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CHANGES IN MICROBIOME ASSOCIATED WITH PREGNANCY

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Abstract

When studying the role of the microbiota in pregnancy, it is crucial to consider the stage at which the essential interaction between the host and its microbes begins. The gut microbiota changes dramatically during pregnancy. The gut microbiota during pregnancy is influenced not only by internal cues, but also by environmental factors, primarily by diet.

The maternal microbiome has emerged as an important factor in gestational health and outcome and is associated with risk of preterm birth and fetuses morbidity. Microbial metabolites, e.g. short-chain fatty acids affect gut-brain signaling and the immune response. Pregnancy is shown to alter the maternal gut microbiota. Recent studies have suggested that changes to the microbiota during pregnancy may influence these pregnancy-associated metabolic changes.

The vaginal microbiome becomes dominated by Lactobacilli species during pregnancy. Bacterial infections during pregnancy can be caused by a single species of bacteria, by an imbalance in the microbiomes, or by gut dissemination of bacteria. In pregnancy dramatical changes of the maternal microbiota affects neonatal immune responses and maturation the design product.

Clinically, abnormal changes in the vaginal microbiome have been associated with preterm birth. It is, therefore, not surprising that there are also significant changes in the microbiome during pregnancy when there is an excess of weight with metabolic and immunological changes occur. We believe that the microbial alterations observed during pregnancy are vital for a healthy pregnancy.

In this review, I summarize the known changes in microbial composition throughout pregnancy in the gut, vagina, oral cavity and placenta.

Keywords:

pregnancy, microbiome, bacterial infections, probiotics

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The vaginal microbiome is critically important to a healthy pregnancy, and studies have shown that vaginal dysbiosis during pregnancy can lead to infection and preterm birth.

Hormonal changes during and after pregnancy are linked with modifications in the maternal microbiota. The vaginal microbiome becomes dominated by Lactobacilli species during pregnancy.

Healthy pregnancy is characterized by an increase in the bacterial load and profound alterations in the composition of gut microbiota.

In the first trimester of pregnancy, the gut microbial composition is similar to that of healthy, non-pregnant women. However, from the first to the third trimester of pregnancy, the gut microbiota composition changes dramatically. It has been suggested that progesterone and estrogen affect the microbiota during pregnancy.

In this review, I describe the pronounced microbial changes that occur in the pregnant female, thus offering an overview of the initial exposure of the fetus to microbiotafrom the placenta, through birth and infancy.

In this review, we describe the changes in the compositions of the gut, oral and vaginal microbiome that occur in connection with pregnancy. In this review, we describe the pronounced microbial changes that occur in the pregnant female. The meaning of modifications in the gut microbiota has been investigated.

The aim of the present study was to analyse the microbiota composition of pregnant women in the understanding of the role of the microbiota in the health status of pregnant woman.

In this review, changes in gut, oral and vaginal microbiome composition that occur in association with pregnancy are described.

The significance of changes in gut microbiota was investigated.

Gestation is a complex and continuously changing physiological process (1). Pregnancy is a remarkable biological process involving simultaneous changes in many physiological systems to support the development of healthy progeny. Important changes in the maternal gut microbiota have been observed during pregnancy (2).

Recent evidence suggests that microbial alterations seen during pregnancy may help maintain homeostasis and aid the required physiological changes occurring in pregnancy (3).

Evidence supports the hypothesis that maternal dysbiosis could act as a trigger for preterm birth (4).(Fig,1).

Resident endometrial microbiota has only been defined recently. However, questions remain regarding the main components of the endometrial microbiota and their impact on the reproductive tract concerning both fertility and pregnancy outcomes.

Periodontal infections that are transmitted to other locations can lead to premature birth, low birth weight, and preeclampsia so that virtually all pregnant women require periodontal care (5). (Fig,2).

The microbial changes during pregnancy are likely coordinated with the immune, endocrine, and metabolic states (6).

In the first trimester of pregnancy, the gut microbial composition is similar to that of healthy, non-pregnant women (7).

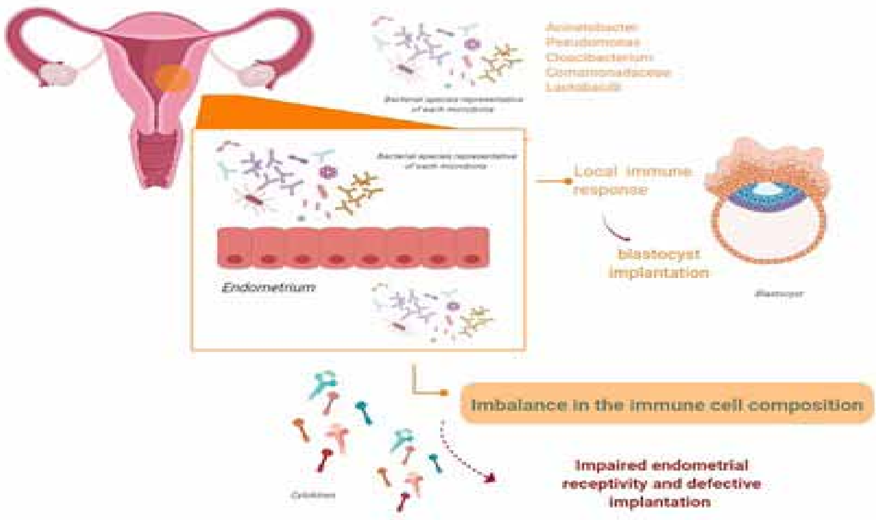

Fig. 1 The endometrial microbiota. The endometrium is not a sterile tissue (5).

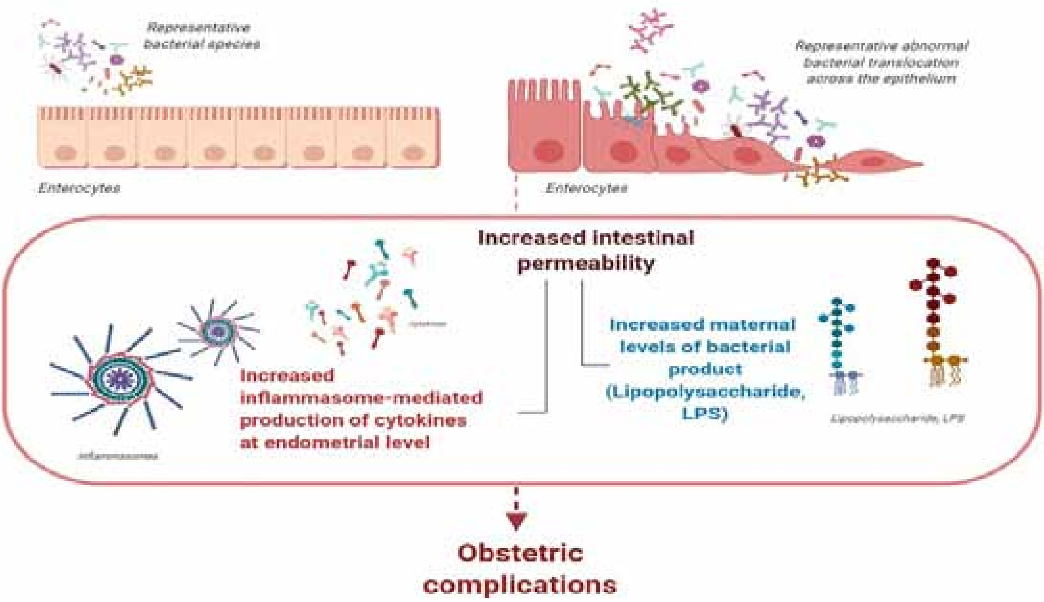

Fig. 2 During pregnancy, the gut microbiota undergoes profound changes (5)

However, from the first to the third trimester, the gut microbiota composition changes dramatically (8).

The dramatic changes in microbiome composition that take place during gestation have only recently been appreciated (9).

The gut microbiota in the first trimester of pregnancy resembles the microbiota of healthy nonpregnant women (10).

The maternal microbiome not only affects the success of a pregnancy, but may play an indispensable role in shaping the metabolism, behavior, and immunity of the offspring.

The gut microbiota during pregnancy is a critical determinant of offspring health (11).

Recent studies have suggested that changes to the microbiota during pregnancy may influence these pregnancy-associated metabolic changes.

Several studies support the hypothesis that changes in the gut microbiota during early pregnancy are associated with an increased risk of gestational diabetes and hypertension.

These changes are associated with an increase in maternal body weight and dietary changes (12).

During pregnancy, maternal fat deposition and food intake increase progressively.

In the second and third trimesters, maternal metabolic changes include increased gluconeogenesis, lipolysis, and insulin resistance.

Maternal dysbiosis during pregnancy has been associated with a number of pregnancy complications, including preeclampsia, preterm birth, and gestational diabetes.

Some other studies, however, found no consistent changes in the gut microbiome during pregnancy or postpartum (9,13).

Pregnancy history affects both the maternal gut microbiome during gestation and the infant gut microbiome postpartum (14).

The postpartum period is also characterized by significant changes in the microbiota, and it has been reported that at least 1 month after birth the mothers' microbiotas do not yet return to their baseline (15, 37) (Fig,3).

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The postpartum period is also associated with dramatic hormonal changes including a significant decrease in progesterone and estrogen levels. se various alterations may persist for as long as a year after delivery.

These various alterations may persist for as long as a year after delivery.

The changes that occur in the gut throughout pregnancy are complex and mediated by maternal factors, such as diet and antibiotic usage (16).

A better understanding of how changes of the maternal microbiome may underlie the vulnerability of pregnant women to metabolic syndromes and infections.

Studies have reported changes in the maternal microbiome in the gut, vagina, and oral cavity during pregnancy; it remains unclear whether/how these changes might be related

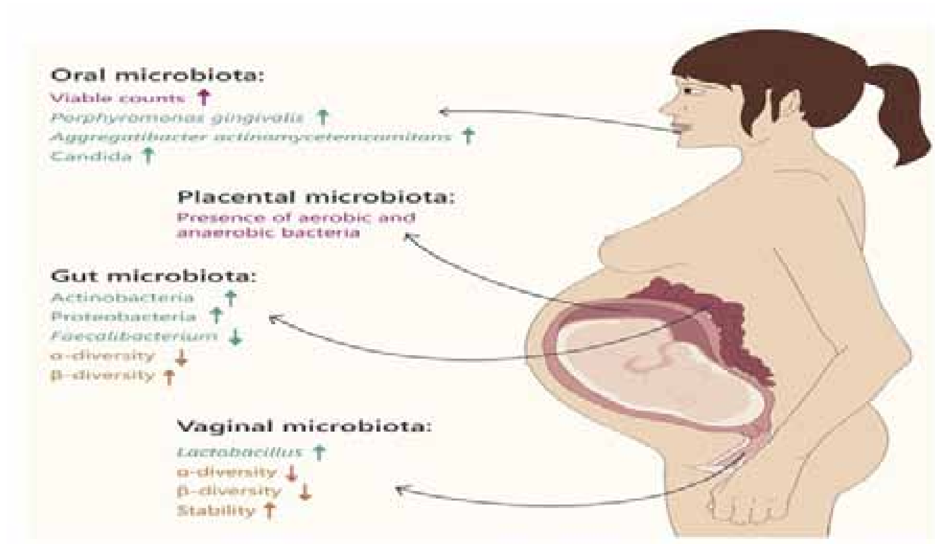

Fig. 3 Vaginal microbial composition influences inflammation and T cell abundance (10)

to maternal immune responses, metabolism, and susceptibility to infections during pregnancy.

Methods to analyze the bacterial communities include culturing methods, which are limited to only a subset of species easily culturable, and more commonly used next generation sequencing techniques including 16S rRNA gene surveys and metagenomics (17).

Dysbiosis of the gut microbiome during pregnancy is associated with gestational diabetes, preeclampsia and restricted fetal growth. The relationship between the immune system, gut microbiota, and metabolism of pregnant women is unclear (18), (Fig,4).

Microbial metabolites produced in the maternal gut can be detected in the placenta and fetal tissues, where they drive postnatal innate immune development (19).

During pregnancy, the gastrointestinal (gut) microbiota undergoes profound changes that lead to an increase in lactic acid-producing bacteria and a reduction in butyrate-producing bacteria.

We find that increased intestinal permeability in early pregnancy is associated with increased maternal levels of LPS, excessive inflammasome-mediated production of cytokines at the endometrial level, and last, increased risk of pregnancy loss (20).

Therefore, we suggest that, during early pregnancy, gut bacterial products from the intestinal lumen are translocated into the maternal circulation.

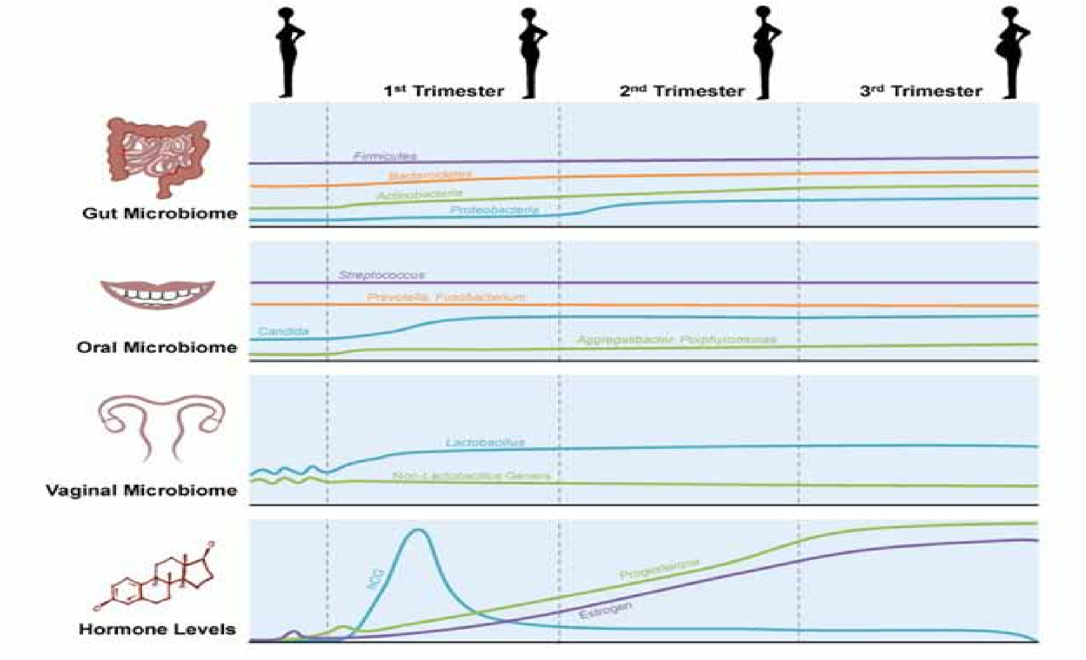

Fig. 4 General changes in the gut, oral, and vaginal microbiomes in parallel with the hormonal changes throughout pregnancy (18)

This is likely associated with increased intestinal permeability and may increase the risk of obstetric complications.

During the third trimester of pregnancy, butyrate-producing bacteria with anti-inflammatory activities decline, whereas bifidobacteria, proteobacteria, and lactic acid–producing bacteria increase (21).

Hormonal changes during and after pregnancy are linked with modifications in the maternal microbiota.

These changes include hormonal changes, weight gain, immune system modulation, and others, which must all be synchronized to preserve the health of both the mother and the offspring.

Hormonal changes during pregnancy instigate numerous physiological changes aimed at the growth and delivery of a healthy baby.

Hormonal and dietary changes during pregnancy underlie the changes in microbial richness and diversity.

During this period, levels of secreted hormones (especially progesterone and estrogens) rise dramatically, and there are major alterations in the immune response (22).

Estrogen and progesterone have previously been shown to perturb the gut microbiome.

The increase in circulating estrogen is thought to be important for Lactobacilli colonization, so it makes sense that the rapid decrease in estrogen decreases Lactobacilli abundance.

Progesterone can also directly influence the composition of the gut microbiome in pregnant women. The increase in circulating estrogen is thought to be important for Lactobacilli colonization.

And hormonal factors during pregnancy also drive changes in the composition of the intestinal microbiota, e.g. elevated levels of progesterone can lead to an increased abundance of Bifidobacterium in the gut (23).

It has been proposed that such bacterial composition improved the ability of the host to extract energy from the diet and to store this energy in the adipose tissue

The human vaginal microbiota is a key component in the defense system against microbial and viral infections, conferring protection against disease.

Although obesity is an important health issue during pregnancy, the relationships between the gut microbiota composition and obesity has been scarcely studied in pregnant women (24).

The human vaginal microbiota is a key component in the defense system against microbial and viral infections, conferring protection against disease.

The vaginal microbiome during pregnancy becomes more stably dominated by species of Lactobacillus, thereby decreasing in overall diversity (18, 25).

Romero and colleagues (26,30) also observed the dominance of Lactobacillus species during pregnancy, suggesting that the vaginal microbiome is relatively more stable during pregnancy than in the nonpregnant state.

Clinically, abnormal changes in the vaginal microbiota have been associated with preterm birth.

The Lactobacilli are thought to prevent pathogens from colonizing the vagina because they produce lactic acid which decreases the overall pH of the vagina, and they secrete antibacterial toxins (27).

The dominance of Lactobacillus species in the vaginal microbiome, and the resulting increase in acidity, might confer protection against urinary tract infections during pregnancy.

The Lactobacilli are thought to prevent pathogens from colonizing the vagina because they produce lactic acid which decreases the overall pH of the vagina, and they secrete antibacterial toxins.

These Lactobacilli are also important as they are normally the first to colonize the new infants' guts after they pass through the birth canal.

These vaginal microbial changes during pregnancy might be partly related to increased glycogen levels induced by estrogen (28).

The human vagina has its own microbiota, and changes in vaginal microbiota are related to several pregnancy-related complications.

The endometrium is not a sterile site. Resident endometrial microbiota has only been defined recently.

Vertical transmission of bacteria from mother to newborn contributes to developing the microbiota of the infant gastrointestinal (gut); emerging evidence suggests that this influence may begin in utero.

Vaginal dysbiosis, which is linked to inflammatory states, is associated with adverse obstetric outcomes.

In the presence of dysbiosis, the vaginal microbiota increases the levels of vaginal inflammatory cytokines, which, in turn, increases the risk of spontaneous preterm birth. The vaginal microbiome undergoes a shift in diversity during pregnancy (19,29), characterized by a decrease in diversity and richness in pregnant women.

Antibiotic use during pregnancy has been associated with the development of metabolic and allergic disorders later in childhood, including obesity and asthma infants.

The vaginal microbiome is critically important to a healthy pregnancy, and studies have shown that vaginal dysbiosis during pregnancy can lead to infection and preterm birth (30).

Bacterial vaginosis (BV) and uterine infections may also occur as a result of an imbalance of bacteria or by dissemination of bacteria into inappropriate regions. Bacterial vaginosis is an infection resulting from dysbiosis in the vaginal microbiome.

Bacterial vaginosis represents a dysbiosis of the vaginal microbiome that is associated with significant adverse healthcare outcomes, including increased risk of abnormal pregnancy outcomes. B V is associated with dramatic shifts in the vaginal microbiota, characterized by a change from Lactobacillis sp. dominance to dominance by a mixture of organisms including Gardnerella vaginalis, various anaerobic species, and the genital mycoplasmas (31).

Markers of bacterial vaginosis that are used by clinicians to diagnose bacterial vaginosis include the following: (1) vaginal secretions with a pH of >4.5, (2) a fishy odor that is best elicited by mixing vaginal secretions with a 10% potassium hydroxide solution, (3) ≥20% of microscopically observed vaginal epithelial cells coated with bacteria ("clue cells"), and (4) a white, skim milk-like vaginal discharge.

Women with bacterial vaginosis have an increased risk of preterm labor and delivery of babies that are small for gestational age (32).

More specifically, the microbiome in pregnant women contains a larger proportion of, in particular, Bifidobacterium, but also of Proteobacteria and Actinobacteria (33,37).

Early studies on the endometrial microbiota reported the dominance of Lactobacillus species.

Finally, endometrial bacterial composition was different from that of the vagina.

The role of the endometrial microbiota in female reproduction is not fully understood (38).

Prolonged postnatal empirical antibiotic use is associated with changes in preterm gut microbiome.

Antibiotic use during pregnancy has been associated with the development of metabolic and allergic disorders later in childhood, including obesity and asthma infants (39).

Recent studies have implicated a possible association between altered gut microbiome in children and increased risk of asthma and autism (40).

Bacterial infections during pregnancy can be caused by a single species of bacteria, by an imbalance in the microbiomes, or by gut dissemination of bacteria (41).

At the same time, it appears that following antibiotic treatment, supplementary probiotics can lower the vaginal pH to an optimal value hence promoting the restoration of vaginal microbiota, thereby preventing the reduction in levels of anti-inflammatory cytokines (42).

For example, changes in the endocrine system in response to maternal factors such as diet and usage of antibiotics influence the compositions of the gut and oral microbiome (43).

Women planning to have a family could be asked to consume specific nutrients, foods, and probiotics as well as making appropriate lifestyle changes (44).

Given the causal role for the microbiome in a wide range of human diseases, our data suggest that the microbiome merits further exploration as a possible contributing factor to parity-associated outcomes in maternal and infant health (45).

An appropriate microbiota is essential for healthy early development, pregnancy maintenance, and the first years of childhood.

Therefore, understanding the role of the microbiome throughout pregnancy and early development, as well as its role in health and disease, is of great importance for opening new research avenues, establishing developmental concepts, and perhaps even suggesting new therapeutic approaches (46).

Conclusion

A new study shows that pregnancy alters microbe populations in the gut. The gut microbiota during pregnancy is influenced not only by internal cues, but also by environmental factors, primarily by diet.

The gut microbiome plays a central role in the regulation of the immune system, metabolism, and resistance to infections.

The hormonal, immunological and metabolic changes that pregnant women undergo influence these compositions and vice-versa, appropriate adaptation is required to support optimal fetal growth and development.

Imbalances in the microbiota can lead to complications of pregnancy such gestational diabetes, preterm delivery and preeclampsia.

Manipulating microbiome composition during pregnancy through probiotics could result in improved maternal health and pregnancy outcomes.

Conflict of interest

The author declare no conflict of interest

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