genital microbiota on outcomes of assisted reproductive techniques. Biomedicine 13(6):1332. https://doi.org/10.3390/biomedicines13061332
15. Pendharkar S, Skafte-Holm A, Simsek G, Haahr T (2023) Lactobacilli and their probiotic effects in the vagina of reproductive age women. Microorganisms 11(3):636. https://doi.org/10.3390/microorganisms11030636
16. Nori SRC et al (2025) Strain-level variation among vaginal Lactobacillus crispatus and Lactobacillus iners as identified by comparative metagenomics. NPJ Biofilms Microbiomes 11(1). https://doi.org/10.1038/s41522-025-00682-1
17. Avitabile E, Menotti L, Croatti V, Giordani B, Parolin C, Vitali B (2024) Protective mechanisms of vaginal lactobacilli against sexually transmitted viral infections. Int J Mol Sci 25(17):9168. https://doi.org/10.3390/ijms25179168
18. Johana Karin SMO, Carmen VDR (2022) Impact of bacterial vaginosis on the reproductive outcomes of IVF: meta-analysis. Obstet Gynecol Int J 13(4):191–202. https://doi.org/10.15406/ogij.2022.13.00649
19. Darville T (2021) Pelvic inflammatory disease due to *Neisseria gonorrhoeae* and *Chlamydia trachomatis*: immune evasion mechanisms and pathogenic disease pathways. J Infect Dis 224(Supplement_2):S39–S46. https://doi.org/10.1093/infdis/jiab031
20. Silveira RC, Ting JY (2024) Maternal-fetal-neonatal microbiome and outcomes associated with prematurity. BMC Pediatr 24(1):1–3. https://doi.org/10.1186/s12887-024-04536-1
21. Dobbler P, Mai V, Procianoy RS, Silveira RC, Corso AL, Roesch LFW (2019) The vaginal microbial communities of healthy expectant Brazilian mothers and its correlation with the newborn's gut colonization. World J Microbiol Biotechnol 35(10):159. https://doi.org/10.1007/s11274-019-2737-3
22. Flores Ventura E, Esteban-Torres M, Gueimonde M, Van Sinderen D, Koren O, Hallnpj LJ (2025) Mother-to-infant vertical transmission in early life: a systematic review and proportional meta-analysis of *Bifidobacterium* strain transmissibility. Biofilms Microbiomes 11(1):121. https://doi.org/10.1038/s41522-025-00720-y
23. Mesa MD (2020) The evolving microbiome from pregnancy to early infancy: a comprehensive review. Nutr 12:133. https://doi.org/10.3390/nu12010133

24. Bogaert D, Van Beveren GJ, De Koff EM, Parga PL, Lopez CEB, Koppensteiner L, Clerc M (2023) Mother-to-infant microbiota transmission and infant microbiota development across multiple body sites. Cell Host Microbe 31(3):447–460. https://doi.org/10.1016/j.chom.2023.01.018
25. Dubé-Zinatelli E, Mayotte E, Cappelletti L, Ismail N (2025) Impact of the maternal microbiome on neonatal immune development. J Reprod. https://doi.org/10.1016/j.jri.2025.104542
26. Liu X, Zhou J, Chen J, Li L, Yuan L, Li S, Sun X, Zhoue X (2024) Risk of asthma and allergies in children delivered by cesarean section: A comprehensive systematic review. J Allergy Clin Immunol Pract 12(10):2764–2773. https://doi.org/10.1016/j.jaip.2024.06.022
27. Xu H et al (2025) Vaginal colonization of lactobacilli: mechanism and function. Microb Pathog 198:107141. https://doi.org/10.1016/j.micpath.2024.107141
28. Shen J, Sun H, Chu J, Gong X, Liu X (2024) Cervicovaginal microbiota: a promising direction for prevention and treatment in cervical cancer. Infect Agent Cancer 19(1):13. https://doi.org/10.1186/s13027-024-00573-8
29. Elias M et al (2005) The presence of Mycoplasma hominis and Ureaplasma urealyticum in the cervical canal of uterus. Ginekol Pol 76(1):28–32. Available: https://europepmc.org/article/med/15846863. Accessed: Apr. 02, 2026
30. Rumyantseva T, Khayrullina G, Guschin A, Donders G (2019) Prevalence of *Ureaplasma* spp. and *Mycoplasma hominis* in healthy women and patients with flora alterations. Diagn Microbiol Infect Dis 93(3):227–231. https://doi.org/10.1016/j.diagmicrobio.2018.10.001
31. Lacroix G, Gouyer V, Gottrand F, Desseyn JL (2020) The cervicovaginal mucus barrier. Int J Mol Sci 21(21):8266. https://doi.org/10.3390/ijms21218266
32. De Tomasi JB, Opata MM, Mowa CN (2019) Immunity in the cervix: interphase between immune and cervical epithelial cells. J Immunol Res 2019(1):7693183. https://doi.org/10.1155/2019/7693183
33. Banchi P, Colitti B, Opsomer G, Rota A, Van Soom A (2023) The dogma of the sterile uterus revisited: does microbial seeding occur during fetal life in humans and animals? Reproduction 167(1):e230078. https://doi.org/10.1530/rep-23-0078
34. Toson B, Simon C, Moreno I (2022) The endometrial microbiome and its impact on human conception. Int J Mol Sci 23(1):485. https://doi.org/10.3390/ijms23010485
35. Moreno I et al (2022) Endometrial microbiota composition is associated with reproductive outcome in infertile patients. Microbiome 10(1):1–17. https://doi.org/10.1186/s40168-021-01184-w
36. Kaluanga Bwanga P et al (2023) The endometrial microbiota: challenges and prospects. Medicina 59(9):1540. https://doi.org/10.3390/medicina59091540
37. Al-Nasiry S et al (2020) The interplay between reproductive tract microbiota and immunological system in human reproduction. Front Immunol 11:378. https://doi.org/10.3389/fimmu.2020.00378
38. Gao X, Louwers YV, Laven JSE, Schoenmakers S (2024) Clinical relevance of vaginal and endometrial microbiome investigation in women with repeated implantation failure and recurrent pregnancy loss. Int J Mol Sci 25(1):622. https://doi.org/10.3390/ijms25010622
39. Chen L, Ke Y, Guo H, Wu B, Liu L (2025) The relationship between vaginal and endometrial microbiota and the outcome of frozen-thawed embryo transfer during hormone replacement cycles. BMC Microbiol 25(1):494. https://doi.org/10.1186/s12866-025-04167-1
40. Panzer JJ et al (2023) Is there a placental microbiota? A critical review and re-analysis of published placental microbiota datasets. BMC Microbiol 23(1). https://doi.org/10.1186/s12866-023-02764-6
41. Kennedy KM et al (2023) Questioning the fetal microbiome illustrates pitfalls of low-biomass microbial studies. Nature 613:639–649. https://doi.org/10.1038/s41586-022-05546-8
42. Sterpu I et al (2021) No evidence for a placental microbiome in human pregnancies at term. Am J Obstet Gynecol 224(3):296.e1-296.e23. https://doi.org/10.1016/j.ajog.2020.08.103
43. Ruiz-Triviño J, Álvarez D, Cadavid J ÁP, Alvarez AM (2023) From gut to placenta: understanding how the maternal microbiome models life-long conditions. Front Endocrinol 14:1304727. https://doi.org/10.3389/fendo.2023.1304727
44. J. R. Fowler and L. V. Simon, "Chorioamnionitis," Chorioamnionitis, pp. 1–156, Sep. 2023. https://doi.org/10.31260/repertmedcir.v22.n4.2013.752
45. Jain VG, Willis KA, Jobe A, Ambalavanan N (2021) Chorioamnionitis and neonatal outcomes. Pediatr Res 91(2):289. https://doi.org/10.1038/s41390-021-01633-0
46. Jung E et al (2023) Clinical chorioamnionitis at term: definition, pathogenesis, microbiology, diagnosis, and treatment. Am J Obstet Gynecol 230(3 Suppl):S807. https://doi.org/10.1016/j.ajog.2023.02.002
47. Dodson B, Suner T, Haar ELV, Han YW (2025) Oral microbiome and adverse pregnancy outcomes. Am J Reprod Immunol 93(6):e70107. https://doi.org/10.1111/aji.70107
48. Delgado-Diaz DJ et al (2022) Lactic acid from vaginal microbiota enhances cervicovaginal epithelial barrier integrity by promoting tight junction protein expression. Microbiome 10(1):141. https://doi.org/10.1186/s40168-022-01337-5
49. Schwecht I, Nazli A, Gill B, Kaushic C (2023) Lactic acid enhances vaginal epithelial barrier integrity and ameliorates inflammatory effects of dysbiotic short chain fatty acids and HIV-1. Sci Rep 13(1). https://doi.org/10.1038/s41598-023-47172-y
50. Dong M, Dong Y, Bai J, Li H, Ma X, Li B, Wang C, Li H, Qi W, Wang Y, Fan A, Han C, Xue F (2023) Interactions between microbiota and cervical epithelial, immune, and mucus barrier. Front Cell Infect Microbiol 13. https://doi.org/10.3389/fcimb.2023.1124591
51. Miko E, Barakonyi A (2023) The role of hydrogen-peroxide (H_2O_2) produced by vaginal microbiota in female reproductive health. Antioxidants Basel 12(5):1055. https://doi.org/10.3390/antiox12051055
52. Vinitha G, Balakrishnan J, Nagarajan P, Kannan S (2025) Reconnoitering the Association of Vaginal Microbiota Composition in the Female Reproductive Tract with Health and Disease. Open Microbiol J 19(1). https://doi.org/10.2174/0118742858375414250428060224
53. Zhu M et al (2024) Vaginal *Lactobacillus* fatty acid response mechanisms reveal a metabolite-targeted strategy for bacterial vaginosis treatment. Cell 187(19):5413-5430.e29. https://doi.org/10.1016/j.cell.2024.07.029
54. Webber CA, Glick VJ, Simmons LE, Martin MC, Ahmad M, Kim CH (2024) Vaginal *Lactobacilli* produce anti-inflammatory β-carboline compounds. Cell Host Microbe 32(11):1897–1909. https://doi.org/10.1016/j.chom.2024.09.014
55. Cheng Q, Lv S, Yin N, Wang J (2025) Microbial regulators of physiological and reproductive health in women of reproductive age: their local, proximal and distal regulatory roles. npj Biofilms Microbiomes 11(1):207. https://doi.org/10.1038/s41522-025-00839-y
56. Vieira-Baptista P, Bornstein J (2019) Candidiasis, Bacterial Vaginosis, Trichomoniasis and Other Vaginal Conditions Affecting the Vulva. Vulvar Dis Break Myth 167–205. https://doi.org/10.1007/978-3-319-61621-6_24
57. Amabebe E, Anumba DOC (2018) The vaginal microenvironment: the physiologic role of *Lactobacilli*. Front Med 5(JUN):389042. https://doi.org/10.3389/fmed.2018.00181
58. Moreno I et al (2016) Evidence that the endometrial microbiota has an effect on implantation success or failure. Am J Obstet Gynecol 215(6):684–703. https://doi.org/10.1016/j.ajog.2016.09.075
59. Keburiya LK et al (2022) Does the uterine microbiota affect the reproductive outcomes in women with recurrent implantation failures? BMC Womens Health 22(1):1–10. https://doi.org/10.1186/s12905-022-01750-w
60. Chen L, Li J, Xiao B (2024) The role of sialidases in the pathogenesis of bacterial vaginosis and their use as a promising pharmacological target in bacterial vaginosis. Front Cell Infect Microbiol 14:1367233. https://doi.org/10.3389/fcimb.2024.1367233
61. Gensollen T, Iyer SS, Kasper DL, Blumberg RS (2016) How colonization by microbiota in early life shapes the immune system. Science (80-) 352(6285):539–544. https://doi.org/10.1126/science.aad9378
62. Balakrishnan SN, Yamang H, Lorenz MC, Chew SY, Than LTL (2022) Role of vaginal mucosa, host immunity and microbiota in vulvovaginal candidiasis. Pathogens 11(6):618. https://doi.org/10.3390/pathogens11060618
63. Subramanyam PNB, Yeddula SGR (2024) Antimicrobial Peptides in Reproductive Health and Therapeutic Applications. Evol Antimicrob Pept From Self-Defense to Ther Appl 349–373. https://doi.org/10.1007/978-3-031-67515-7_13
64. Pelayo P et al (2024) *Prevotella* are major contributors of sialidases in the human vaginal microbiome. Proc Natl Acad Sci U S A 121(36):e2400341121. https://doi.org/10.1073/pnas.2400341121
65. Agarwal K et al (2023) Resident microbes shape the vaginal epithelial glycan landscape. Sci Transl Med 15(724). https://doi.org/10.1126/scitranslmed.abp9599
66. Lithgow K, Buchholz V, D'Aubeterre A, Sycuro L (2022) Collagenase activity of vaginal microbes associated with preterm labour. Am J Obstet Gynecol 226(2):302. https://doi.org/10.1016/j.ajog.2021.11.1299
67. Foessleitner P et al (2021) Screening pregnant women for bacterial vaginosis using a point-of-care test: A prospective validation study. J Clin Med 10(11). https://doi.org/10.3390/jcm10112275
68. Agarwal K, Lewis AL (2021) Vaginal sialoglycan foraging by *Gardnerella vaginalis*: mucus barriers as a meal for unwelcome guests? Glycobiology 31(6):667–680. https://doi.org/10.1093/glycob/cwab024
69. Zheng S et al (2023) Differential enrichment of bacteria and phages in the vaginal microbiomes in PCOS and obesity: shotgun sequencing analysis. Front Microbiomes 2. https://doi.org/10.3389/frmbi.2023.1229723

70. Chudzicka-Strugała I et al (2024) Bacterial vaginosis (BV) and vaginal microbiome disorders in women suffering from polycystic ovary syndrome (PCOS). Diagnostics 14(4):404. https://doi.org/10.3390/diagnostics14040404
71. He Y et al (2020) Lactic acid bacteria alleviate polycystic ovarian syndrome by regulating sex hormone related gut microbiota. Food Funct 11(6):5192–5204. https://doi.org/10.1039/c9fo02554e
72. Franasiak JM, Moreno I, Simon C (2018) Microbiome in embryonic implantation and implantation failure. Recurr. Implant. Fail. Etiol. Clin. Manag. pp 175–195. https://doi.org/10.1007/978-3-319-71967-2_11
73. Ruiz-Alonso M, Moreno I, Vilella F, Simon C (2023) Diagnosis of endometrial receptivity, embryo-endometrial dialogue, and endometrial microbiome. Textb. Assist. Reprod. Tech. Vol. 1 Lab. Perspect. sixth Ed., vol 1. pp 280–291. https://doi.org/10.1201/9781003268598-26
74. Kumar M et al (2025) Microbiome-maternal tract interactions in women with recurrent implantation failure. Microorganisms 13(4):844. https://doi.org/10.3390/microorganisms13040844
75. Li Y, Chen D, Feng YK, Li Q, Mao W, Yu P, Zhang Y (2025) A pilot study of cervicovaginal microbiome patterns associated with embryo implantation outcomes in endometriosis-associated infertility. Front Med 12:1642770. https://doi.org/10.3389/fmed.2025.1642770
76. Guan W, Dong S, Wang Z, Jiao J, Wang X (2023) Impact of a *Lactobacillus* dominant cervical microbiome, based on 16S-FAST profiling, on the reproductive outcomes of IVF patients. Front Cell Infect Microbiol 13:1059339. https://doi.org/10.3389/fcimb.2023.1059339
77. Wu Y, Shi L, Jin Z, Chen W, Wang F, Wu H, Li H, Zhang C, Zhu R (2025) A nomogram prediction model for embryo implantation outcomes based on the cervical microbiota of the infertile patients during IVF-FET. Microbiology Spectrum 13(4). https://doi.org/10.1128/spectrum.01462-24
78. Tindal K, Filby CE, Cousins FL, SJ (2024) The composition of menstrual fluid, its applications, and recent advances to understand the endometrial environment: a narrative review. F&S Rev 5(3):100075. https://doi.org/10.1016/j.xfnr.2024.100075
79. Jain M, Mladova E, Shichanina A, Kirillova K, Povarova A, Scherbakova L (2023) Microbiological and cytokine profiling of menstrual blood for the assessment of endometrial receptivity: a pilot study. Biomedicines 11(5):1284. https://doi.org/10.3390/biomedicines11051284
80. Zhang X, Zhang L, Li T, Zhang Z, Shang X, Bai H, Liu Y, Zo X, Shang C, Song D, Zhang X (2024) Investigating bacteria-induced inflammatory responses using novel endometrial epithelial gland organoid models. Front Reprod Heal 6. https://doi.org/10.3389/frph.2024.1490520
81. Wecke A, Guilbert IT, Lambert C, Plainvert C, Goffinet F, Poyart C, Méhats C, Fou A (2021) Streptococcus pyogenes infects human endometrium by limiting the innate immune response. J Clin Invest 131(4). https://doi.org/10.1172/jci130746
82. Stoyancheva G, Mihaylova N, Gerginova M, Krumova E (2025) Endometrial microbiome and reproductive receptivity: diverse perspectives. https://doi.org/10.3390/ijms262110796
83. Samama M, Ueno J, Carvalho de Arruda Veiga E, Piscopo RCCP, Ikeda. F (2025) Vaginal microbiome and its relationship with assisted reproduction: a systematic review and meta-analysis. Life Basel 15(9):1382. https://doi.org/10.3390/life15091382
84. Baud A, Hillion KH, Plainvert C, Tessier V, Tazi A, Mand L. Poyart C, Kennedy SP (2023) Microbial diversity in the vaginal microbiota and its link to pregnancy outcomes. Sci Rep 13(1). https://doi.org/10.1038/s41598-023-36126-z
85. Ferrante M, Oliveri Conti G, Pulvirenti E, Favara C, Fiore M, Cristaldi A (2025) The vaginal microbiota and preterm birth: A systematic review. Eur J Obstet Gynecol Reprod Biol 311. https://doi.org/10.1016/j.ejogrb.2025.114007
86. Gudnadottir U, Debelius JW, Du J, Hugerth LW, Danielsson H, Schuppe-Koistinen I (2022) The vaginal microbiome and the risk of preterm birth: a systematic review and network meta-analysis. Sci Rep 12(1):1–8. https://doi.org/10.1038/s41598-022-12007-9
87. Huang C, Gin C, Fettweis J, Foxman B, Gelaye B, MacIntyre DA, Subramaniam A, Frase W (2023) Meta-analysis reveals the vaginal microbiome is a better predictor of earlier than later preterm birth. BMC Biol 21(1):199. https://doi.org/10.1186/s12915-023-01702-2
88. Jiang X, Bao Y, Li X, Qu X, Mao X, Dong J, Wang L, Liu X, Zhang F, Ying H (2025) Characteristics of the vaginal microbiota associated with recurrent spontaneous preterm birth: a prospective cohort study. J Transl Med 23(1):1–13. https://doi.org/10.1186/s12967-025-06460-z
89. Yang Y, Liu Z, Chen X, Qin F, Zhou W (2023) Association between vaginal microbiomes and neonatal septicemia in pregnant women with preterm premature rupture of membranes based on metagenome sequencing. Am J Transl Res 15(7):4544–4557
90. Cicinelli E, Matteo M, Tinelli R, Lepera A, Alfonso R, Indraccolo U, Marrocchella S, Greco P (2015) Prevalence of chronic endometritis in repeated unexplained implantation failure and the IVF success rate after antibiotic therapy. Hum Reprod 30(2):323–330. https://doi.org/10.1093/humrep/deu292
91. Huang L, Cai M, Li L, Zhang X, Xu Y, Xiao J, Huang Q, Luo G, Zeng Z, Jin C, Jin Y (2021) Gut microbiota changes in preeclampsia, abnormal placental growth and healthy pregnant women. BMC Microbiol 21(1):1–9. https://doi.org/10.1186/s12866-021-02327-7
92. Gensollen T, Blumberg RS (2017) Correlation between early-life regulation of the immune system by microbiota and allergy development. J Allergy Clin Immunol 139(4):1084–1091. https://doi.org/10.1016/j.jaci.2017.02.011
93. Al Jehani AN, Shuaib M, Alsharif A, Alsubaie KA, Khraisat A, Alsharif A, Altaf M, Almasry RH (2025) Impact of maternal microbiota composition on neonatal immunity and early childhood allergies: a systematic review. Pediatr Rep 17(3):67. https://doi.org/10.3390/pediatric17030067
94. Mueller NT, Differding MK, Sun H, Wang J, Levy S, Deopujari V, Appel LJ, Blaser MJ (2023) Maternal bacterial engraftment in multiple body sites of cesarean section born neonates after vaginal seeding-a randomized controlled trial. MBio 14(3). https://doi.org/10.1128/mbio.00491-23
95. Liu J, Liu ZA, Liu Y, Cheng L, Yan L (2022) Impact of antibiotic treatment for chronic endometritis on pregnancy outcomes in women with reproductive failure: A systematic review and meta-analysis. Front Med. https://doi.org/10.3389/fmed.2022.980511
96. Vodstrcil LA, Muzny CA, Plummer EL, Sobel JD, Bradshaw CS (2021) Bacterial vaginosis: drivers of recurrence and challenges and opportunities in partner treatment. BMC Med 19(1). https://doi.org/10.1186/s12916-021-02077-3
97. Armstrong E, Hemmerling A, Miller S, Huibner S, Kulikova M, Crawford E, Castañeda GR (2024) Vaginal *Lactobacillus crispatus* persistence following application of a live biotherapeutic product: colonization phenotypes and genital immune impact. Microbiome 12(1). https://doi.org/10.1186/s40168-024-01828-7
98. Amabebe E, Anumba DOC (2020) Female gut and genital tract microbiota-induced crosstalk and differential effects of short-chain fatty acids on immune sequelae. Front Immunol 11:553047. https://doi.org/10.3389/fimmu.2020.02184
99. Yang S, Reid G, Challis JRG, Gloor GB, Asztalos E, Money D, Seney S, Bocking AD (2020) Effect of oral probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 on the vaginal microbiota, cytokines and chemokines in pregnant women. Nutr 12(2):368. https://doi.org/10.3390/nu12020368
100. Pérez-Castillo ÍM, Fernández-Castillo R, Lasserrot-Cuadrado A, Gallo-Vallejo JL, Rojas-Carvajal AM, Aguilar-Cordero MJ (2021) Reporting of perinatal outcomes in probiotic randomized controlled trials. A systematic review and meta-analysis. Nutr 13(1):256. https://doi.org/10.3390/nu13010256
101. Blancafort C, Llácer J (2023) Can probiotics enhance fertility outcome? Capacity of probiotics as a single intervention to improve the feminine genital tract microbiota in non-symptomatic reproductive-aged women. Front Endocrinol 13:1081830. https://doi.org/10.3389/fendo.2022.1081830
102. Lev-Sagie A, Goldman-Wohl D, Cohen Y, Dori-Bachash M, Leshem A, Mor U, Strahilevitz J (2019) Vaginal microbiome transplantation in women with intractable bacterial vaginosis. Nat Med 25(10):1500–1504. https://doi.org/10.1038/s41591-019-0600-6
103. Grewal K, MacIntyre DA, Bennett PR (2021) The reproductive tract microbiota in pregnancy. Biosci Rep 41(9). https://doi.org/10.1042/bsr20203908
104. Malloy E, Kates AE, Dixon J, Riley C, Safdar N, Hanson L (2024) Vaginal and rectal microbiome changes following administration of a multi-species antenatal probiotic: A randomized control trial. Gut Microbes Rep 1(1). https://doi.org/10.1080/29933935.2024.2334311
105. Noormohammadi M, Eslamian G, Kazemi SN, Rashidkhani B (2022) Association between dietary patterns and bacterial vaginosis: A case-control study. Sci Rep 12(1):1–9. https://doi.org/10.1038/s41598-022-16505-8
106. Nelson DB, Lafferty A, Venkatraman C (2022) Association of vaginal progesterone treatment with prevention of recurrent preterm birth. JAMA Netw Open 5(10). https://doi.org/10.1001/jamanetworkopen.2022.37600
107. Escobar MF, Hincapie MA, Barona JS (2020) Immunological role of the maternal uterine microbiota in postpartum hemorrhage. Front Immunol 11:504. https://doi.org/10.3389/fimmu.2020.00504

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