



## MATERNAL MICROBIOME, PREGNANCY, AND ORAL HEALTH: A COMPREHENSIVE REVIEW OF BIDIRECTIONAL INTERACTIONS AND IMPLICATIONS FOR MATERNAL-FETAL OUTCOMES

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### ABSTRACT

Pregnancy induces profound immunological, hormonal, metabolic, and microbial alterations that influence oral health and systemic physiology. Increasing evidence indicates that maternal gut and oral microbiota serve as interconnected regulatory systems that influence pregnancy outcomes, fetal development, and long-term offspring health. This narrative review synthesizes evidence from recent studies (2021–2025) examining the influence of maternal microbiome changes on oral health, periodontal inflammation, gestational diseases, and fetal gut-brain axis (GBA) development. Pregnancy shifts gut microbiota toward reduced alpha diversity and increased inflammatory taxa, driven by progesterone-mediated gastrointestinal changes, enhanced metabolic demands, and immune modulation. Similarly, the oral microbiome exhibits increased abundance of anaerobic, pathogenic species linked to pregnancy gingivitis, periodontitis, and elevated systemic inflammatory markers. Dysbiosis in either system—oral or gut—has been shown to contribute to gestational diabetes, preeclampsia, preterm birth, maternal inflammation, altered placental signaling, and impaired fetal neurodevelopment. Emerging evidence also suggests microbial translocation from the maternal gut or oral cavity to the placenta and amniotic fluid, shaping early fetal immune priming and meconium colonization. Maternal diet, obesity, stress, infection, and medication use (antibiotics, antidepressants) are major drivers of dysbiosis with downstream consequences on the fetal HPA axis, neuroinflammation, and future metabolic risk. Given the high global burden of periodontal disease in pregnancy and its potential to worsen systemic inflammation, integrating oral healthcare into prenatal care may reduce adverse outcomes. Understanding the interconnected maternal microbiome systems may guide future preventive and therapeutic interventions.

### KEYWORDS :

#### INTRODUCTION

Pregnancy represents a unique physiological state characterized by dynamic endocrine, immunological, and metabolic transitions required to sustain fetal growth. These changes are accompanied by profound alterations in the maternal microbiome, particularly within the gut and oral cavity—two major microbial reservoirs with systemic influence. Traditionally, oral health and gut physiology were studied independently; however, contemporary research has shifted toward understanding their bidirectional influence on maternal-fetal outcomes.<sup>1</sup>

The maternal oral microbiome, comprising over 700 bacterial species, changes markedly during pregnancy. Elevated estrogen and progesterone enhance vascular permeability, increase gingival crevicular fluid (GCF), and promote colonization by *Prevotella*, *Porphyromonas*, *Fusobacterium*, and other periodontal pathogens. This predisposes pregnant women to gingivitis, periodontitis, and oral infections. Periodontal inflammation generates systemic inflammatory mediators—IL-6, CRP, TNF<sup>α</sup>—which can enter the maternal circulation, influencing placental vascular function, metabolic homeostasis, and fetal immune priming. Studies have consistently associated periodontal disease with adverse outcomes such as preterm birth, low birth weight, preeclampsia, and gestational diabetes.<sup>2</sup>

Simultaneously, the maternal gut microbiota undergoes trimester-specific reorganization characterized by reduced diversity, enrichment of Actinobacteria and Proteobacteria, and a decline in butyrate-producing bacteria such as *Faecalibacterium*. These shifts contribute to physiologic insulin resistance, enhanced energy storage, and metabolic flexibility essential for fetal development. However, aberrant gut dysbiosis—often driven by maternal obesity, high-fat diets, stress, infection, or antibiotic exposure—can result in

systemic inflammation, increased intestinal permeability, and altered metabolite profiles, including short-chain fatty acids (SCFAs). These changes impair placental signaling, disrupt fetal neurodevelopment, and alter offspring gut-brain axis maturation.<sup>3</sup>

Importantly, the gut-oral axis plays a central role in pregnancy health. Oral pathogens have been identified in placental tissues, amniotic fluid, and meconium, indicating hematogenous translocation during pregnancy. Similarly, gut microbial metabolites cross the placenta, influencing fetal brain development, immune maturation, and hormonal regulation. This suggests that early microbial exposures—maternal or translocated—shape long-term neonatal outcomes.<sup>4</sup>

Given the rising interest in prenatal microbiome science, this narrative review synthesizes findings from recent peer-reviewed articles (2021–2025) to explain:

1. Pregnancy-associated changes in gut and oral microbiota
2. Mechanisms linking dysbiosis to oral disease and systemic inflammation
3. How maternal microbes influence fetal development
4. Factors that exacerbate dysbiosis
5. Implications for oral healthcare in prenatal medicine

#### 1. Pregnancy-Induced Changes in the Maternal Gut Microbiome

Pregnancy triggers profound physiological adjustments in the gastrointestinal system, largely mediated by hormonal and metabolic changes that reshape the maternal gut microbiome to meet the growing fetus's nutritional and developmental needs. Early in gestation, rising levels of human chorionic gonadotropin and progesterone slow gastrointestinal transit, increasing the duration of nutrient-microbe interaction. This extended transit time enhances nutrient extraction and

supports the expansion of microbial groups that efficiently harvest additional energy from the maternal diet. As pregnancy advances, the gut microbiome undergoes characteristic trimester-specific transitions. During the second trimester, overall microbial richness tends to decline, with a shift toward greater abundance of Actinobacteria and a reduction in beneficial genera such as *Bifidobacterium* and *Faecalibacterium*. By the third trimester, a more striking rise in inflammation-associated Proteobacteria emerges along with increased beta diversity and higher proportions of Firmicutes, changes that promote energy storage. Although these adaptations support fetal growth, the resulting microbial profile closely resembles that seen in metabolic dysfunction and may increase maternal inflammation and insulin resistance.<sup>5</sup>

Along with these compositional changes, the functional output of the maternal gut microbiota undergoes important modifications. Gut bacteria produce critical metabolites—short-chain fatty acids, folate, vitamins, amino acids, and neurotransmitter precursors—that readily cross the placenta and influence fetal metabolic pathways, neural development, and immune maturation. A reduction in butyrate-producing bacteria lowers anti-inflammatory signaling, while elevated acetate levels enhance placental growth but may alter immune programming in the fetus. When these adaptive changes shift toward imbalance, maternal gut dysbiosis can occur. This state is characterized by an overrepresentation of pathogenic taxa and a depletion of beneficial commensals and has been associated with gestational diabetes, hypertensive disorders of pregnancy, preterm birth, excessive gestational weight gain, and altered immune development in the fetus. Obesity during pregnancy further amplifies dysbiosis through an increased Firmicutes-to-Bacteroidetes ratio, greater intestinal permeability, and disrupted placental nutrient transfer.<sup>6</sup>

Together, these observations underscore the central role of the maternal gut microbiome as a dynamic, regulatory system that supports maternal adaptation, guides fetal development, and influences pregnancy outcomes.

## 2. Changes In The Maternal Oral Microbiome During Pregnancy

The oral microbiome also undergoes marked transformation during pregnancy, driven largely by fluctuations in estrogen and progesterone that influence vascularity, saliva composition, and immune responsiveness. These hormonal changes create an environment that favors the proliferation of certain periodontal organisms while altering the balance between protective and pathogenic species. Increased levels of sex hormones provide growth substrates for several anaerobic bacteria, encouraging their expansion and enhancing their virulence potential. As a result, pregnancy is associated with higher colonization by organisms such as *Prevotella intermedia*, *Porphyromonas gingivalis*, *Treponema denticola*, and *Fusobacterium nucleatum*, each of which contributes to dysbiosis and inflammatory activation within periodontal tissues.<sup>7</sup>

These microbial and immunologic alterations help explain the high burden of pregnancy-associated gingival inflammation. A significant proportion of pregnant women experience pregnancy gingivitis, characterized by erythema, edema, and bleeding, while those with preexisting periodontitis often show worsening attachment loss and deepened periodontal pockets. The heightened inflammatory response is linked to elevated levels of cytokines such as IL-6 and IL-1, increased C-reactive protein, oxidative stress, and enhanced activity of matrix metalloproteinases. Together, these processes disrupt collagen integrity and accelerate tissue breakdown, reducing the host's ability to maintain periodontal stability.<sup>8</sup>

Beyond local effects, periodontal inflammation may influence broader pregnancy physiology. Systemic dissemination of inflammatory mediators can impair vascular regulation within the placenta and modify fetoplacental signaling. Observational research has consistently shown associations between maternal periodontal disease and a range of adverse pregnancy outcomes, including preterm birth, low birth weight, gestational diabetes, and hypertensive disorders of pregnancy. Although these relationships are not necessarily causal, the biological plausibility is strengthened by evidence that oral bacteria can translocate through the bloodstream and have been identified in placental tissues, amniotic fluid, and fetal compartments. Among these, *Fusobacterium nucleatum* is frequently detected and is thought to migrate hematogenously from sites of periodontal inflammation.<sup>9</sup>

Collectively, these findings highlight pregnancy as a period of increased vulnerability within the oral environment, in which microbial shifts and amplified inflammatory responses can influence both maternal periodontal health and broader pregnancy outcomes.

## 3. Interaction Between Maternal Gut, Oral Microbiomes, And The Placenta

A consistent finding across emerging research is the recognition that the placenta is not a sterile environment, as once believed. Instead, it harbors a low-diversity microbial community that more closely resembles the maternal oral microbiota than the gut. Although sparse and metabolically restrained, these microorganisms or their components appear to participate in maternal–fetal signaling, influencing immune maturation and fetal development. This paradigm shift has reshaped the understanding of how maternal microbial ecosystems communicate with the intrauterine environment.<sup>10</sup>

Multiple pathways have been proposed to explain how microbes or their products reach the placenta. One mechanism involves hematogenous spread, where oral bacteria enter the maternal bloodstream through inflamed periodontal tissues and subsequently localize within placental structures. Another proposed route involves increased intestinal permeability during pregnancy, which enhances the passage of bacterial metabolites, lipopolysaccharides, and possibly whole bacterial fragments into the circulation. Dendritic cells may facilitate this transport by sampling luminal content and migrating toward systemic compartments. A further layer of interaction is provided by the maternal immune system, in which antigen–antibody complexes originating from maternal gut or oral microbes can cross the placental barrier and serve as early immunologic cues for the fetus.<sup>11</sup>

These microbial exchanges are supported by observations in fetal meconium, which contains detectable microbial DNA overlapping with components of amniotic fluid and select maternal oral taxa. The presence of these microbial signatures suggests that the fetus is exposed to microbial antigens before birth, challenging long-held assumptions of a sterile prenatal environment. Such early exposure may play a role in establishing neonatal immune tolerance, guiding the maturation of the gut–immune interface, and preparing the newborn for the rapid colonization that occurs after delivery.<sup>12</sup>

Together, these insights reinforce the concept of a dynamic maternal–fetal microbial continuum in which subtle microbial signals contribute to fetal development, early immune programming, and postnatal health trajectories.

## 4. Maternal Microbiota and Fetal Gut–Brain Axis Development

The fetal gut–brain axis begins forming well before birth, and

its early architecture is profoundly shaped by the maternal microbial environment. During gestation, maternal microbiota-derived metabolites, immune signals, and microbial components interact with developing neural, immune, and endocrine pathways, laying the foundation for postnatal neurodevelopment and gut-brain communication.<sup>13</sup> The central nervous system is particularly sensitive to these maternal influences. Alterations in maternal gut composition can modify axonal growth, synapse formation, and the development of thalamocortical circuits that govern sensory processing. Microglial cells—the brain's resident immune regulators—are likewise affected, exhibiting changes in activation and maturation when maternal microbial balance is disrupted. Even the integrity of the fetal blood-brain barrier is shaped by microbial signaling, with reduced microbial input linked to a more permeable and immature barrier. Experimental models have demonstrated that depletion of maternal microbiota during pregnancy leads to impaired thalamocortical development and altered sensory responses after birth, highlighting the importance of maternal microbial cues in early neural wiring.<sup>14</sup>

The enteric nervous system, the intrinsic neuronal network of the gastrointestinal tract, also develops in close association with maternal microbiota. Short-chain fatty acids produced in the maternal gut help regulate serotonin synthesis, promote epithelial barrier maturation, and guide the differentiation of enteric neurons. When maternal microbial diversity is reduced or absent, the transfer of these metabolites to the fetus diminishes, resulting in delayed or impaired ENS development.<sup>15</sup>

Fetal immune maturation similarly depends on a steady influx of maternal microbial signals. Microbial metabolites help direct T-cell differentiation, while bacterial DNA and antigen-antibody complexes crossing the placenta provide early exposure to immune-relevant antigens. These interactions prime fetal immunity and support the establishment of tolerance mechanisms that will be essential once the newborn encounters the external microbial world. Low levels of key maternal microbial metabolites have been associated with reduced regulatory T-cell development and an increased susceptibility to inflammatory imbalance.<sup>16</sup>

The endocrine arm of the gut-brain axis, particularly the developing hypothalamic-pituitary-adrenal axis, is also shaped by maternal microbiota. When maternal microbial balance is disrupted, inflammatory mediators and stress-related hormones can cross the placenta in greater amounts, increasing fetal cortisol exposure. This early hormonal environment may hyperactivate the fetal stress-response system, influencing long-term regulation of stress reactivity, metabolism, and emotional behavior.<sup>17</sup>

Together, these interconnected pathways illustrate how closely fetal development is tied to maternal microbial health. Through a continuous molecular dialogue, the maternal microbiome plays a central role in constructing the foundations of the fetal gut-brain axis and shaping lifelong neurodevelopmental and metabolic trajectories.

### 5. Factors Exacerbating Maternal Dysbiosis And Oral Disease

A range of maternal factors can disrupt the normal adaptation of the microbiome during pregnancy, with significant consequences for both maternal physiology and fetal development. Maternal obesity is one of the most influential contributors, leading to a characteristic shift in gut microbial composition marked by an increased Firmicutes-to-Bacteroidetes ratio. This imbalance promotes greater energy harvest, heightens systemic inflammation, and contributes to insulin resistance. As a result, obese pregnant women face a

higher risk of gestational diabetes, hypertensive disorders such as preeclampsia, and altered placental function that can affect fetal growth trajectories.<sup>18</sup>

Maternal diet is another major determinant of microbial balance. Diets high in saturated fats reduce microbial diversity and encourage the growth of proinflammatory bacteria, creating an environment that can disrupt metabolic and immune pathways important for pregnancy. Conversely, deficiencies in micronutrients such as folate and B vitamins compromise neurodevelopmental processes and may increase the risk of structural and functional brain abnormalities in the fetus. These nutritional imbalances shape the maternal microbial output, altering the metabolites available for placental transfer during critical developmental windows.<sup>19</sup>

Psychological stress during pregnancy also exerts measurable effects on the maternal microbiome. Elevated cortisol levels associated with stress alter gut motility, modify microbial composition, and disrupt the production of key metabolites involved in fetal neural and immune development. These changes may sensitize the fetal stress-response system and influence long-term behavioral and metabolic outcomes.<sup>20</sup>

Infectious or inflammatory conditions further complicate the maternal microbial environment. Heightened maternal inflammation can impair placental vascularization, interfere with nutrient and oxygen delivery, and increase the likelihood of preterm birth. Systemic inflammatory mediators can also reach the fetal compartment, influencing early immune priming and neurodevelopment.<sup>21</sup>

Medications used during pregnancy, particularly antibiotics and certain psychotropic drugs, significantly alter maternal microbial ecology. Antibiotics sharply reduce microbial diversity and diminish the availability of beneficial metabolites, while antidepressants can influence gut-brain signaling pathways. These disruptions may influence fetal development indirectly by modifying the maternal microbial signals transmitted across the placenta.<sup>22</sup>

Together, these factors demonstrate how sensitive the maternal microbiome is to physiological, nutritional, psychological, and pharmacological influences during pregnancy, and how changes in microbial composition can ripple across the maternal-fetal interface to shape pregnancy outcomes and early developmental health.

### 6. Clinical Implications: Why Oral Health Must Be Prioritized in Pregnancy

Given the close biological links between the gut microbiome, oral microbial ecology, systemic inflammatory pathways, and placental function, oral health must be recognized as an essential component of prenatal care rather than an isolated dental concern. Pregnancy-associated hormonal shifts create an environment that favors the proliferation of pathogenic oral bacteria, which can enter the bloodstream and contribute to systemic inflammation. This, in turn, may influence placental physiology and fetal development. Although clinical findings on whether periodontal therapy directly reduces preterm birth are mixed, there is consistent evidence that reducing the oral bacterial load lowers systemic inflammatory markers and minimizes the risk of hematogenous spread of periodontal pathogens to the placenta.<sup>23</sup>

Integrating oral healthcare into routine antenatal management helps stabilize the maternal microbial environment and supports overall maternal-fetal wellbeing. Best practices include a comprehensive dental evaluation early in pregnancy, followed by periodontal screening at each

trimester to detect emerging inflammation. Nutritional counseling helps support both oral and gut microbial balance, while regular monitoring of gingival health enables early intervention before tissue damage occurs. Care should be taken to avoid unnecessary antibiotic exposure, which can disrupt maternal microbiota, and incorporating stress-management strategies can indirectly reduce oral inflammation by moderating cortisol-mediated immune dysregulation. Together, these measures create a preventive care framework that supports systemic health, optimizes maternal microbial balance, and promotes healthier pregnancy outcomes.<sup>24</sup>

## CONCLUSION

Pregnancy triggers significant shifts in both gut and oral microbiota, influencing systemic inflammation, placental physiology, fetal immune conditioning, and neurodevelopment. When these microbial ecosystems become dysbiotic-due to obesity, poor diet, infections, stress, or medication use-measurable effects on pregnancy outcomes and long-term offspring health emerge, aligning with the developmental origins of health and disease (DOHaD) framework. The oral cavity functions as a reservoir for pathogens capable of hematogenous spread to the placenta, while the maternal gut microbiome produces metabolites that cross the placenta and directly shape fetal CNS, ENS, immune, and endocrine development. Together, these microbial networks act as modifiable determinants of maternal-fetal wellbeing. Considering the associations between periodontal inflammation, systemic cytokine burden, and adverse obstetric events, incorporating oral health into routine prenatal care is both justified and essential. Future work should explore targeted microbiome interventions-including probiotics, diet optimization, and personalized oral care-to enhance precision prenatal health strategies.

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