

Beyond Birth: The Role of the Maternal Microbiome in Shaping Neonatal Immune and Neurodevelopmental Outcomes

* Shams Muaaz Alkhateeb ¹, Ropafadzo Leocardia Chekera ², Hadi El Natour ¹, Pascal Dourgham ¹, Abir Ghosson ¹, Fatima Soufan ¹

¹ Beirut Arab University, Beirut, Lebanon.

² Nanjing Medical University, Nanjing, China.

Abstract

Background and Aim: The maternal microbiome is an important determinant of neonatal immune and neurodevelopment. Microbial signatures from the mother shape fetal development and direct postnatal immune maturation. Maternal perturbations due to delivery mode, antibiotic use, diet, and metabolic status have been linked to negative birth outcomes. This review summarizes current research on how maternal factors affect the neonatal microbiome and its impact on infant immune and brain development.

Methods: A narrative review was performed using PubMed, Scopus, and Google Scholar. English-language manuscripts were identified using terms related to maternal microbiome, neonatal microbiome, pregnancy, immune development, neurodevelopment, delivery mode, antibiotic exposure, maternal diet, probiotics, and breastfeeding. Relevant human studies, systematic reviews, meta-analyses, and clinically focused reviews were included, with preference for literature published between 2015 and 2025.

Results: Maternal influences affect how newborns acquire initial microbial communities. Vaginally delivered neonates acquire beneficial microorganisms earlier than those delivered by Cesarean section or exposed to antibiotics. Maternal nutrition, metabolic health, and breastfeeding shape the infant microbiome. Probiotic use may help restore balance, but findings vary.

Conclusion: The maternal microbiome plays a key role in early-life development. Targeting modifications may decrease the risk of adverse neonatal outcomes, particularly in high-risk populations. Heterogeneous study designs and a lack of standardized protocols limit clinical translation. Future research should focus on longitudinal cohorts, microbial biomarkers, and well-designed trials.

Key Words: Delivery mode; Maternal microbiome; Neonatal microbiome; Neurodevelopment; Pregnancy; Immune development.

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*Corresponding Author:

Shams Muaaz Alkhateeb; Beirut Arab University; Beirut, Lebanon; Email: shamsalkhateeb2@gmail.com

1- INTRODUCTION

The maternal microbiota encompasses the communities of microorganisms that inhabit the maternal vagina, gut, skin, oral cavity, and breast milk. At the same time, the existence of a distinct placental microbiome remains debated, as presented in Table 1 (1). It can be passed on to the baby with initial colonization of the neonate's gut, skin, and other mucosal surfaces (1,2).

Beyond microbial exposure at birth, maternal microbiome-related metabolites and immune signals may influence fetal development during pregnancy through maternal-placental pathways (3).

The composition and function of the maternal microbiota undergo significant changes during pregnancy. These changes are usually driven by hormonal, metabolic, and immunological shifts to support fetal growth and prepare the maternal host for parturition (4,5).

Furthermore, the early microbial imprinting heavily influences the neonate's susceptibility to a wide range of diseases,

including autoimmune and neurological diseases (4–6). Maternal gut microbiota and maternal milk microbiota also shape neonatal immune homeostasis and gut colonization (7,8).

There are several limitations to the current understanding of this field. Controversy remains over whether microbial exposure begins in utero or primarily at birth (9). If a unique placental microbiome is present, fetal colonization begins in utero, reshaping our understanding of neonatal programming and shifting preventive measures to the prenatal stage. If not, microbial exposure primarily begins at birth, emphasizing delivery mode and early-life environment as the main determinants.

Another limitation lies in the difficulty of fully elucidating the mechanisms by which the maternal microbiome influences offspring development (10). The precise mechanisms, whether through microbial metabolites, maternal immune mediators, or antibody transfer, remain incompletely characterized (5).

Table-1. Comparison of maternal microbiota niches, modes of transmission, and their influence on neonatal colonization and development (11–18).

Maternal Microbiome Niches	Role/Transfer Mode	Function
Vagina	Provides microbes during vaginal delivery through vertical transmission	Primary source of neonatal gut colonization
Gut	Influenced by maternal diet, antibiotics, and metabolism	Shapes infant gut microbiota; disruptions linked to immune and metabolic disorders
Skin	Transferred during direct skin-to-skin contact	Contributes to early skin and gut colonization
Oral	Altered by hygiene, nutrition, and immune status	Poor oral health is associated with preeclampsia, preterm birth, and small-for-gestational-age infants
Placental and amniotic fluid	Possible presence remains debated; microbes may originate from the maternal oral cavity or be contamination.	If genuine, it could initiate in utero exposure; otherwise, birth is the main exposure window.
Breast milk	Contains Bifidobacterium and Lactobacillus species, transferred during breastfeeding	Supports postnatal gut colonization and immune homeostasis

The current body of research is fragmented, with some studies concentrating solely on immunity and others on neurodevelopment. In addition, to determine causal relationships and guide clinical translation, extensive longitudinal cohorts that track children into adolescence are needed. This review aims to synthesize human evidence on how the maternal microbiome shapes neonatal immune maturation and early neurodevelopment through shared microbial, immune, metabolic, endocrine, and gut–brain axis pathways.

2- METHODS

This article is a narrative review of the literature concerning the maternal microbiome and its effect on the neonatal neurological and immunological development. To collect articles on this topic, a narrative literature search was conducted using PubMed, Scopus, and Google Scholar. Search terms included “maternal microbiome,” “pregnancy,” “neonatal microbiome,” “immune development,” “neurodevelopment,” “delivery mode,” “antibiotic exposure,” “maternal diet,” “probiotics,” and “breastfeeding.” In addition, some articles were extracted from the reference lists of key articles.

The included articles are peer-reviewed articles published in English between 2015 and 2025, with greater emphasis on recent studies. However, older foundational studies were included when necessary to support key concepts. Original human studies, systematic reviews, and meta-analyses were prioritized. Primary animal studies were excluded to maintain a clinically focused review based on human neonatal evidence.

2-1. The Maternal Microbiome Landscape

To elaborate further on the intricacies of the maternal microbiome, phyla such as Firmicutes, Bacteroidetes,

Actinobacteria, and Proteobacteria inhabit the gut and vagina (19,20). Vaginal microbiota are often dominated by *Lactobacillus* Species (SPP) in a healthy pregnancy. Deviations toward bacterial vaginosis are associated with adverse outcomes such as preterm birth (21).

Factors that influence the maternal microbiome are substantial. One of the major determinants is maternal dietary diversity, which correlates with shifts in gut microbiome composition and metabolic output. Use of antibiotics can also disrupt bacterial diversity and reduce the abundance of some taxa (22). Other external factors associated with maternal dysbiosis include stress, infections, obesity, and gestational metabolic conditions, e.g., gestational diabetes (23,24).

2-2. Shaping Neonatal Immune Development

2-2-1. Maternal Gut Microbiota and Immune Priming

Maternal gut microbiota affects fetal health through several pathways, including the transfer of antibodies, immune molecules, components of maternal gut microbiota, and immune cells across the placental barrier (25). The maternal gut microbiota is closely associated with the immune microenvironment in the uterus (9,26).

Figure 1, provides a concise schematic overview of the interactions between the maternal microbiome and the developing neonate’s immune system.

2-2-2. Psychosocial Stress and Microbiome Disruption

Furthermore, maternal anxiety, depression, and stress can affect offspring gut microbiome diversity and bifidobacterial abundances by altering maternal hormones and microbial balance (14, 27). Evidence shows that there is an association between the maternal gut

microbiome during pregnancy and the composition of the infant's cord and peripheral blood immune cells in the first year of life (28).

2-2-3. Microbial Metabolites as Immune Modulators

One significant mechanism is the maternal microbiome producing metabolites, which can cross the placenta and impact fetal development directly (4,27,29). They are produced from the fermentation of dietary fiber by maternal gut bacteria. Short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate are crucial signaling molecules that work in shaping the offspring's immune system and can cross the placental barrier (4,27,29).

SCFAs foster the development and function of regulatory T-cells (Tregs), promoting an anti-inflammatory environment (30,31). They also possess a capacity to modulate the immune system through epigenetic control of histone deacetylation (4,32). Tryptophan derivatives also play a vital role in immunomodulation.

Tryptophan is an amino acid that is hydrolyzed by bacteria in the gut. Certain tryptophan-derived metabolites produce indole derivatives that serve as endogenous ligands for aryl hydrocarbon receptors (AhR) (33,34). Tryptophan-derived indoles modulate inflammation, barrier integrity, and neurodevelopment (35,36).

2-2-4. Delivery Mode, Antibiotics, and Environmental Disruptions

Alterations caused by Cesarean section delivery or early antibiotic use are linked to increased risks of asthma, allergies, metabolic disorders, and autoimmune disorders. It also affects the

composition of immune cells in infancy (28).

Additionally, maternal antibiotic use is associated with reduced infant microbiome diversity (37).

2-3. Shaping Neonatal Neurodevelopment

2-3-1. Gut–Brain Axis in Early Life

A critical communication system through which the maternal and neonatal microbiomes influence central nervous system development is the gut-brain axis. Synaptogenesis, myelination, and neurotransmitter production in the developing brain are modulated by microbial metabolites such as short-chain fatty acids, tryptophan derivatives, and GABA precursors, which act as signaling molecules (38). Therefore, changes in the maternal microbiota during pregnancy may influence neonatal neurodevelopment through gut–brain axis signaling.

2-3-2. Human Correlation Studies

Emerging evidence suggests that maternal microbiome composition during pregnancy is linked to offspring neurodevelopmental outcomes. A recent study showed that maternal prenatal gut microbiota was a stronger predictor of neurocognitive outcomes at one year of age than the infant's own postnatal microbiota (39). In particular, the abundance of butyrate-producing taxa in maternal gut communities was associated with increased motor, cognitive, and language development in the offspring (39).

Prepartum maternal systemic inflammation has also been demonstrated to be associated with increased risk of neurodevelopmental disorders, such as ASD and schizophrenia (40).

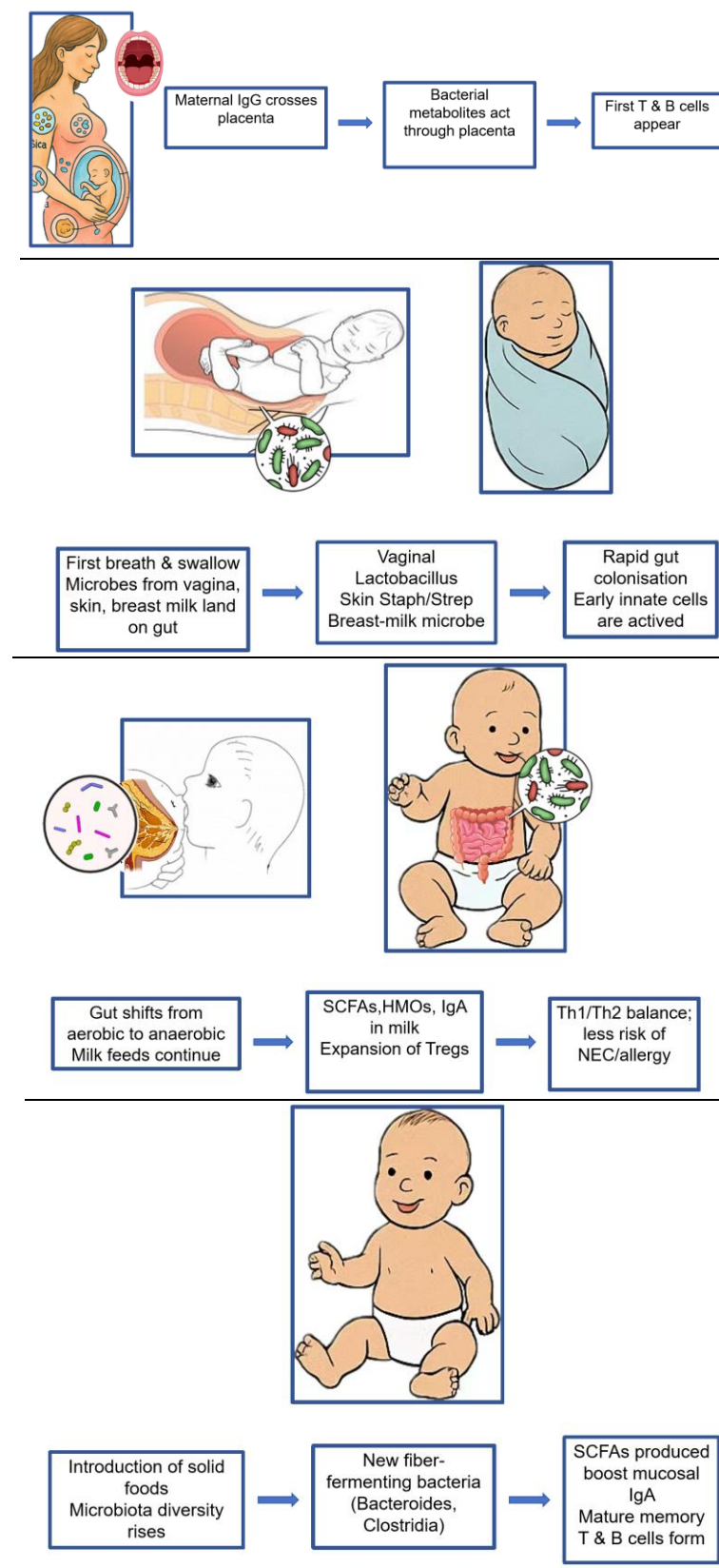


Figure-1: Mechanistic pathways of neonatal immune development influenced by the maternal microbiome.

3- DISCUSSION

This section reviews current evidence on how various maternal factors, including delivery mode, antibiotic exposure, diet, and probiotic use, shape the neonatal microbiome development and affect short- and long-term health outcomes.

3-1. Delivery Mode and Colonization

Vaginal delivery exposes the newborn to maternal vaginal and gut-associated microbial communities, including genera such as *Lactobacillus* and *Prevotella* (41). Changes in the normal composition of the vaginal flora can result in preterm delivery (42). Several cohort studies have demonstrated that low lactobacilli levels or the presence of lactobacilli other than *L. crispatus* are associated with preterm delivery (42). In contrast, cesarean section delays bacterial colonization. Such delay alters neonatal immune development and increases the risk of allergies, asthma, and metabolic disorders (3,4).

Cesarean section remains an important modifier of the neonatal microbiome. This has led to increased interest in vaginal seeding. Vaginal seeding is the practice of exposing newborns delivered via Cesarean section to the maternal vaginal microbiota (8,43,44). Despite this, its efficacy and safety are still under investigation, and it is not considered a standard of care yet (9). This practice remains controversial due to concerns regarding the potential transmission of harmful pathogens to the infant (7). Beyond delivery mode, medical interventions such as antibiotic exposure further influence early microbiome establishment.

3-2. Antibiotics and Microbe Disruption

Antibiotic exposure around delivery, including intrapartum antibiotic prophylaxis and antibiotics administered with cesarean section, can disrupt the early

establishment of the infant gut microbiome (45). Human cohort studies have shown that maternal intrapartum antibiotics, delivery mode, and breastfeeding are associated with differences in infant gut microbiota composition during the first year of life (45).

3-3. Maternal Diet

Alterations in maternal diet during pregnancy and breastfeeding have been associated with undesirable outcomes in the offspring, such as intestinal inflammation and low birth weight (46).

Maternal obesity is associated with several adverse pregnancy and neonatal outcomes. These include an increased risk of preterm birth, neonatal asphyxia, macrosomia, dysbiosis of the infant gut microbiome, and reduced diversity (47,48).

In addition, the effects of maternal diet extend beyond pregnancy through breastfeeding (8). Maternal milk contains bioactive components, such as human milk oligosaccharides (HMO), lactoferrin, and secretory immunoglobulins, which modify the neonatal microbiota (17).

3-4. Probiotics

Probiotics have been proposed as a potential intervention strategy to modulate the maternal microbiome during pregnancy and lactation (49). Some studies suggest that maternal probiotic supplementation may stabilize gut dysbiosis and increase beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, with possible reductions in infant eczema and neonatal jaundice (4,42,50,51). However, evidence remains inconsistent, and there are currently no standardized recommendations regarding probiotic strain, dose, or timing.

3-5. Postbiotics

Postbiotics are defined as preparations of inanimate microorganisms and/or their components that provide a

health benefit to the host (52). Unlike probiotics, they do not contain live microorganisms but may include heat-inactivated microbial cells, cell-wall components, enzymes, peptides, or microbial metabolites that can interact with the intestinal barrier and immune system (52,53). In neonates and infants, postbiotics may offer a safer microbiome-targeted approach because they avoid the potential risks related to administering live microorganisms, especially in vulnerable populations (53). A recent systematic review and meta-analysis of infant formula studies suggested that postbiotic-containing formulas appear generally safe and may influence gastrointestinal and immune-related outcomes, although the available evidence remains heterogeneous (54). Therefore, in the context of maternal and neonatal health, postbiotics represent a promising but still developing intervention, and more human studies are needed to clarify their effects on neonatal immune maturation, gut microbiome development, and long-term neurodevelopmental outcomes (54).

3-6. Regional Differences

Maternal microbiome composition varies between regions due to differences in environmental exposures, dietary patterns, and healthcare access (37,55). These variations influence neonatal microbial outcomes and limit the broad application of microbiome-based interventions across populations (56,57).

4- CONCLUSION

This narrative review highlights the maternal microbiome as a dynamic system that plays a key role in maternal physiology and early-life development. The maternal gut, vaginal, oral, skin, and breast milk microbiota, together with maternal-placental immune and metabolic signaling, may influence early-life development. These interactions influence immune maturation and metabolic

programming in the offspring, placing the maternal microbiome within a broader maternal-fetal continuum.

Emerging evidence suggests that targeted modulation of the maternal microbiome may reduce the risk of adverse neonatal outcomes related to maladjustment of the immune system, metabolic dysfunction, and the development of allergic conditions, particularly in populations at high risk. Nonetheless, most available data are associative, and heterogeneous study designs and outcome measures limit clinical translation.

Future research should focus on longitudinal maternal-infant cohorts, identification of reliable microbial biomarkers, and well-designed clinical trials evaluating the safety, timing, and effectiveness of microbiome-targeted interventions.

5- CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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