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The Effect of Microbes Isolated from The Female Reproductive Tract of Pregnant Women on Fetuses

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ABSTRACT

Objective: *This study explores the role of microorganisms isolated from the female reproductive tract during pregnancy and their potential impact on fetal development and pregnancy complications.* ***Method:*** *A descriptive, literature-based approach was employed to analyze microbial populations across various anatomical sites – vaginal, cervical, endometrial, tubal, and ovarian – focusing on their interactions with the maternal immune system and reproductive outcomes.* ***Results:*** *The findings reveal that microbial imbalance, particularly the reduction of Lactobacillus species, disrupts immune regulation and compromises epithelial integrity, leading to adverse outcomes such as premature labor, miscarriage, infections, and congenital abnormalities. Pathogens including Candida, Trichomonas, Cytomegalovirus, and Group B Streptococcus were identified as major contributors to these complications.* ***Novelty:*** *Unlike prior studies that often examine isolated reproductive sites, this research integrates microbiome data from both upper and lower reproductive tracts, offering a comprehensive view of organ-specific dysbiosis and its influence on maternal-fetal health. These insights suggest new directions for preventive strategies, targeted therapies, and the development of biomarkers aimed at restoring microbial equilibrium to safeguard pregnancy outcomes.*

INTRODUCTION

The balance and diversity of microorganisms during pregnancy play a vital role in the health of the mother and fetus, as they have a direct impact on regulating pregnancy hormones and inflammation, as well as immune responses and maintaining the integrity of the female reproductive system through their direct interaction with the body, any disruption in the work of these organisms causes several problems or various complications (such as infection, premature birth, and recurrent miscarriages),when a change occurs in the natural microbe, it leads to the growth of organisms that cause inflammation in the urinary tract and vaginal infections. Therefore, any disruption in the microbial balance may lead to premature birth or miscarriage by hindering the process of fetal development [1][2]. In the context of the widespread prevalence of various vaginal infections during pregnancy or its early stages, the need for new strategies to diagnose and treat these infections emerges to avoid any diseases that lead to the loss of the fetus at any stage of its development [3][4].

The female reproductive tract is one of the most important mucosal environments, colonized by diverse microbes that naturally interact with the host to form a delicate and complex relationship that can be termed an ecosystem [5][6]. Most research has shown

that the reproductive tract microbiome plays a fundamental role in this microenvironment, interacting precisely with anatomical structures and immune responses, and holding significant potential for maintaining maternal health [7][8]. One of the major influences on human physiological and pathological functions is the existence of natural, symbiotic relationships between organisms and their hosts throughout the healthy body, including the female reproductive system. Each part has its own microbe, representing 9% of the total bacteria in the female body, such as the ovaries, fallopian tubes, endometrium, cervix, and vagina [9][10]. These parts have their own microbiome[11] . Lactobacillus bacteria are responsible for vaginal health in women. The upper genital tract (UGT) contains a less dense but highly diverse bacterial population [12][13].

MATERIAL AND METHODS

The methodology of this study was based on an integrative and descriptive analysis of microbial populations within the female reproductive tract, aiming to understand their influence on fetal development and pregnancy outcomes. The researchers adopted a literature-based, cross-sectional approach supported by observational data on microbial communities isolated from various anatomical regions, including the vagina, cervix, endometrium, fallopian tubes, and ovaries. Through a combination of microbiological characterization and analysis of clinical case findings, the study systematically identified dominant microbial taxa particularly Lactobacillus species and contrasted their presence in healthy versus dysbiotic states. Sources of microbial dysbiosis were categorized into bacterial, fungal, viral, and parasitic agents, with emphasis on clinical correlations such as premature birth, miscarriage, and congenital abnormalities. Data interpretation involved comparative analysis between microbial profiles under normal and pathological conditions, examining shifts in immune responses, epithelial barrier integrity, and cytokine activity. In addition, findings from peer-reviewed studies were synthesized to evaluate microbial-host interactions and their implications for maternal and fetal immune regulation. The method integrated tables and figures to illustrate differences in microbial composition and immune activation across reproductive tract compartments. By aligning microbial patterns with clinical indicators, the methodology not only enabled the identification of pathogenic mechanisms but also informed the development of preventive and therapeutic strategies. The approach relied on secondary data from microbiome research, immunological assays, and infection outcomes, enabling the formulation of hypotheses about microbiota-driven complications in pregnancy. This comprehensive methodology served as the basis for linking microbial dysbiosis to specific reproductive and fetal health risks.

RESULT AND DISCUSSION

Result

Pregnancy

Pregnancy occurs inside a woman's uterus, either with one fetus or multiple fetuses, as in the case of twins. Pregnancy can occur as a result of several processes, which may occur naturally after vaginal intercourse or through assisted reproductive techniques [14].

Components of the Female Reproductive System

The female reproductive system consists of two parts: the lower and the upper. The lower system includes the vulva and vagina (The birth canal), while the upper system consists of the ovaries (A pair of organs that produce eggs and female hormones such as estrogen), fallopian tubes, uterus (An internal organ where the fetus develops and develops before birth), and cervix (The round, thick end of the uterus, with an opening through which menstrual blood and the baby exit during birth) [15][16].

Vaginitis

When vaginitis occurs, the fetus is at risk of premature birth due to membrane rupture and microbial imbalance. It is one of the most important causes of congenital malformations caused by organisms present in the reproductive tract, such as chlamydia, mycoplasma, and ureaplasma. This can also lead to congenital malformations in fetuses or stillbirth [17].

Discussion

Symptoms of genital tract infections:

Vaginal itching, burning, pain, or irritation. Internal itching or irritation. Pain during intercourse. Pain during urination [18].

Causes of miscarriage

During pregnancy, many physiological changes occur. Pregnancy is a complex process that requires many changes to contain and nourish the fetus with essential nutrients such as fatty acids, amino acids, vitamins, and minerals. The female reproductive tract (FGT) is also exposed to numerous sexually and non-sexually transmitted diseases, which can lead to infections [19][20].

1. Bacterial cause

One of the most common bacteria found in the female reproductive tract Group B streptococcus (GBS), can cause infections in newborns, such as meningitis and pneumonia. Therefore, the mother should be given antibiotics before delivery to prevent transmission (Table 1).

Table 1. Shows the parts of the female reproductive system and some of the microbes that can infect it.

1-lower reproductive tract	**1**_Vaginal microbiome	The vagina is considered the entrance to the female reproductive tract and contains the highest bacterial biomass. Lactobacillus is found in a higher relative abundance (over 89%), while	(Chen et al., 2017; Ravel et al., 2011; Integrative,

		the presence of Staphylococcus, Synthetia, Veillonella, Streptococcus, Prevotella, and others remains controversial.	2019; Santella et al., 2022).
	2_Cervical microbiome	It was previously believed that the cervical microbiome was the same as the vaginal microbiome; however, recent studies have confirmed differences between the two phyla . Firmicutes was found to be the most abundant phylum among the cervical microbiome, and Lactobacillus was the dominant genus within this phylum . L. crispatus in the cervix was found to produce lactic acid and antimicrobial compounds, thus preventing many infections and acting as a shield against many diseases. Bacteroidetes is the second most abundant phylum, with Prevotella bacteria being the dominant .	(Chen et al., 2017). (Onywera et al., 2019a; Onywera et al., 2019b). genus (Keburiya et al., 2022).
2-upper reproductive tract	**1**_Endometrial microbiome	Some studies have shown that Acinetobacter, Lactobacillus, Methylobacterium, Sphingobium, and Streptococcus dominate the endometrium. Several previous studies have also revealed that Lactobacillus is dominant in the endometrial microbiome (Lactobacillus >90%, other bacteria <10%), and that clinical pregnancy rates and live birth rates (i.e., reproductive success) are higher. However, a decrease in these bacteria (Lactobacillus <90%, other bacteria >10%) leads to microbial imbalance, which increases pregnancy complications, such as preterm birth, recurrent miscarriage, recurrent implantation failure, and biochemical pregnancies .Currently, the presence of an endometrial microbiome is considered a positive predictor of	(Chen B. et al., 2021). (Moreno et al., 2016). (Bonzon-Jimenez and Labarta, 2021).

	reproductive success, which may provide new insights and research directions for the prevention and treatment of pregnancy complications.	
2_Tubal microbiome	The entire reproductive tract of women who had undergone total hysterectomy was studied and the results showed the presence of Shigella bacteria in the fallopian tubes	(Walther-Antonio et al., 2016).
3_Ovarian microbiome	Many studies have described the gut microbiome as rare in healthy individuals but found in malignant diseases	(Miles et al., 2017; Zhou et al., 2019; Banerjee et al., 2017).

The female reproductive system consists of organs that are continuously and sequentially involved in the birth of new life and are predisposed to resist many diseases that cause prenatal miscarriage ,Figure (1) illustrates the most important interactions between the microbiome and the female reproductive system in both normal and pathological conditions [21][22]. The Lactobacillus microbiome and its main metabolites, especially lactic acid, create a healthy environment for the female reproductive system, enhancing the integrity of the epithelial barriers and mucosal membranes. It also stabilizes local immune defenses, creating an efficient immunological environment [23][24].

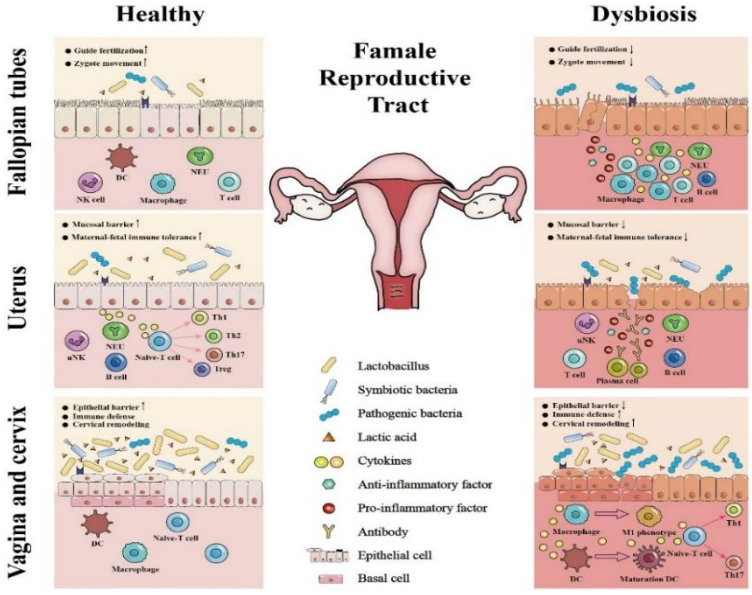

Figure 1. The figure shows the reproductive system in a state of health and dysbiosis.

The table 2 compares the vaginal and cervical microenvironment in healthy and dysbiotic states. In health, *Lactobacillus* dominance, intact epithelial barriers, and anti-inflammatory responses maintain immune balance. In contrast, dysbiosis features increased pathogenic bacteria, disrupted barriers, elevated pro-inflammatory cytokines, and macrophage-mediated inflammatory responses, compromising reproductive tract immunity and function [25][26].

Table 2. Vagina and Cervix

No.	Healthy	Dysbiosis
1	Dominated by **Lactobacillus** (yellow rods).	Increase in **pathogenic bacteria** (pink and purple).
2	**Lactic acid** and **anti-inflammatory cytokines** are present.	Disrupted epithelial barrier.
3	Epithelial barrier is intact.	More **pro-inflammatory cytokines.**
4	Macrophages and T-cells maintain immune homeostasis.	Macrophages release **pro-inflammatory mediators.**

The table 3 highlights microbial and immunological differences between healthy and dysbiotic vaginal and cervical environments. Healthy states are marked by *Lactobacillus* dominance, intact epithelial barriers, and anti-inflammatory conditions. Dysbiosis involves increased pathogenic bacteria, epithelial disruption, elevated pro-inflammatory cytokines, and macrophage activation, contributing to compromised mucosal immunity and increased risk of reproductive complications [27][28].

Table 3. Uterus

No.	Healthy	Dysbiosis
1	Immune tolerance is maintained by anti-inflammatory cytokines and regulatory T-cells.	Immune tolerance is impaired.
2	Balanced microbiota supports a favorable environment for implantation and pregnancy.	Elevated inflammatory cytokines**.**
3		Increased recruitment of neutrophils (NE) and reduced regulatory T-cell activity.

The table 4 presents the impact of microbial balance in the fallopian tubes. A healthy state supports fertilization and early zygote movement through balanced microbiota and cytokines. In contrast, dysbiosis disrupts the fertilization environment, where inflammation and microbial imbalance hinder sperm-egg interaction or zygote transport, potentially impairing reproductive success [29][30].

Table 4. Fallopian Tubes

N.	**Healthy**	**Dysbiosis**
1	Support for **fertilization** and early **zygote movement**.	Disruption of fertilization environment.
2	Balanced microbiota and cytokines.	Inflammation and bacterial imbalance can interfere with **sperm-egg interaction** or **zygote transport.**

2. Fungal cause

Fungal diseases are considered one of the most important causes of clinical diseases [31]. Hippocrates and Galen identified the oldest types of infection, fungal infections, which can be chronic, superficial, or deep [32]. Vaginal infections caused by yeast-like fungi of the genus Candida are the main infection during pregnancy, Fungi were identified in the 19th century as infections of the reproductive system during pregnancy and newborns, and how they interact with each other [33][34].The infection can be transmitted to the fetus via ascending (from the vagina) or through the bloodstream in exceptional cases, even when the placenta and fetal membranes are protective against infection. They can cross the barrier without damaging the mucous membranes ,As a result of congenital candidiasis and Candida fungi invading the membranes, a serious infection occurs in newborns in the twenty-third week of pregnancy, leading to intrauterine infection with Candida fungi,This causes elevated levels of inflammation in the mother's blood (leukocytes, procalcitonin, C-reactive protein), which are also detected in the baby's blood after birth. Therefore, it is preferable to terminate the pregnancy early [35][36].

3. Parasitic cause

Trichomoniasis is a sexually transmitted parasitic infection that affects the reproductive system. During pregnancy, trichomoniasis may increase the risk of premature birth and low birth weight [37].

4. Viral Cause

Viral infections are among the most important factors that increase the risk of miscarriage, stillbirth, fetal brain injury, hearing loss, intrauterine growth retardation, cataracts, and other fetal abnormalities [38][39]. The placenta also acts as an immune shield to protect the fetus from pathogens during maternal viral infections. However, most viruses have evolved mechanisms to match the pathogenesis of the disease. In response to infection, the mother's immune system increases cytokine activation, which negatively affects the fetus. Cytomegalovirus (CMV) is one of the most important viral infections and the most common cause of birth defects in fetuses [40]. It is a viral infection that can infect the body at any age. Once infected, the virus remains in the body for life, and the disease often does not produce any signs or symptoms and is not detected until after diagnosis. However, its symptoms may appear in some patients, especially those with weakened immunity, as it is transmitted to cells through direct contact with the body fluids of an infected person, such as urine, sweat, blood, and semen. It may also be

transmitted from mother to child during pregnancy or breastfeeding. It is called cytomegalovirus because it enlarges the size of the infected cell, slowly replicating within it [41].

Maternal immune system

The effect of the microbiome on the fetal immune system and its development,The diversity of the maternal microbiome contributes to the development of the immune system through exposure to multiple antigens and may lead to the maturation of the immune system, especially microbes that help in the production of short-chain fatty acids (SCFAs), These acids have anti-inflammatory properties, which can reduce the risk of diseases in children [42].

The placenta and its role

The placenta was previously believed to be a completely sterile environment, but research has proven otherwise. It contains a unique community of organisms that directly influence the fetus, particularly its growth and the development of the maternal immune system. It also guides fertilization and promotes zygote transfer. However, any disruption of the microbial balance and the invasion of pathogenic bacteria negatively impact reproductive function through several factors, as shown in Table (5) ,it is important to highlight these interactions and the essential role of the microbiome in regulating physiological processes within the female reproductive tract, including fertilization, embryo implantation, fetal development, childbirth, and protection against infection.

The table 5 outlines key pathological effects of microbial imbalance in the female reproductive tract. Dysbiosis leads to reduced barrier integrity, heightened immune activation, premature cervical remodeling, impaired maternal-fetal immune tolerance, and decreased ciliary function. These disruptions collectively compromise reproductive health and increase the risk of adverse pregnancy outcomes.

Table 5. Factors Contributing to Microbial Dysbiosis-Induced Reproductive Complications

No.	Factors	Low/High
1	Damage to epithelial and mucosal barriers	↓ barrier integrity
2	Overstimulation of immune responses	↑ immune activation
3	Causing premature cervical remodeling	↑ cervical changes
4	Impairment of maternal and fetal immune tolerance	↓ tolerance
5	Causing edema, necrosis, and loss of fallopian tube cilia function	↓ ciliary function

Sexually Transmitted Diseases (STIs)

One of the direct causes of early miscarriage is sexually transmitted infections (STIs). Most research focuses on the fact that changes in the composition and stability of the reproductive tract microbiome may also predispose individuals to a greater risk of STIs. Immune responses, through microbial variations in the vagina, affect the integrity

of the mucosal barrier. Any changes in the vaginal microbiome can exacerbate pregnancy complications caused by STIs, even during pregnancy, which can exacerbate pregnancy complications.

Prevention and treatment

Vaginal infections during pregnancy are very common and can be prevented and treated if the causative agent is identified, which may be bacterial, fungal (such as a yeast infection), or parasitic (such as trichomoniasis), Topical treatments (such as metronidazole and clindamycin) can be used to prevent them through good personal hygiene, changing wet clothes, avoiding irritants, wearing cotton underwear, and practicing safe sex.

CONCLUSION

Fundamental Finding : This study establishes a strong link between maternal reproductive tract microbiota composition and fetal health, revealing that microbial dysbiosis—especially the depletion of beneficial *Lactobacillus* species—can disrupt immune regulation, weaken epithelial barriers, and elevate the risk of adverse outcomes such as miscarriage, preterm birth, and congenital infections. **Implication :** These findings underscore the clinical potential of microbiome monitoring and modulation as a preventative and therapeutic strategy in maternal-fetal medicine, offering new avenues for early diagnosis and personalized interventions to improve pregnancy outcomes. **Limitation :** However, the study is primarily based on secondary data and lacks empirical validation through direct clinical or experimental trials, limiting the generalizability of its conclusions. **Future Research :** Subsequent studies should focus on longitudinal, multi-omics analyses of maternal microbiomes, including mechanistic investigations of host-microbiota interactions, to better understand causal pathways and support the development of microbiome-targeted therapies in obstetric care.

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