Maternal microbiome and metabolic health program microbiome development and health of the offspring

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ABSTRACT

The maternal nutritional, metabolic, and physiological statuses, as well as exposure to various environmental factors during conception, gestation, and lactation, play a fundamental role in the health programming of the offspring. Therefore, alterations affecting the maternal microbiota could indirectly influence fetal development. In addition, such alterations could be transmitted to the progeny at different stages of the infant development (e.g., pre-conception, pre-natal, post-natal), thereby favoring the development of an altered microbiota in the neonate. Microbial changes of this kind have been linked to an increased risk of non-communicable diseases, including obesity and metabolic syndrome, allergy-related problems, and diabetes. This review summarizes the relevance of the maternal microbiota to fetal-neonatal health programming, with a focus on the maternal nutritional and metabolic statuses.

Keywords: microbiota, nutrition, lactation, C-section, antibiotic, obesity, diabetes, neonatal health

The relevance of nutrition in health programming

The intimate interrelationship that exists between an individual's diet, microbiome and health has been widely recognized in studies explaining susceptibility to disease, including allergic, autoimmune, and inflammatory diseases, as well as to obesity [1].

Epidemiological studies have highlighted the relevance of perinatal nutrition to the physiology and structural biology of fetal and neonatal development having an impact on "health programming" [2, 3]. Both the maternal and paternal nutritional statuses prior to conception have pivotal implications for the offspring's growth and development, as well as for the offspring's health outcomes in the short and long term [4, 5]. Nevertheless, preconception and perinatal interventions intended to improve the outcomes for both mothers and neonates remain limited, and additional evidence is required in this regard [6].

Developmental programming in utero may be affected by prenatal exposure to environmental factors. Fetal development requires an adaptation to the *in-utero* environment, which affects fetal physiology and metabolism. Alterations of the homeostasis during embryonic and fetal development may result in an increased risk of non-communicable diseases (NCDs) later in life [3]. Adaptation to the maternal nutritional status (both under- and overnutrition) occurs through changes in the fetal-placental physiology, hormonal alterations, and metabolic modifications [3, 7]. In fact, the perinatal period is considered the most critical time span in terms of the risk of developing NCDs [8, 9]. Recent studies have provided strong evidence that prenatal exposure to unhealthy dietary patterns, xenobiotics or stress may increase the risk of adverse health outcomes, such as obesity, diabetes, and allergy/asthma, among other diseases [10]. These environmental conditions may act through diverse mechanisms that include epigenetic mechanisms as well as cellular and physiological routes that affect neonatal development and metabolism, thereby leading to an increased risk of NCDs [9]. Detailed mechanisms on epigenetic link between maternal diet, microbiome and offspring are outside the scope of this and authors refer to [11].

The human microbiota and its impact on health

The human body harbors complex communities of microorganisms comprised of bacteria, yeast, and fungi, as well as viruses, and archaea, which perform essential functions in terms of human physiology, metabolism, nutrition, and immunity throughout the entire human life span [12]. The development of the human microbiota is a complex and step-wise process, which is thought to be initiated at birth, when the infant first encounters maternal microbes through delivery, and then supported by breastfeeding [12]. Historically, the human womb has been considered sterile in healthy pregnancies, however, recent data suggests the possibility of prenatal colonization of the gut [13]. This hypothesis is based on the presence of microbial DNA in amniotic fluid, meconium and placenta; however, the role of prenatal microbial colonization is still open to debate [14]. The microbial contact prior to birth may be a possible mechanism of NCD programming, as the most critical time for the establishment of genome-wide epigenetic profiles occurs during early embryogenesis [11, 15]. Microbial colonization plays a decisive role in relation to both gut physiology and the homeostatic balance, but it also shapes the maturation of the immune system and cognitive development [16-18]. The immune system of fetus, newborn and infant evolve in a dynamic and complex fashion to adapt to the different challenges and requirements occurring during specific developmental periods [19].

The link between nutrition, maternal microbiota and neonatal immune system has previously been described [20].

The order and timing of species arrival to the neonatal host (priority effects), may influence the early stages of community assembly and development, which in turn would have long-lasting consequences to the human gut microbiota and host health, still largely understood [21]. These critical processes can be adversely affected by several factors, including the mode of birth (caesarean [C]-section), antibiotic use, prematurity, and formula feeding, which have all been linked to an increased risk of NCDs [12, 22].

At birth, the neonate first encounters an immense quantity and diversity of maternal microbes from the maternal reproductive tract, gut, and skin, in addition to those from the environment.

Vaginally delivered infants are in exposed to maternal vaginal and fecal microbiota, resulting in neonatal gut colonization by vagina-associated microbes (e.g. *Lactobacillus* and *Prevotella*), significantly differing from C-section infants, especially during the first week after birth [23]. The effect of maternal diet and metabolic parameters during pregnancy and pre-birth on vaginal microbiome and the possible consequences for infant gut colonization warrants further research.

During breastfeeding, the neonate's microbiome evolves and becomes more diverse and complex, and following the introduction of food, it shifts to an adult-type microbiome at between two and four years of age [24]. It has previously been shown that the key factor shaping neonatal microbiota development is the mother's breastfeeding status, whether exclusive or partial [25]. Furthermore, the mode of birth, as well as the adopted breastfeeding practices and antibiotic treatments during the first two years of life, have been found to be associated with a distinct oral and gut bacterial composition at a later age [26, 27].

Maternal influence on infant microbiota is well recognized, but the role of paternal impact on progeny's health still needs to be appreciated. The effect of environmental factors such as paternal diet, nutritional status, xenobiotics exposure, or physical activity, is key in shaping both sperm and seminal plasma composition, which transmit paternal modulatory signals to influence the developmental programming of the offspring [28, 29].

In summary, a growing body of evidence suggests the early life period, that is, from conception through the first two years of life, to be pivotal for microbial colonization, and at same time, for immune system maturation, cognitive development, and metabolic stimulation (**Figure 1**). Hence, this period is considered to be a window of opportunity during which dietary or other changes will have a strong impact on the metabolic, immunological, and microbiological programming of a child, thereby affecting the health, physical, and intellectual development of that child [12, 16, 18].

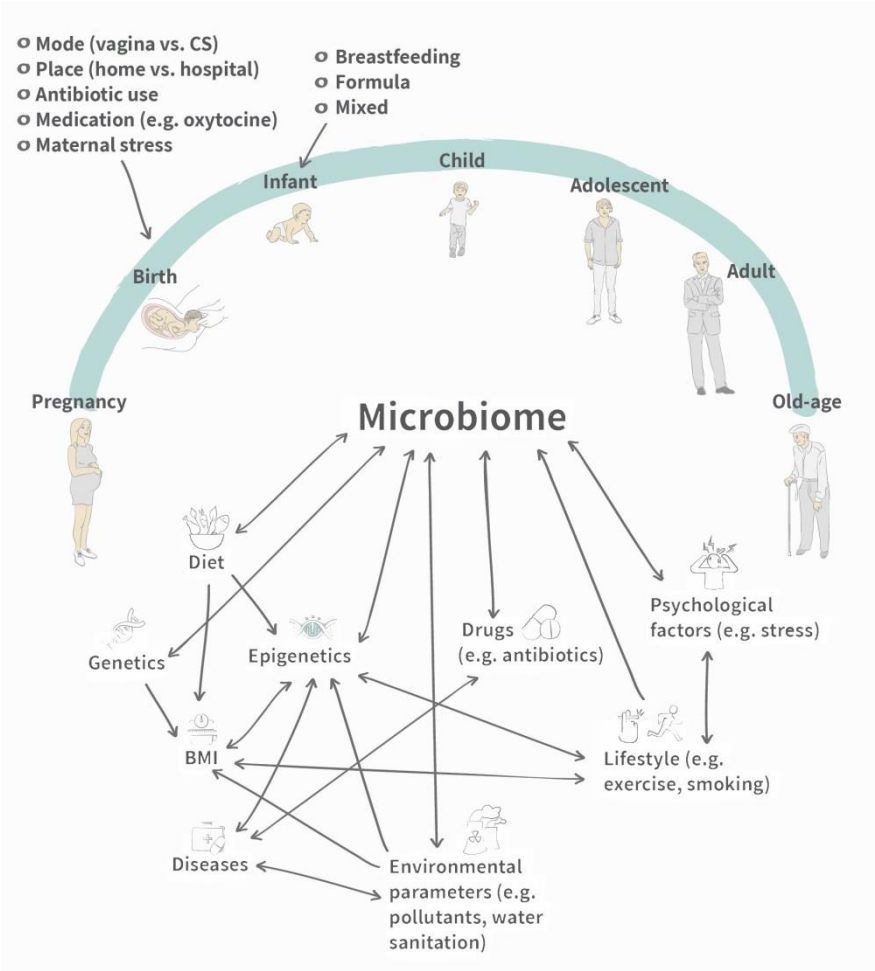

Figure 1. Maternal Microbiota Contribute Significantly to the Initial Microbial Colonization of the Neonate, with Both Short- and Long-Term Impacts. Different factors shape and alter the maternal microbiota and maternal dysbiosis is transferred to the neonate. The early-life period, from conception through the first 2 years of life, is pivotal for microbial colonization, immune system maturation, cognitive development, and metabolic stimulation. Abbreviations: BMI, body mass index; CS, cesarean section.

Maternal adaptation during pregnancy: impact on the microbiota

The physiology, metabolism, and immunity of women alter during pregnancy to allow for an optimal intrauterine environment that favors fetal development and growth [30]. Physiological changes during gestation, including shifts in the endocrine, immunological, and metabolic levels, favor a proinflammatory status, analogous to the alterations reported in relation to diabetes, obesity, and metabolic syndrome, which are reflected in the maternal microbiota, including the oral cavity, gut, and vaginal microbiota [31]. However, this pro-inflammatory status is also implicated in metabolic alterations during pregnancy, which contribute to ensuring a healthy pregnancy. The microbial changes in the gut mainly manifest as an increase in Actinobacteria and Proteobacteria phylum, alongside a reduction in microbial diversity and butyrate-producing bacteria [32]. Some studies have identified shifts in the gut microbiota during pregnancy [33, 34], while others have failed to identify any microbial changes during gestation [35].

Correlations between the gestational metabolic variables and the gut microbiota during pregnancy have previously been described, including direct relationships between the levels of

Collinsella and circulating insulin, triglycerides, and very-low-density lipoproteins; *Sutterella* and C-reactive protein; Ruminococcaceae/Lachnospiraceae and leptin; Bacteroidaceae and ghrelin; and *Coprococcus* and gastrointestinal polypeptide (GIP). Moreover, inverse relationships have been reported between *Blautia* and insulin values; *Faecalibacterium*/*Fusobacterium* ratios and the blood glucose level; *Odoribacter* and arterial blood pressure; Ruminococcaceae and GIP ; and Prevotellaceae and ghrelin level [36]. Recently, it has also been shown that progesterone, a major hormone during pregnancy, influences the composition of the gut bacteria in pregnant women, and more specifically, increases the relative abundance of *Bifidobacterium* [34].

Therefore, the gut microbiota may contribute to gestational metabolic changes, although the exact mechanisms behind this contribution remains unknown. Moreover, it has been suggested that multiple childhood difficulties (e.g., chronic stress or abuse) program an exaggerated adult inflammatory response to stress and thereby drive changes in the gut microbiota during pregnancy [37].

Does the maternal diet during pregnancy affect the maternal-neonatal microbiota and metabolism?

Evidence obtained from animal models and epidemiological data show that maternal obesity during pregnancy, as well as a high-fat diet, imprint a long-lasting metabolic signature on the neonatal microbiota and immune system, which predisposes the offspring to both obesity and metabolic diseases [38]. Limited data are currently available concerning the impact of the maternal diet during gestation on the maternal microbiota [39-41], with some of the available studies having focused on the relationship between maternal overweight and obesity and gestational diabetes (GDM) [36, 42, 43] (**Table 1**). Interestingly, it has been reported that stress and adverse childhood experiences (ACEs) affect the maternal microbiota at a later age during pregnancy [37]. In rodents, the consumption of dietary omega-3 fatty acids (including docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) during adulthood was able to modulate the shifts caused by ACE in the maternal gut microbiota [44]. These data also emphasize the relevance of the maternal diet to both maternal and fetal health, as well as its influence on the gut-brain axis. However, additional studies are needed to identify which foods, macro- and micro-nutrients, and specific dietary compounds influence the perinatal microbiota in both the mother and her offspring [45]. Yet, Savage and collaborators [46] did not find an association between the maternal diet during gestation and the infant's microbiota, which suggests that the infant's diet has a stronger influence on the composition of the microbiome.

Table 1. Evidence of effect of maternal diet during pregnancy on maternal and/or neonatal microbiota.

Study population	volunteers	Diet record	Effects*	Reference
Pregnancy microbiota Norwegian NoMIC cohort	N= 60 - Dietary records in 2nd trimester - Microbiota 4 days after birth	FFQ covering 255 food items	↑Monounsaturated fatty acids (MUFAs) ↑Firmicutes, Proteobacteria, and Bacteroidetes ↑vitamin E intake ↓Proteobacteria ↓fiber intake ↓reduced gut microbiota diversity and richness ↑ *Sutterella*, ↑vitamin D, mono-unsaturated fat, cholesterol, and retinol ↑Proteobacteria	[41]
Pregnancy microbiota	N=100 Overweight and	3-d food record	↑dietary fiber and n–3 polyunsaturated fatty acids (PUFAs) ↑microbiota richness ↓serum zonulin levels	[47]

Women with OW/OB	obese women (BMI ~30) early pregnancy (≤17 weeks)			
Pregnancy microbiota SPRING (Study of Probiotics IN Gestational diabetes)	N= 57 overweight N= 73 obese 16 weeks gestation	Victoria Cancer Council FFQ (Version DQES V2.0)	↓fiber intake ↓gut microbiota diversity and richness ↑ *Collinsella*	[42]
Pregnancy microbiota gestational diabetes mellitus (GDM)	N=41 - 2nd trimester - 3rd trimester	3-day food record and the Minnesota-Leisure-Time-Physical Activity Questionnaire	↑adherence to dietary recommendations ↓metabolic and inflammatory pattern ↓ Bacteroides	[43]
Pregnancy microbiota SPRING study (Study of Probiotics IN Gestational diabetes)	N=9 vegetarian N=18 omnivorous 16 weeks gestation	Victoria Cancer Council FFQ (Version DQES V2.0)	Vegetarian diets: ↑ *Roseburia* and *Lachnospiraceae* ↓*Collinsella, Holdemania*, no difference in α-diversity compared to omnivorous	[39]
Mother–infant dietary intervention trial (NCT01922791) Pregnancy microbiota Women with OW/OB	N=100 Overweight and obese women (BMI ~30) early pregnancy (≤17 weeks)	3-d food record	↑high-fat ↓fiber intake ↓gut microbiota diversity and richness and ↓ Bacteroidaceae. ↑microbiota richness ↓ low-grade inflammation marker GlycA.	[48]
Pregnancy microbiota Women with OW/OB	N=84 Overweight and obese women (BMI ~30) early pregnancy (≤17 weeks)	Dietary quality measured by a validated index of diet quality (IDQ)	↑IDQ score ↑ microbial diversity (Shannon index) ↑*Coprococcus* (family Lachonspiraceae) ↑ *Faecalibacterium prausnitzii* (family Ruminococcaceae) ↓ *Sutterella*	[49]
Vitamin D Antenatal Asthma Reduction Trial	N=323	FFQ	Marginal associations between maternal diet during pregnancy and infant gut microbiome: high maternal intake of vegetables and low intake of processed meats and deep fried foods ↑*Lactobacillus* spp in infant stool Solid food introduction:↑*Clostridium* spp	[46]
Infant gut microbiome 6 weeks post-delivery New Hampshire Birth Cohort Study	N=145	FFQ	↑maternal fruit intake associated with infant gut microbial community structure In vaginally delivered infants: ↑ fruit intake ↑odds of infants belonging to the high *Streptococcus/Clostridium* group In C-Section infants: maternal dairy intake ↑ odds of infants belonging to the high *Clostridium* cluster	[50]

Abbreviations: OW: overweight; OB: obese; GWG: gestational weight gain; FFQ: Food Frequency Questionnaire; GlycA: glycoprotein acetylation.*The effects are related to the mothers, otherwise stated in the table

Impact of metabolic complications on the maternal microbiota during pregnancy

Evidence obtained from human studies suggests that shifts in the gut microbiota during pregnancy are sensitive to the maternal pre-gestational body mass index (BMI), as well as to weight gain during pregnancy [51, 52]. Reduced levels of *Bifidobacterium* spp. have been reported in the obese maternal gut, as well as in women with excessive weight gain during pregnancy, when compared to the levels reported in lean mothers and those with appropriate weight gain during pregnancy [51]. Higher levels of *Staphylococcus* and Enterobacteriaceae (mainly *Escherichia coli* spp.), as well as lower levels of *Bacteroides* spp., were observed in Spanish obese pregnant women when compared to the levels observed in lean pregnant women [45, 52]. Maternal obesity and excessive weight gain were found to be associated with

lower microbial diversity, in addition to shifts in the Christensenellaceae family and the levels of *Lachnospira*, *Parabacteroides*, *Bifidobacterium*, and *Blautia*; however, such shifts were not correlated with the infant gut microbiota composition during the first two years of life [53].

Moreover, GDM has a significant impact on the gut microbiota during both gestation and lactation [54, 55], and also in breastmilk microbiota and composition [56]. In fact, GDM was found to modify the gut microbiota of pregnant women during the third trimester of pregnancy, and the identified differences were maintained for eight months after delivery [54]. A higher increase in the Ruminococcaceae levels early in pregnancy (12 weeks) has been found to be associated with GDM [57]. Changes in the gut microbiota have been reported in pregnant mothers with GDM between the second and third trimesters, leading to increased microbial richness, an increase in the Firmicutes levels, and a reduction of Bacteroidetes and Actinobacteria phyla [43]. It has previously been reported that the levels of *Faecalibacterium* spp. are associated with fasting glucose levels, that higher levels of *Collinsella* and lower levels of *Blautia* are associated with insulin levels and the homeostasis model assessment of insulin resistance, and that the *Sutterella* genus is linked to C-reactive protein level [43]. Pregnant mothers with GDM are known to harbor a higher abundance of Actinobacteria phylum and certain specific bacteria, including *Rothia*, *Collinsella*, *Clostridium* (sensu stricto), *Veillonella*, and *Desulfovibrio,* as well as a reduced abundance of *Faecalibacterium* and *Anaerotruncus*. A lower alpha diversity and a lower relative abundance of the *Prevotella* and *Lactobacillus* groups in the meconium of the progeny of mothers with GDM have also been reported [58]. Moreover, maternal GDM status is known to have a significant impact on the neonatal microbiota, resulting in an increased viral load and altered microbial metabolism [59].This suggests that metabolic abnormalities on the part of the mother can have an indirect effect (e.g., through lactation) on the infant's microbiota. Long-term and mechanistic studies focused on assessing the effect of microbial change on infant or adult health warrant further investigation.

It has previously been demonstrated that the maternal pre-pregnancy BMI and the level of weight gain during pregnancy impact the gut microbiota of six-week-old infants [60]. In vaginally delivered infants, higher infant gut microbial diversity, as well as higher levels of *Bacteroides fragilis, Escherichia coli*, and *Veillonella dispar*, were found to be associated with maternal obesity, while no associations were observed in infants delivered by C-section [60].

However, a pilot study (n = 16) showed that the identified shifts in the composition and diversity of the maternal vaginal *Lactobacilli* were linked to a higher prevalence of type 1 diabetes in children [61].

Furthermore, their gut microbiota can shape the development of the central and peripheral nervous system, through modulating neurotransmitters or host biosynthesis pathways, secreting short chain fatty acids or other bioactive metabolites, stimulating vagal nerve responses, affecting the permeability of the blood brain barrier or shaping the response to stress via hypothalamic-pituitary-adrenal (HPA) axis [62]. Accordingly, a higher maternal BMI during gestation has been linked to lower levels of salivary cortisol in the offspring during adulthood [63]. Likewise, maternal obesity alters the HPA axis activity toward lower maternal cortisol, which has been linked to an increased birthweight and a prolonged pregnancy [64]. Maternal obesity during pregnancy has also been linked to an increased risk of neurodevelopmental disorders in the offspring, including autism spectrum disorder (ASD) [65].

Impact of gestational and early-life antibiotic use

Antibiotics are widely used during pregnancy, and they are often administered during a C-section, thereby impacting the maternal microbiota [66]. Perinatal antibiotics administered to the mother have been found to shape the infant's microbiota for up to three months [67], including the promotion of an increased abundance of Enterobacteriaceae [68]. Further, intrapartum antibiotics shape the early neonatal gut microbiota toward an increase in the Proteobacteria and Firmicutes levels and a reduction in the level of Actinobacteria phylum [69, 70]. In fact, antibiotics administered during delivery shape the neonatal oral microbiome, thereby resulting in higher levels of Proteobacteria phylum following antibiotic treatment [71]. This could have important consequences in terms of child development. Relatedly, it has been observed that children who were exposed to antibiotic treatment during the second and third trimesters exhibited an 84% higher risk of developing obesity [72]. Additionally, *Neisseria* and *Streptococcus mitis/dentisani* were found to be present in significantly higher levels in seven-year old children who did not take antibiotics early in life [26].

Table 2. Selected studies describing factors affecting microbiota profiles of offspring, with emphasis on influence of parental diet on infant weight gain and metabolic parameters.

Study population	Factor of study	Effects	Reference
Canadian Healthy Infant Longitudinal Development (CHILD birth cohort) n = 935	Effect of birth mode and maternal BMI on infant gut microbiota and offspring BMI z-score at 1 and 3 years	Infants from overweight or obese mothers had 3-fold (vaginal delivery) or 5-fold risk (CS delivery) of becoming overweight at the age of one year with a similar risk at the age of 3 years. Abundance of Lachnospiraceae in microbiota of the infant gut was directly associated with child obesity in early infancy	[73]
New Hampshire Birth Cohort N= 335 mother-infant pairs in	Effect of birth mode and maternal BMI and weight gain	In the vaginal-delivery group, ↑maternal overweight or obesity was associated with ↑infant microbial diversity and ↑relative abundance of *Bacteroides fragilis*, *Escherichia coli*, *Veillonella dispar*, *Staphylococcus* and *Enterococcus*. No associations in the Cesarean-delivered group,	[60]
FinnBrain Birth Cohort n = 46	BMI and gestational weight gain in mid-pregnancy	↑ gestational weight gain and ↓ α-diversity in mid-pregnancy is associated with Bacteroidetes-dominated gut microbiota in offspring	[74]
EPOCH study n= 107	Associations among gut microbiota, diet and HFF in adolescents	↑HFF was associated with ↓ α-diversity. 32% of the variation in HFF can be explained by the combination of *Bilophila* and *Paraprevotella* abundances, dietary intake of monounsaturated fatty acids, and BMI z-scores	[75]
Finnish Gestational Diabetes Prevention Study (RADIEL) n =109	Gestational diabetes mellitus (GDM)	↑ *Anaerotruncus* in children of women with GDM ($p < 0.001$).	[76]
Norwegian birth cohort (NoMIC) n = 165	Maternal OW/OB or GWG, infant early life microbiota, BMI at age 12	Gut microbiota composition at 2 years can explain 53% of the variability in BMI z-scores at 12 years Overlap between maternal gut microbiota associated with OW/OB, or excessive GWG and infant gut microbiota associated with elevated BMI in children (e.g., *Bifidobacterium bifidum*, *Blautia spp*.)	[53]
Norwegian birth cohort (NoMIC) n = 267 (mother-child pairs)	Effect of environmental toxins in breastmilk on gut microbiome of infants (1 month)	Exposure to PBDE-28 and PFOS from milk reduced microbiome diversity. *Lactobacillus* had lower abundance in infants with high exposure to toxins (> 80th percentile). Breast milk toxins affected acetic and propionic SCFA production	[77]
$ARCH_{GUT}$ or $BABY_{GUT}$ cohorts n = 42	Pre-pregnancy BMI	OW mothers had lower alpha diversity and higher abundance of *Bacteroides, Acidaminococcus* and *Dialister*, and lower *Phascolarctobacterium*. Infants from N and OW women had lower abundances of *Megashpaera*. *Staphylococcus* was	[78]

		lowest in infants of OB women	
PREOBE study cohort n = 39	Effect of pre-pregnancy BMI on the microbiome functions of infants at 18 months (transition to solid food)	Infants from obese mothers had higher abundance of *Bacteroidetes*, and gut microbiota functional shifts: enrichment in streptomycin biosynthesis, sulphur metabolism, taurine and hypotaurine metabolism, and lipopolysaccharide biosynthesis pathways	[79]
KOALA Birth Cohort Study N=281	Effect of early diet and breastfeeding duration on microbiota and metabolic phenotype in the children at school age	Children with a bacterial gene number < 600,000 exhibited ↑BMI z-score and no pattern was observed in lean children children dominated by *Bifidobacterium* showing the lowest gene number and the lowest diversity compared to children enriched with *Bacteroides* or *Prevotella*, ↓breast-feeding duration in the *Bifidobacterium*-dominated enterotype in school-age children	[80]
Bibo (n=87) and Flora (n=75) cohorts	Effect of early life microbiota composition and antibiotic exposure on infant BMI	Children minimally exposed to antibiotics: positive association between BMI and *Bacteroidetes* (*Bacteroides ovatus*, *Bacteroides vulgatus*, and *Prevotella tannerae*). Multiple antibiotic courses: positive association of phylum Firmicutes (streptococci) and BMI. Actinobacteria (particularly *B. infantis, B. pseudocatenulatum, B. longum, and B. thermophilum*) were negatively associated with BMI.	[81]
81 maternal (oral, intestinal and vaginal) and 248 neonatal (oral, pharyngeal, meconium and amniotic fluid)	Maternal GDM in maternal-neonatal microbiota	*Prevotella, Streptococcus, Bacteroides* and *Lactobacillus* were prevalent in multiple sample types of maternal and neonatal microbiota, reflecting their possible significance to GDM	[59]

Abbreviations: BMI: body mass index; GDM: gestational diabetes mellitus; N: normal weight; OW: overweight; OB: obese; GWG: gestational weight gain; HFD: high-fat diet; HFF: Hepatic fat fraction

Maternal metabolic impact on breast milk composition

Human milk is considered to be the "gold standard" for infant nutrition due to its many epidemiologically demonstrated advantages for both mothers and infants, most notably the decreased risk of NCDs, including obesity and other metabolic-related problems [82]. In addition to its nutritional components, breast milk contains a complex and varied mixture of bioactive compounds, including proteins, peptides, lipids, micronutrients, nucleotides, hormones, growth factors, immunomodulatory agents, human milk oligosaccharides (HMO), and microbes [83].

The maternal pre-gestational BMI shapes the milk microbiota [84]. The mother's BMI has been found to be positively associated with colostrum *Lactobacillus* and *Staphylococcus* levels, as well as negatively associated with *Bifidobacterium* count, in milk samples. These findings were

confirmed by mixed model analyses, which also identified an increase in the total number of bacteria in milk with an increasing maternal BMI [84]. Similarly, an association between gestational weight gain and the human milk microbiota has been reported, with the microbiome being less diverse with an increased gestational weight gain [84]. A recent study involving 393 breast milk samples obtained at three to four months postpartum [85] demonstrated that the composition and diversity of the milk microbiota were associated with maternal BMI, parity, mode of delivery, breastfeeding practices, and sex of the offspring. Furthermore, a number of studies have highlighted the impact of the maternal BMI on human milk components such as the leptin and insulin hormones, fatty acids, and some cytokines [86-88]. Modulation of breastmilk composition through dietary, pre-, pro-, post-biotic interventions, aiming to beneficially steer the gut microbiome establishment in early life and infant metabolic homeostasis is an area of research still to be explored.

Breastfeeding and the gut microbiota: a key interaction to reduce obesity and metabolic diseases

A recent meta-analysis [89], which included seven studies conducted in different locations (>1825 gut samples obtained from 684 infants), reported that exclusive breastfeeding practices shape the gut microbiota by promoting higher relative abundances of Bacteroidetes and Firmicutes. This change in bacterial composition is accompanied by increases in predicted microbial pathways related to carbohydrate, lipid and vitamin metabolism, as well as detoxification pathways, when compared to non-exclusively breastfed neonates. The identified differences in the predicted microbial pathways were higher in the non-breastfed neonates delivered by C-section when compared to the vaginally delivered neonates. Recently, it has been demonstrated that the shifts induced by C-section delivery on infant gut microbiome may be partially reestablished to a similar-vaginal birth microbiota by exclusive breastfeeding [90]. Furthermore, exclusive breastfeeding practices of a longer duration were associated with lower gut microbiota dysbiosis related to diarrhea. The gut microbiota differences between the exclusively and non-exclusively breastfed neonates persisted until six months of age, suggesting the short- and long-term benefits of exclusive breastfeeding in terms of the gut microbiota across different populations.

Concluding remarks

The maternal metabolic status both before and during gestation exerts a significant influence on the infant microbiota at the beginning of life. Although the maternal diet has an influence on the infant microbiota, it appears that early-life nutritional patterns (e.g. breastfeeding, formula fed) have a stronger effect on the microbiota.

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