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The role of the maternal gut microbiome in regulating endocrine function during pregnancy and postpartum: implications for neonatal health

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Abstract

Objective: This systematic review aims to examine the role of the maternal gut microbiome in regulating endocrine function during pregnancy and the postpartum period, and its effects on neonatal health. Additionally, it assesses the effectiveness of microbiome-targeted interventions and identifies knowledge gaps in the current literature to inform future research directions.

Design and Methods: A systematic literature review was conducted following PRISMA 2020 guidelines. Searches were performed in PubMed, Scopus, and the Cochrane Library. Out of 94 identified records, 19 studies met the inclusion criteria based on the PICOST framework. The included studies were critically appraised using the Caldwell framework.

Results: Findings indicate that metabolites derived from the maternal gut microbiome influence maternal endocrine function, affecting maternal weight and neonatal outcomes such as birth weight and length. Specific microbial profiles were found to predict gestational age and neonatal development, while some were linked to excessive fetal growth. In cases of gestational diabetes mellitus, notable dysbiosis was observed in both mothers and their newborns, with significant implications for health. The use of probiotics showed mixed results, beneficial in some studies, ineffective in others.

Conclusion: The maternal gut microbiome plays a critical role in maternal and neonatal health by interacting with the endocrine system and influencing key developmental outcomes. However, this emerging field remains under-researched. Further longitudinal and mechanistic studies are needed to clarify causal pathways and to evaluate the clinical utility of microbiome-based interventions during pregnancy.

Keywords: Maternal Gut Microbiome; Pregnancy; Postpartum Period; Endocrine Function; Hormonal Regulation; Neonatal Health

1. Introduction

Understanding the role of the maternal gut microbiome in regulating endocrine function during pregnancy and postpartum is a growing area of interest in maternal-child health. The gut microbiota influences host metabolism, immunity, and hormonal balance functions that are especially critical during gestation. Disruptions in microbial composition have been associated with adverse pregnancy outcomes and long-term consequences for neonatal health [1–3]. This systematic review aims to synthesize current findings on this topic and highlight gaps in the literature.

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1.1. The Role of the Gut Microbiome in Humans

The human gut microbiome comprises approximately 35,000 bacterial species, alongside archaea, fungi, and viruses, forming a complex and symbiotic ecosystem [1–5]. While viruses are often excluded from formal definitions, they are present within the microbiome [6]. The composition of the gut microbiota varies by geography, diet, lifestyle, age, genetics, medications, and environmental exposures, including breastfeeding and maternal oral microbiota [1,6–9]. The dominant phyla in a healthy gut are Firmicutes and Bacteroidetes, followed by Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia [10]. Key genera include Lactobacillus, Clostridium, Bacteroides, Prevotella, and Bifidobacterium [11].

The gut microbiome contributes to nutrient and xenobiotic metabolism, energy homeostasis, immune maturation, intestinal barrier function, and neurological development [2,6,7,12]. It also plays a role in host-microbe communication via neuroendocrine and immunometabolic pathways and is thus considered a vital organ [1,6,10]. Short-chain fatty acids (SCFAs), mainly acetate, propionate, and butyrate, produced by microbial fermentation of dietary fibers and human milk oligosaccharides, support epithelial integrity, modulate inflammation, and regulate appetite, blood pressure, weight, and glucose metabolism [4,6,13–16]. SCFAs interact with G-protein-coupled receptors, influence hormone secretion, and are linked to insulin sensitivity and reduced adiposity [16-18]. Butyrate, in particular, has anti-inflammatory and possibly antitumor effects [6], while higher levels of SCFAs are associated with reduced asthma and atopy risk [19]. The microbiome plays a dual role with the immune system, influencing T cell differentiation, neutrophil regulation, and immune tolerance [1,19–22]. Dysbiosis is associated with immune-related diseases such as eczema and allergies, marked by shifts in bacterial families [7,12]. Via the gut–brain axis, gut microbes affect neurotransmitter production and are linked to emotional and cognitive functions [10,11,14]. Gut bacteria also synthesize vitamins and regulate bile acid metabolism, affecting lipid peroxidation, hepatic fatty acid synthesis and triglyceride storage [1,6,20].

Moreover, the gut microbiome modulates absorption of iodine, selenium, iron, and zinc [17], contributing to micronutrient homeostasis [15]. It also regulates endocrine function by interacting with insulin, estrogens, and androgens [17,18]. Alterations in microbial taxa are associated with insulin resistance and glucose levels [14,17,23]. Microbiota-related mechanisms include inflammation modulation, fat storage, and amino acid and bile acid metabolism [24]. Overall, the gut microbiome plays a pivotal role in human physiology, particularly during pregnancy, where it can influence hormonal balance, immune tolerance, and metabolic adaptation.

1.2. The Gut Microbiome During Pregnancy

Pregnancy is characterized by profound hormonal, metabolic, and immunological changes essential for fetal development, which also influence the maternal gut microbiome [9]. The microbiota, mainly residing in the colon, undergoes trimester-specific alterations influenced by maternal age, pre-pregnancy BMI, height, residence, and hematological factors [14,25,26]. Throughout pregnancy, microbial diversity and composition shift: alpha diversity declines, while beta diversity increases, along with elevated Firmicutes/Bacteroides ratios and increased abundance of Actinobacteria, Proteobacteria, Blautia, Collinsella, and Bifidobacterium species [10,27]. These changes are associated with reduced insulin sensitivity and enhanced nutrient absorption to support gestation [10,27]. A rise in pro-inflammatory cytokines and gut bacteria helps mobilize fat stores to fuel fetal growth, while increased SCFA production, elevated leptin, insulin, and insulin resistance further adapt maternal metabolism [11,15,28,29].

Notably, the third-trimester gut microbiome resembles a dysbiotic state, similar to that seen in metabolic syndrome, yet is physiologically beneficial during pregnancy [8,27]. A progressive decrease in microbial diversity is observed, alongside increases in Proteobacteria, Actinobacteria, Enterobacteriaceae, and Streptococcus spp. [17]. Cytokine levels rise significantly in late gestation, with low-grade mucosal inflammation [27]. The endocrine environment, particularly rising levels of progesterone and estrogens, modulates the microbiome through mechanisms such as reduced gut motility [11,17]. Progesterone may promote vertical transmission of beneficial microbes, like Bifidobacterium, which increase in late pregnancy and support infant gut and immune health [7,18]. The gut microbiota also impacts maternal-fetal energy metabolism. Taxa such as Bacteroides, Staphylococcus, Lachnospiraceae, Prevotellaceae, and Ruminococcaceae are associated with adiposity and metabolic profiles [17]. Elevated Firmicutes, Proteobacteria, and Actinobacteria in late gestation contribute to fetal weight gain and glucose transfer, but may induce maternal hyperglycemia [11]. Cortisol levels increase under CRH influence toward term, aiding in metabolic homeostasis and preparation for labor. Changes in insulin and glycogen also support maternal-fetal glucose balance [5]. Dysbiosis during pregnancy may contribute to complications and affect offspring health. Thus, maintaining microbial balance through nutrition and probiotics/prebiotics is considered essential [14].

1.3. Initiation of Gut Microbiome Colonization

Recent studies using advanced techniques have identified bacterial DNA in the amniotic fluid, uterus, placenta, and meconium, challenging the long-standing view of the womb as a sterile environment [6,7]. These findings suggest that microbial colonization may begin in utero through maternal–fetal microbial exchange, potentially influencing fetal immune system development. However, many studies fail to detect a distinct fetal microbiome, attributing previous findings to contamination during sampling, as no viable bacterial colonies were observed [6,7]. Despite the ongoing debate, the neonatal gut is widely believed to encounter its first significant microbial exposure during passage through the birth canal [30]. A recent systematic review comparing evidence for in utero colonization versus the sterile womb hypothesis concluded that the majority of data supports the sterility of the intrauterine environment, with only limited and inconclusive evidence against it [31].

1.4. Interaction Between the Maternal Gut Microbiome and the Fetus

The fetal and neonatal gut microbiome is shaped by the maternal gut microbiota and perinatal factors [10]. Maternal microbes may be vertically transmitted via the placenta, facilitated by increased gut permeability and altered placental integrity, allowing microbial components to reach the fetus [23]. While direct bacterial transfer remains under debate, it is well established that immune molecules and microbiota-derived metabolites, such as TLR ligands, SCFAs, neurotransmitters, B vitamins, folate, and polyphenols, cross the placenta and influence fetal gene expression, neurodevelopment, and the gut–brain axis [11,21]. These factors support immune and nervous system maturation, thalamocortical development, and brain connectivity, with long-term effects on cognition and behavior. For instance, maternal microbiome diversity and butyrate-producing bacteria have been associated with reduced anxiety behaviors in children [11]. The maternal microbiota also influences fetal HPA axis regulation, cortisol production, and early stress responses through microbial antigens and cytokines [11]. Maternal stress and dysbiosis can disrupt this system, contributing to necrotizing enterocolitis and impaired fetal development [5]. Additionally, SCFAs modulate IL-6, T cell function, epithelial integrity, and neuroimmune development [11,32,33]. Gut eubiosis promotes fetal myelination, whereas dysbiosis may lead to neuroinflammation and neuronal damage [11]. Low maternal acetate is linked to preeclampsia, while SCFA signaling may protect against offspring obesity [11, 18].

1.5. The Neonatal Gut Microbiome

At and after birth, the neonatal gut is colonized by microbes from the maternal gut, vagina, mouth, skin, and the environment [34]. Maternal sources contribute differentially, fecal, vaginal, oral, and skin microbiota, with fecal influence increasing over time [34]. Vertical transmission is key, as maternally derived microbes are more likely to persist than those from external sources [7], though evidence remains limited [25]. Gut colonization is influenced by gestational age, sex [34], maternal genetics, delivery mode, breastfeeding, diet, antibiotic exposure, and smoking [19,21]. Vaginal delivery promotes maternal-like gut colonization [35], while cesarean delivery is linked to reduced diversity, delayed immune development, and higher risk of asthma and allergies [21].

Breastfeeding fosters Bifidobacteria through natural probiotics, while formula feeding promotes Clostridia and Bacteroides [22]. Breast milk provides immunoglobulins, cytokines, and protective IgG against E. coli [21]. It contributes ~27% of the infant's microbiome in the first year; another 10% comes from maternal skin [21]. The neonatal microbiome supports immune maturation, nutrient metabolism, and pathogen defense [25,36]. Early colonizers include Enterococcus, Staphylococcus, and Enterobacteriaceae, followed by Lactobacillus, Clostridium, Bifidobacterium, and Bacteroides [37]. By age one, microbial diversity increases, approaching adult-like composition dominated by Actinobacteria, Firmicutes, and Bacteroidetes [35,37]. Development progresses in three phases, developmental (0–14 months), transitional (15–30 months), and stabilization (31–46 months) [19], with a shift from facultative to obligate anaerobes as gut oxygen levels drop [21]. The neonatal microbiome, composed mainly of Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, and Verrucomicrobiae, is more adaptable than the adult microbiome [6,21].

1.6. Gut Microbiome Dysbiosis

During pregnancy, maternal gut dysbiosis refers to the imbalance or maladaptation of the gut microbiome, influenced by factors such as obesity, diet, inflammation, stress, infections, and medication use [11]. Dysbiosis has been linked to adverse maternal and neonatal outcomes, including preeclampsia, gestational diabetes, intrauterine growth restriction, and increased risk of metabolic, immune, and neurodevelopmental disorders in the offspring, such as obesity and autism [1,16,26,30,38]. Vertical transmission of a dysbiotic microbiome may occur during gestation or delivery, affecting neonatal gut colonization and development [15,23]. For example, gestational diabetes alters maternal and neonatal microbiota composition, reducing microbial diversity and promoting pro-inflammatory bacterial profiles [10,19,23]. Similarly, maternal stress and elevated cortisol levels are associated with reduced beneficial bacteria and increased potential pathogens in the neonate [18]. Early-life dysbiosis has been associated with conditions such as NEC, sepsis,

asthma, eczema, and metabolic dysfunction [6,33,34]. Probiotic use during pregnancy may help restore microbial balance and support maternal and neonatal health [39].

1.7. Probiotics and Prebiotics

Probiotics are live microorganisms which, when administered in adequate amounts, confer health benefits to the host [40]. They modulate gut microbiota composition and function, aiming to counteract the negative effects of dysbiosis [41,42]. Generally considered safe, probiotics support maternal and neonatal health by promoting symbiotic bacteria, enhancing intestinal barrier function, and regulating immune responses [14]. They also help restore deficiencies in the neonatal microbiome [34], prevent inflammatory gut disorders [12], and stimulate the growth of beneficial microbes, including bacteria and fungi [43].

During and after pregnancy, probiotic supplementation may reduce the risk of gestational diabetes, preterm birth, mastitis, constipation, postpartum depression, infant atopic dermatitis, and Group B Streptococcus colonization. They are also associated with improved glucose metabolism, reduced inflammation, and enhanced neonatal gut colonization [43]. Prebiotics, typically non-digestible oligosaccharides, support probiotic activity. When combined with probiotics, they form synbiotics. These fibers are selectively fermented by gut bacteria to produce SCFAs, which contribute to intestinal health [2]. Prebiotics enhance gut motility, epithelial integrity, and mucosal maturation, while limiting pathogen growth [12]. Postnatal maternal intake of prebiotics increases SCFA levels in offspring, which may cross the blood–brain barrier and influence brain function [33].

1.8. Antibiotics

Antibiotic use disrupts the maternal vaginal microbiome, a major contributor to neonatal gut colonization [21]. This disruption is associated with increased asthma severity, heightened anxiety and reduced social behavior in offspring [14], and a higher risk of childhood-onset Crohn's disease [39]. Notably, amoxicillin/clavulanic acid use has been linked to a fourfold increased risk of NEC [30]. Prenatal antibiotic exposure alters neonatal gut microbiota. For instance, intrapartum antibiotic prophylaxis for Group B Streptococcus is transferred via the umbilical cord and reduces beneficial Bifidobacterium, while increasing potentially pathogenic Escherichia and Enterococcus strains [7]. It also reduces Lactobacillus, essential for dendritic cell maturation, potentially delaying neonatal immune responses and increasing the risk of early-onset sepsis [21]. Co-administration of probiotics is recommended to mitigate the adverse effects of antibiotics [39]. These findings underscore the gut microbiome's crucial role in systemic homeostasis across life stages, particularly in conditions like gestational diabetes and obesity. Restoring microbiome balance through probiotics and prebiotics has shown promise and is a growing area of research. The following sections of this review will explore in detail the maternal gut microbiome's role in hormonal regulation, fetal development, neonatal outcomes, and the impact of maternal dysbiosis and microbiome-targeted interventions on neonatal endocrine and metabolic health.

2. Design and Methods

To identify the literature for review, a structured search was conducted in the electronic databases PubMed/Medline, Scopus, and Cochrane Library. The searches were performed between November 2024 till May 2025. covering literature published from 2014 to 2024. Initially, a broad search strategy was applied, which was then refined into three specific search algorithms, each targeting key concepts: (1) gut microbiome, (2) endocrine function, (3) pregnancy, (4) postpartum period, and (5) neonatal outcomes.

The search terms included both MeSH terms and free-text keywords combined using Boolean operators (AND/OR). Table 1 below presents the databases used, the specific search algorithms applied in each, and the central research question that guided the search process. Only English language articles were considered. Inclusion criteria comprised peer-reviewed original research studies, systematic reviews, and meta-analyses focusing on the maternal gut microbiome and endocrine interactions during pregnancy and their effects on neonatal health. Studies involving animals, non-pregnant populations, or unrelated outcomes were excluded. After removing duplicates, titles and abstracts were screened for relevance, and full-text articles were assessed based on predefined eligibility criteria. Systematic theoretical reviews provide valuable insights into medical practices and help identify research gaps across a wide range of medical and social issues. They aim to identify all relevant studies that address a specific research question [44]. This systematic theoretical literature review was conducted in accordance with the steps outlined in the PRISMA Statement [45].

Table 1 Search Algorithms and Research Question per Database

Search Algorithm No.	Database	Search Terms	Research Question
1	PubMed/Medline	(Gut-microbiome OR Gut-microbiota OR Intestinal-microbiota OR Gastrointestinal-microbiome OR Dysbiosis OR Microbiome-composition OR Probiotics OR Prebiotics) AND (Endocrine-function OR Hormonal-regulation OR Insulin OR Cortisol OR Thyroid-hormones OR Estrogen OR Progesterone OR Glucocorticoids OR Adiponectin OR Leptin OR Ghrelin OR HPA-axis OR Hypothalamic-Pituitary-Adrenal-axis) AND (Pregnancy OR Postpartum OR Gestation OR Prenatal OR Perinatal OR Maternal) AND (Neonatal-health OR Neonatal-outcomes OR Neonatal-endocrine-function OR Neonatal-metabolism OR Birth-weight OR Neonatal-growth OR Neonatal-immune-development OR Neonatal-obesity OR Neonatal-diabetes OR Neonatal-metabolic-syndrome	To investigate the role of the maternal gut microbiome in regulating endocrine function during pregnancy and childbirth: implications for neonatal health.
2	Scopus	(“Gut microbiome” OR “Gut microbiota” OR “Intestinal microbiota” OR “Gastrointestinal microbiome” OR “Dysbiosis” OR “Microbiome composition” OR “Probiotics” OR “Prebiotics”) AND (“Endocrine function” OR “Hormonal regulation” OR “Insulin” OR “Cortisol” OR “Thyroid hormones” OR “Estrogen” OR “Progesterone” OR “Glucocorticoids” OR “Adiponectin” OR “Leptin” OR “Ghrelin” OR “HPA axis” OR “Hypothalamic Pituitary Adrenal axis”) AND (“Pregnancy” OR “Postpartum” OR “Gestation” OR “Prenatal” OR “Perinatal” OR “Maternal”) AND (“Neonatal health” OR “Neonatal outcomes” OR “Neonatal endocrine function” OR “Neonatal metabolism” OR “Birth weight” OR “Neonatal growth” OR “Neonatal immune development” OR “Neonatal obesity” OR “Neonatal diabetes” OR “Neonatal metabolic syndrome”)	To investigate the role of the maternal gut microbiome in regulating endocrine function during pregnancy and childbirth: implications for neonatal health.
3	Cochrane Library	(Gut AND microbiome OR Gut AND microbiota OR Intestinal AND microbiota OR Gastrointestinal AND microbiome OR Dysbiosis OR Microbiome AND composition OR Probiotics OR Prebiotics) AND (Endocrine AND function OR Hormonal AND regulation OR Insulin OR Cortisol OR Thyroid AND hormones OR Estrogen OR Progesterone OR Glucocorticoids OR Adiponectin OR Leptin OR Ghrelin OR HPA AND axis OR Hypothalamic AND Pituitary AND Adrenal AND axis) AND (Pregnancy OR Postpartum OR Gestation OR Prenatal OR Perinatal OR Maternal) AND	To investigate the role of the maternal gut microbiome in regulating endocrine function during pregnancy and childbirth: implications for neonatal health.

		(Neonatal AND health OR Neonatal AND outcomes OR Neonatal AND endocrine AND function OR Neonatal AND metabolism OR Birth AND weight OR Neonatal AND growth OR Neonatal AND immune AND development OR Neonatal AND obesity OR Neonatal AND diabetes OR Neonatal AND metabolic AND syndrome)	

2.1. Inclusion and Exclusion Criteria

To determine the inclusion and exclusion criteria of the studies, the PICOST framework was applied [46]. Specifically, studies were included if they involved pregnant women (Population), investigated the maternal gut microbiome (Intervention), and included a comparison related to endocrine function (Comparison). Eligible studies were required to report outcomes associated with neonatal health (Outcome). Regarding study design, only primary research studies, both quantitative and qualitative, were considered; studies not available in full text or published in languages other than English were excluded. Finally, with respect to timeliness, the review was limited to studies published between 2014 and 2024; those published outside this period were not included.

2.2. Search Results and Data Extraction

The initial search was conducted in the PubMed, Scopus, and Cochrane Library databases. A total of 109 records were identified. Among these, 25 were retrieved from PubMed/Medline, 83 from Scopus, and 1 from the Cochrane Library. After removing 25 duplicate records, 84 unique records remained for screening. Table 2 provides an overview of the number of articles retrieved from each database, the total number of duplicate entries, and the final number of articles included after de-duplication.

Table 2 Number of Articles by Database and Deduplication Process

Database				**Total with Duplicates**	**Duplicate Entries**	**Total without Duplicates**
PubMed/Medline	Scopus		Cochrane Library	109	25	84
25	83		1			

Following the initial database search, each article was carefully screened to determine its relevance to the study topic. The first level of screening involved a review of article titles and abstracts to eliminate those unrelated to the research question: the role of the maternal gut microbiome in the regulation of endocrine function during pregnancy and childbirth, and its implications for neonatal health.

As noted above, not all studies were deemed eligible. Following the initial screening, 74 articles were excluded. The remaining 10 articles were assessed in detail. During the full-text retrieval phase, 1 article was found to be inaccessible, resulting in 9 articles eligible for analysis. An additional 10 relevant articles were identified and added, bringing the total number of included studies to 19. All studies were evaluated for methodological quality using the Caldwell appraisal framework [47], which is suitable for both quantitative and qualitative research. The selection process is visually presented in the PRISMA 2020 flow diagram shown in Figure 1.

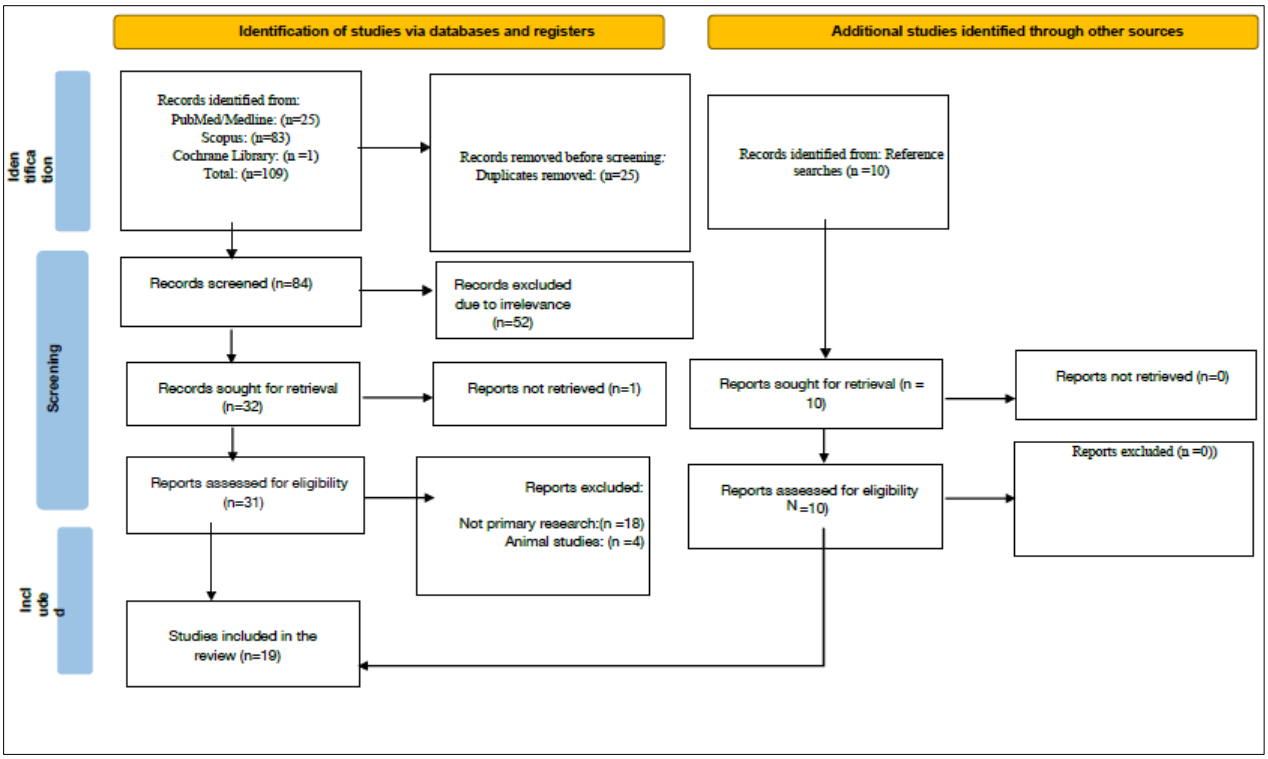

Figure 1 PRISMA 2020 Flow Diagram

Subsequently, the following variables were extracted from the selected studies: the first author, year of publication, type of study, sample size relevant to the target population, overall sample size, method and type of data collection, comparison group (if available), main findings of each study, specific findings related to the research question on mode of delivery, follow-up with the sample (if applicable), study limitations, journal of publication, and country in which the study was conducted.

3. Results

A total of 19 scientific articles published between January 1, 2014, and January 1, 2024, were analyzed. These studies investigated the role of the maternal gut microbiome in regulating endocrine function during pregnancy and childbirth, as well as the implications for neonatal health. The studies were conducted across various countries, including China (n=8), Australia (n=2), Ireland (n=2), Malta (n=1), Denmark (n=1), the United States (n=1), Israel (n=1), Zimbabwe (n=1), Germany (n=1), and Finland (n=1).

Each article was reviewed in detail, and essential data were extracted and recorded in a Microsoft Excel spreadsheet, organized in ascending chronological order based on the publication date, as outlined in Subsection 2.2. Table 3 presents a summary of key findings from the 19 reviewed studies, with a particular focus on the role of the maternal gut microbiome in hormonal regulation.

Table 3 Concise overview of the principal characteristics and findings of the reviewed studies

	First Author	Title	Year	Journal of Publication	Country	Type of Study	Participants	Target Group	Measurement and Data Collection Method	Comparison Group	Measured Outcome	Main Findings	Specific Findings Related to Mode of Delivery	Follow-up with Sample	Study Limitations
1	Abela, Alexia G	Prenatal and early life factors and type 1 diabetes	2022	Endocrine	Malta	Retrospective case-control study	A total of 89 mothers of children with type 1 diabetes and 89 mothers of healthy children participated.	89 mothers of children with type 1 diabetes	An interview was conducted.	89 mothers of healthy children	The possible role of prenatal and perinatal factors as causes in the development of type 1 diabetes was investigated.	Handwashing before meals, bathing frequency, and the overall stress score were found to be positively associated with the development of type 1 diabetes.	Regarding the mode of delivery, 16.9% of patients with type 1 diabetes and 18% of healthy individuals were born by cesarean section.	No follow-up contact with the sample was reported.	Limitations of the present study include the lack of assessment of childhood behavioral habits through the questionnaire, as well as the retrospective study design rather than a prospective one.

2	Lan Yehui	The relationship between gut microbiota, short-chain fatty acids, and glucolipid metabolism in pregnant women with large for gestational age infants	2023	Journal of Applied Microbiology	China	Observational prospective cohort study	A total of 49 pregnant women participated, of whom 4 participants were excluded.	Eighteen women who gave birth to large-for-gestational-age neonates.	Fecal samples were collected from each pregnant woman prior to delivery for the analysis of gut microbiota composition and short-chain fatty acids. Additionally, blood samples were obtained at 24–28 weeks of gestation, as well as shortly before delivery	27 women who gave birth to neonates appropriate for gestational age.	The association between the gut microbiota of SCFAs and glucolipid metabolism was investigated in women with large-for-gestational-age infants.	Multiple distinct taxonomic strains, particularly the phylum Firmicutes and the genera Prevotella and Clostridium, may contribute to excessive fetal growth and the birth of large-for-gestational-age neonates. Additionally, these strains might be associated with lower serum HDL levels.	No findings regarding the mode of delivery were reported.	No follow-up contact with the sample was reported.	Limitations of the present study include the inability to account for lifestyle and dietary factors of the population, which may influence the gut microbiome, SCFAs, and glucose-lipid metabolism, as well as the small sample size.
3	Halkjær Sofie I.	No effect of multi-strain probiotic supplementa	2023	Nutrition, Metabolism and	Denmark	Randomized, double-blind placebo-controlled study	A total of 50 obese pregna	The focus group consist	Two visits were conduct	The comparison group	The effects of probiotic suppleme	After probiotic supplementation,	From the group of	There was no follow-up	Limitations of the present study

		tion on metabolic and inflammatory markers and newborn body composition in pregnant women with obesity: Results from a randomized, double-blind placebo-controlled study		Cardiovascular Diseases			nt women participated, of whom 49 completed the study.	ed of 25 women who received the probiotic.	ed at 27–30 weeks and 36–37 weeks of gestation, and one visit postpartum. During each visit, fasting blood samples were collected to measure specific factors. At the first postpartum visit, a DXA scan was performed on the neonate.	consisted of 24 women who received the probiotic placebo.	ntation during pregnancy on metabolic and inflammatory markers, as well as on offspring development, were investigated.	no significant changes were detected in the measured biomarkers, offspring development, GLP-1, or glucagon. However, GLP-1 levels measured from umbilical cord blood were positively associated with offspring fat levels in the probiotic group.	women who received the probiotic, 6 delivered by cesarean section and 10 delivered vaginally, while in the placebo group, 3 women delivered by cesarean section and 17 vaginally. Preterm births were excluded.	contact with the sample reported.	include the small sample size, the short duration of probiotic administration, the low probiotic dose, as well as the lack of precise information regarding the fasting status of the women before sample collection.

4	Lindsay Karen L.	Probiotics in obese pregnancy do not reduce maternal fasting glucose: A double-blind, placebo-controlled, randomized trial (Probiotics in Pregnancy Study)	2014	American Journal of Clinical Nutrition	Irland	Single-center double-blind, placebo-controlled, randomized trial	A total of 175 pregnant women participated, of whom 138 completed the study.	The focus group consisted of 63 pregnant women who received the probiotic.	Fasting blood samples were collected during pregnancy, fetal biometric ultrasound was performed, and blood samples were taken from the umbilical cord after delivery.	The comparison group consisted of 75 pregnant women who received the placebo probiotic.	The effects of probiotic administration on maternal fasting glucose levels in obese pregnant women were investigated.	After probiotic administration, no effect was observed on maternal fasting glucose levels, metabolic profile, or pregnancy outcomes.	From the group of women who received the probiotic, 20 delivered by cesarean section, whereas in the group that received the placebo capsule, 25 delivered by cesarean section.	There was no follow-up contact with the sample reported.	Limitations of the present study include the lack of stool sample collection and the fact that the randomization of the women occurred several weeks before the start of capsule administration.

5	Nachum Zohar	The effect of oral probiotics on glycemic control of women with gestational diabetes mellitus, a multicenter, randomized, double-blind, placebo-controlled trial	2024	American Journal of Obstetrics and Gynecology MFM	Israel	Multicenter prospective randomized, double-blind, placebo-controlled trial	A total of 93 pregnant women participated, of whom 85 completed the study.	The focus group consisted of 44 pregnant women who received the probiotic.	After receiving clear instructions, each participant individually completed daily glucose monitoring charts.	The control group consisted of 41 pregnant women who received the probiotic placebo.	The effects of a probiotic strain mixture were investigated in mothers with gestational diabetes mellitus, specifically on maternal glycemic parameters, particularly fasting and postprandial glucose level, as well as on pregnancy outcomes.	After probiotic administration, no effect was observed on glycemic control in women with gestational diabetes mellitus.	Among the women who received the probiotic, 18 delivered by cesarean section, whereas among the women who received the placebo capsule, 7 delivered by cesarean section.	There was no follow-up contact with the sample reported.	The limitations of the study are that the sample size is not powered for maternal and neonatal outcomes. In addition, our sample size was calculated to demonstrate a reduction in treatment failure in the probiotic group by half but was insufficient to detect a smaller treatment effect.
6	Yajuan Xu, X	Differential intestinal and oral	2020	Am J Physiol Endocri	China	Randomized clinical trial	A total of 61 pregna	The focus group	Stool and saliva	The control group	The primary objective	It was observed that gut	All deliveries	There was no follow-	Limitations of the present

		microbiota features associated with gestational diabetes and maternal inflammation		nol Metab			nt women participated, including 30 women with gestational diabetes mellitus and 31 healthy women.	consisted of 30 women with gestational diabetes mellitus.	samples were collected, routine blood draws were performed, and C-reactive protein levels were measured. Additionally, between 24 and 28 weeks of gestation, insulin use was recorded, an oral glucose tolerance test was conducted, and glycated hemoglobin levels were	consisted of 31 healthy women.	of the present study is to further investigate the composition and diversity of the gut and oral microbiome in pregnant women, aiming to evaluate the presence of bacterial characteristics associated with GDM during pregnancy.	and oral microorganisms during pregnancy are directly associated with the status of GDM during the third trimester. Furthermore, changes in gut and oral microbiota may serve as non-invasive biomarkers for monitoring health and managing GDM throughout pregnancy.	were performed by cesarean section.	up contact with the sample reported.	study include the small sample size, its cross-sectional design, as well as geographic factors and dietary habits that impose regional constraints.

									measured. Finally, immediately after birth, blood glucose levels were measured for the first time in the group with GDM.						
7	Lindsay Karen L.	Impact of probiotics in women with gestational diabetes mellitus on metabolic health: A randomized controlled trial	2015	American Journal of Obstetrics and Gynecology	Ireland	Double-blind placebo-controlled randomized trial	A total of 149 pregnant women participated, of whom 49 were excluded.	The focus group consisted of 74 women who received the probiotic, of whom 48 completed the study.	Blood samples were collected at regular intervals following probiotic administration to measure metabolic parameters. Additionally,	The control group consisted of 75 women who received the placebo capsule, of whom 52 completed the study.	The effects of probiotic supplementation on maternal metabolic parameters and pregnancy outcomes were investigated in women with GDM.	No effect on glycemic control was observed following probiotic use. However, a reduction in LDL cholesterol was noted, independent of the physiological increase	Among the women who received the probiotic, 73 delivered by cesarean section, while among the women who received the	There was no follow-up contact with the sample reported.	Limitations of the present study include the 18% dropout rate of participants after the administration of the probiotic, and the fact that the study was not powered to detect

									umbilical cord blood was collected after delivery, where feasible.			typically associated with pregnancy.	placebo capsule, 74 delivered by cesarean section.		changes in LDL cholesterol levels. It is possible that the observed finding occurred by chance due to multiple outcome analyses.
8	Jiayang Wan	Effects of galactooligosaccharides on maternal gut microbiota, glucose metabolism, lipid metabolism and inflammation in pregnancy: A randomized controlled pilot study	2023	Frontiers in Endocrinology	China	Prospective double-blinded randomized clinical trial	A total of 52 healthy pregnant women participated.	The focus group consisted of 26 women who received the probiotic.	Blood and stool samples were collected, and a questionnaire was completed.	The control group consisted of 26 women who received the placebo capsule.	The feasibility and acceptance of the probiotic in healthy pregnant women, the effects of this intervention on pregnancy, and its impact on the gut microbiota were investigated.	It was observed that prebiotics containing galacto-oligosaccharides are safe and well-tolerated during pregnancy, and induced changes in the composition of the gut microbiome. However, no	In the group of women who received the probiotic, 6 delivered by cesarean section and 20 vaginally, whereas in the group who receiv	There was no follow-up contact with the sample reported.	Limitations of the present study include the small sample size and the fact that it was conducted in a single hospital, which may obscure potential regional differences.

												changes were observed in glucose levels or lipid metabolism.	ed the placebo capsule, 12 delivered by cesarean section and 14 vaginally.		
9	Priyadarshini Medha	Maternal short-chain fatty acids are associated with metabolic parameters in mothers and newborns	2014	Translational Research	USA	Prospective study	A total of 20 pregnant women participated.	A total of 20 pregnant women participated.	Blood samples were collected between 36 and 38 weeks of gestation, and neonatal anthropometric measurements were taken after delivery.	No control group is reported.	The possible correlation between serum LOBA levels and key metabolic parameters in the mother and neonate was investigated.	It was observed that acetate levels are associated with maternal weight gain and adiponectin levels, while propionate levels are negatively correlated with maternal leptin levels, as well as neonatal length and weight.	The mode of delivery is not reported.	There was no follow-up contact with the sample reported.	Limitations of the present study include the relatively small sample size and its conduction in a single hospital setting, which may limit the generalizability of the findings and obscure potential

															regional variations.
10	Gao Yuan	Maternal gut microbiota during pregnancy and the composition of immune cells in infancy	2022	Frontiers in Immunology	Australia	Cohort study	A total of 286 mother–infant pairs participated	A total of 286 pregnant women and their newborns participated as mother infant pairs.	Stool samples were collected from pregnant women at 36 weeks of gestation, umbilical cord blood was obtained at birth, and peripheral blood samples were collected from infants at 6 and 12 months of age.	No control group is mentioned	The relationship between the maternal gut microbiome during pregnancy and the composition of the infant's immune cells in umbilical cord blood and peripheral blood during the first year of life was investigated.	It was found that the maternal gut microbiome during pregnancy contributes to the shaping of both innate and adaptive components of the infant's immune system after birth.	The mode of delivery is not reported.	There was no follow-up contact with the sample reported.	Limitations of the present study include the use of immunological measures that are non-functional and limited to samples from umbilical cord blood and peripheral blood. Moreover, with regard to bacterial groups, not all taxa have been studied in detail, nor have the distinct biological

															functions and the specific significance of each group been fully investigated.
11	Gough Ethan K.	Maternal fecal microbiome predicts gestational age, birth weight and neonatal growth in rural Zimbabwe.	2021	EBioMedicine	Zimbabwe	Cluster-randomized trial	A total of 207 mothers and their newborns participated.	A total of 207 mothers and their newborns participated.	Stool samples were collected from the women during pregnancy and one month postpartum.	No control group was reported	The identification of maternal microbes and metabolic functions potentially influencing gestational age at birth, birth size, or neonatal growth was investigated. Additionally, the effects of the SHINE WASH intervention, baseline	It was found that the maternal fecal microbiome during pregnancy, particularly the abundance of resistant starch degraders, is a significant factor contributing to birth weight and neonatal growth, and to a lesser extent to gestational age, in	195 women delivered vaginally.	Follow-up with the sample was conducted one month postpartum with the mothers, along with intensive blood collection from the infants at 1, 3, 6, 12, and 18 months of age.	A limitation of the present study is that a large fraction of the sequenced reads could not be assigned.

											hygiene, hygiene-related factors, and maternal characteristics on the maternal fecal microbiome were examined.	infants of rural Zimbabwean mothers consuming a maize-rich diet.			
12	Sanjay Patole	Effect of Bifidobacterium breve M-16V supplementation on fecal bifidobacteria in preterm neonates--a randomised doubleblind placebo controlled trial	2014	PLOS One	Australia	Randomised Double Blind Placebo Controlled Trial	A total of 159 newborns participated.	The focus group consisted of 79 newborns who received the probiotic.	Stool samples were collected from the newborns before and after 3 weeks of supplement administration.	The control group consisted of 80 newborns who received the placebo capsule.	The product quality was investigated, and it was hypothesized that supplementation with Bifidobacterium breve M-16V would increase the number of B. breve in stool without	It was found that supplementation with B. breve M-16V is safe and effective in increasing B. breve levels in the stool of very low birth weight preterm infant	A total of 107 newborns were delivered by cesarean section, of whom 58 received the probiotic and 49 received the placebo capsule.	There was no follow-up contact with the sample reported.	A limitation of the present study is that the administration of the study supplement began as soon as the neonate was ready for feeding, without waiting for meconium passage.

											adverse effects.				
13	Minglian Su	Diversified gut microbiota in newborns of mothers with gestational diabetes mellitus	2018	PLOS One	China	Observational, cross-sectional study	A total of 34 full-term newborns participated, of whom the mothers of 20 had GDM.	The focus group consisted of 20 newborns whose mothers developed GDM.	Meconium samples were collected from the newborns.	The control group consisted of 14 newborns whose mothers did not develop GDM.	The potential impact of maternal gestational diabetes on the neonatal gut microbiota was investigated.	Taxonomic analyses indicated that the overall bacterial composition differed significantly according to maternal diabetes status, with the microbiome of the GDM group exhibiting lower alpha diversity compared to the control group. However, bacteria in the newborns of the class A2 GDM group showed	Thirty-four newborns were delivered by cesarean section.	There was no follow-up contact with the sample reported.	A limitation of the present study is the small sample size, as well as the possible administration of treatment for GDM in some mothers.

												no statistically significant variation compared to those of control newborns, which could be attributed to the additional insulin intervention.			
14	Niels van Best	Influence of probiotic supplementation on the developing microbiota in human preterm neonates	2020	Gut Microbes	Germany	Longitudinal observational study	A total of 80 preterm newborns participated.	A total of 80 preterm infants participated.	Stool samples were collected from the newborns.	The control group consisted of newborns who did not receive probiotics.	The effect of probiotic administration on microbiota development in preterm infants was investigated.	Successful transient colonization by probiotic bacteria was observed, along with a significant impact on the endogenous microbiota, characterized by a reduced abundance of bacterial	The majority of neonates were delivered by cesarean section.	There was no follow-up contact with the sample reported.	Limitations of the present study include the relatively small sample size, the observational nature of the study, and the sequential enrollment of the three patient groups.

												taxa associated with the development of NEC.			
15	Wang Jinfeng	Dysbiosis of maternal and neonatal microbiota associated with gestational diabetes mellitus	2018	Gut	China	Observational, cross-sectional study	A total of 140 newborns and 346 pregnant women participated.	A total of 140 newborns and 346 pregnant women participated.	Samples of saliva, pharyngeal aspirates, meconium, and amniotic fluid were collected from the newborns, while saliva, stool, and vaginal secretions were collected from the pregnant women.	No control group was reported.	Potential dysbiosis of the maternal and neonatal microbiota associated with gestational diabetes mellitus was investigated, and the possible risks of microbial alterations in the newborns were assessed.	It was observed that gestational diabetes mellitus may alter the microbiome of both pregnant women and their newborns at birth, shedding light on an alternative form of inheritance and emphasizing the importance of understanding microbiome establishment in early life.	Seventy-six newborns were delivered by cesarean section, and seventeen were delivered vaginally.	There was no follow-up contact with the sample reported.	No limitations were reported.

16	Yang Hongling	Systematic analysis of gut microbiota in pregnant women and its correlations with individual heterogeneity	2020	npj Biofilms and Microbiomes	China	Comprehensive review	A total of 1,479 pregnant women participated.	A total of 1,479 pregnant women participated.	Stool, urine, and blood samples were collected, and a questionnaire was completed.	No control group was reported	The structure and diversity associated with gestational age were investigated, along with correlations with gut microbiome factors during pregnancy and microbe–host interactions.	It was observed that the gut microbiome of pregnant women exhibits an overall structure similar to that of non-pregnant women of comparable age. A range of exogenous and endogenous host factors were found to be strongly associated with variations in the composition and function of the intestinal microbial community. In	The mode of delivery is not reported.	There was no follow-up contact with the sample reported.	Limitations of the present study include the restricted study design, as each participant provided only a single stool sample for analysis, and the fact that the study does not offer any mechanistic explanation for the observed variation in host and gut microbiome heterogeneity.

												addition, microbial and functional markers were identified that correlated with age, pre-pregnancy body mass index, residence status, and pre-pregnancy and gestational health conditions.			
17	Yassour Moran	Strain-Level Analysis of Mother-to-Child Bacterial Transmission during the First Few Months of Life	2018	Cell Host and Microbe	Finland	Prospective longitudinal cohort study	A total of 44 pregnant women and their newborns participated.	A total of 44 pregnant women and their newborns participated.	Stool samples were collected from the mothers and their newborns.	No control group was reported.	Cases of bacterial transmission from mother to offspring and the prevalence of antibiotic resistance genes within each family were	Two inheritance patterns were observed across multiple species, where the dominant maternal strain is often transmitted to the infant, but secondary	Seven neonates were born via cesarean section, and thirty-seven were born vaginally.	There was no follow-up contact with the sample reported.	No limitations were reported.

											investigated.	strains occasionally colonize the infant's gut. In families where the secondary strain of Bacteroides uniformis was inherited, the infant harbored a starch utilization gene cluster absent from the mother's dominant strain, suggesting a selective advantage of the secondary maternal strain in the infant gut.			
18	Wenqing Yang	Ongoing Supplementation of Probiotics to	2021	American Journal of	China	Randomized controlled trial	A total of 26 neonates	The focus group consist	Stool samples were collecte	The control group consist	The effects of probiotics on the	It was observed that after 28 days of	Twenty-three neonat	There was no follow-up	Limitations of the present study

		Cesarean-Born Neonates during the First Month of Life may Impact the Gut Microbial		Perinatology			participated.	ed of 14 neonates born via cesarean section who received the probiotic.	d from the neonates.	ed of 3 neonates born vaginally and 9 neonates born via cesarean section, none of whom received the probiotic.	gut microbiome of neonates born via cesarean section were investigated.	probiotic administration, the alpha and beta diversity of the gut microbiota in infants born via cesarean section were similar to those of infants born vaginally, while the abundances of Lactobacillus and Bifidobacterium significantly increased from the third day of probiotic administration.	es were born via cesarean section, and three were born vaginally.	contact with the sample reported.	include the small sample size and its short duration.
19	Hui Zhong	Impact of probiotics supplement on the gut	2021	World Journal of Pediatrics	China	Open-label single-center randomized parallel controlled study	A total of 55 neonates	The focus group included 25	Stool samples were collected from	The control group consisted of 17	The effects of probiotics on the gut	It was observed that early administration of	Nineteen neonates were	There was no follow-up contact	Limitations of the present study include

		microbiota in neonates with antibiotic exposure: an open-label single-center randomized parallel controlled study					participated.	neonates who received probiotics concurrently with antibiotic treatment, and 13 neonates who received probiotics after the completion of antibiotic therapy.	the neonates.	neonates who received neither antibiotic treatment nor probiotics.	microbiome of infected neonates were investigated, when administered either concurrently with antibiotics or during the recovery period following antibiotic treatment.	probiotics may have the potential to reshape the gut microbiome during recovery from antibiotic treatment.	born via cesarean section, and thirty-six were born vaginally.	with the sample reported.	the small sample size, the use of 16S rRNA sequencing technique, and the insufficient follow-up period to fully observe the long-term clinical or microbiological effects of exposure to antibiotics and supplemental probiotics.

3.1. Role of the Maternal Gut Microbiome in Hormonal Regulation

SCFAs, particularly acetate and propionate, are key fermentation products of the gut microbiota and are known to increase during weight gain, including in pregnancy [48]. These SCFAs were associated with maternal adiponectin and leptin levels, as well as with neonatal weight and length [48]. Specifically, a negative correlation was observed between maternal propionate levels and both leptin levels and neonatal anthropometric measures, while a positive correlation was noted between serum acetate levels and maternal adiponectin concentrations [48]. Adiponectin, a hormone involved in weight regulation, may play a role in gestational weight gain. Overall, the maternal gut microbiome, along with specific microbial taxa, appears to influence pre-pregnancy weight, gestational weight gain, and neonatal birthweight [49].

3.2. Impact on Fetal Development and Neonatal Outcomes

Differences in maternal gut microbiome composition have been linked to excessive fetal growth. In particular, mothers of large-for-gestational-age (LGA) neonates exhibited higher levels of Firmicutes and lower levels of Prevotella [16], suggesting a potential role in metabolic dysregulation contributing to fetal overgrowth. Elevated levels of Clostridium, through butyrate production, may also contribute to the LGA phenotype [16]. Furthermore, reduced maternal HDL cholesterol levels were noted in this group, which may serve as a predictive marker. These findings support the hypothesis that microbiome-targeted interventions could reduce the risk of excessive fetal growth. A study from Zimbabwe further demonstrated that maternal gut microbiota composition, particularly starch-degrading resistant microbes in maize-based diets, significantly influenced neonatal birthweight and postnatal growth [15]. Additional research indicated that maternal gut microbes during pregnancy contribute to the early programming of the neonatal immune system [50].

3.3. Vertical Transmission and Neonatal Immune-Endocrine Programming

During the first two weeks of life, the infant gut microbiome undergoes rapid shifts but remains less diverse than the adult microbiota. Despite overall dissimilarities between maternal and neonatal microbiota, certain bacterial strains, such as Bifidobacterium longum, Bacteroides vulgatus, B. dorei, B. uniformis, and Bifidobacterium adolescentis, were shared, indicating vertical transmission [25]. Dominant maternal strains tend to colonize the infant gut, while selective transmission of subdominant strains occurs based on their adaptive benefits [25]. Each microbial species appears to exhibit distinct transmission patterns, suggesting a highly selective and functionally relevant maternal-infant microbial transfer.

3.4. Dysbiosis and the Risk of Neonatal Endocrine or Metabolic Disorders

Maternal health status, particularly GDM, influences both maternal and neonatal gut microbiome composition. Women with GDM showed marked alterations in beta-diversity and increased levels of Gammaproteobacteria and Haemophilus, which may serve as non-invasive biomarkers for GDM diagnosis and management [24]. Commonly identified genera in these women included Bacteroides, Bifidobacterium, Blautia, Coprococcus, and Faecalibacterium [24]. Evidence suggests vertical transmission of GDM-associated microbial traits from mother to infant [36]. These alterations were linked to impaired metabolic pathways related to nutrient absorption and energy metabolism in neonates [36]. Furthermore, infants of diabetic mothers demonstrated increased prevalence of herpesviruses, poxviruses, papillomaviruses, and mastadenoviruses in their gut microbiome [36]. High levels of Lactobacillus iners may promote abnormal microbiota development by impairing amino acid metabolism in neonates [36]. Additionally, Blautia was associated with GDM onset, while Gemmiger showed a positive correlation with neonatal birthweight [24,49]. Overall, severe dysbiosis in infants of GDM mothers may predispose them to future gastrointestinal and metabolic disorders [51]. Environmental hygiene and maternal stress also influence early microbiome development. Frequent cleaning and excessive hygiene practices in early life were associated with increased risk of type 1 diabetes, whereas exposure to less sterile environments appeared protective [41].

3.5. Interventions During Pregnancy and Their Impact on Neonatal Health

Probiotic administration aims to reshape the gut microbiome and reduce adverse metabolic outcomes associated with dysbiosis. In a study by Halkjær and de Knegt, administration of a multi-strain probiotic to obese pregnant women showed a positive correlation between neonatal fat mass and glucagon-like peptide-1 levels in umbilical cord blood, though further investigation is warranted [38]. Across the reviewed studies, probiotics did not significantly improve neonatal outcomes such as birthweight, length, head or abdominal circumference, gestational age at birth, NICU admissions, Apgar scores, or metabolic biomarkers [29,38,40,52]. However, probiotic supplementation was also recommended for neonates born via cesarean section, especially when combined with breastfeeding [53]. In these cases, probiotic use enhanced both alpha and beta microbial diversity, aligning it more closely with that of vaginally delivered

neonates, and increased the abundance of Lactobacillus and Bifidobacterium species [53]. Additional studies reported increases in Bifidobacterium and Enterobacterium, alongside reductions in Escherichia coli, Enterococcus, and Klebsiella, and a reduced risk of NEC in preterm infants [54,55]. Moreover, no significant impact was observed on neonatal hypokalemia or hypomagnesemia [42].

With respect to maternal health, prebiotic supplementation with galacto-oligosaccharides (GOS) was found to be safe during pregnancy and led to increased abundance of Paraprevotella and Dorea, and decreased Lachnospiraceae UCG_001 [52]. Probiotic intake was associated with reductions in total and LDL cholesterol levels during pregnancy [29]. Nonetheless, no significant improvements were observed in fasting glucose, GDM incidence, gestational weight gain, preeclampsia, pharmacological treatment requirements, or glycemic control in women with GDM [29,40,42]. Antibiotic exposure, specifically piperacillin-tazobactam, was associated with reduced microbial richness in term infants and potential inhibition of Bifidobacterium and Lactobacillus proliferation [56]. Notably, concurrent administration of probiotics and antibiotics was found to support microbiome restoration, particularly increasing Bifidobacterium abundance [56]. Delayed probiotic supplementation, however, did not yield measurable benefits. These findings underscore the importance of timely probiotic co-administration in managing microbiota disruptions due to antibiotic use in neonates.

4. Discussion

This systematic review utilized a comprehensive literature search to identify evidence regarding the role of the maternal gut microbiome in regulating endocrine function during pregnancy and childbirth, and its implications for neonatal health. Overall, the findings indicate that the gut microbiome exerts multifaceted effects on both the mother and offspring. Specifically, microbial metabolites such as SCFAs are crucial determinants of maternal weight before and during pregnancy, as well as neonatal birth weight. Certain microbes have also been linked to the birth of large-for-gestational-age neonates [16,48,49]. For example, excessive gestational weight gain is positively associated with an increased abundance of Bacteroides/Prevotella, while overweight pregnant women exhibit higher levels of Clostridium species [16]. Moreover, metabolic hormones, together with the gut microbiome, synergistically influence metabolic health in overweight or obese pregnant women, as both hormone levels and microbiome profiles differ significantly in this population [17].

Additionally, maternal gut microbiota can predict birth weight, neonatal growth, and gestational age. The microbiome also substantially contributes to the development of the neonatal immune system [15,50]. Extracellular vesicles produced by the gut microbiota play a significant role in prenatal immune system regulation, a field still limited in research and warranting further investigation since most studies focus on postnatal microbial transmission [14]. Vertical transmission primarily involves dominant maternal microbial strains, with selective transmission of secondary strains based on their functional benefits to the host. Notably, different microorganisms exhibit unique transmission patterns [18].

Regarding dysbiosis, GDM induces significant alterations in both maternal and neonatal microbiomes, profoundly affecting offspring health [36,51]. Women with GDM showed decreased abundance of butyrate-producing Coprococcus and lactate-producing Streptococcus, alongside increased abundance of imidazole propionate-producing Megasphaera and Eggerthella [16]. These findings implicate the maternal gut microbiome and SCFAs in the pathogenesis of metabolic disorders [16]. Furthermore, lactobacilli possess anti-inflammatory properties potentially linked to reduced insulin resistance, alongside Butyricimonas and Firmicutes, which may mitigate excessive fetal growth via modulating maternal glucose metabolism [16]. The increase of Akkermansia spp. in the gut microbiome may inhibit obesity, insulin resistance, and gut inflammation, thereby improving glucose homeostasis [24]. Strong correlations between specific oral microbes and glucose tolerance measures support their potential as biomarkers for GDM, especially since oral samples are easier to obtain [36].

Excessive hygiene, cleanliness, and early-life stress can disrupt the gut microbiome, increasing the risk of type 1 diabetes, consistent with the hygiene hypothesis, which links reduced early microbial exposure to increased autoimmune diseases [41]. Reduced environmental microbial diversity since the 19th century may explain the rise in chronic inflammatory diseases in developed countries [41]. Probiotic and prebiotic supplementation during pregnancy and lactation is generally safe, with mild gastrointestinal side effects most commonly reported [43,52]. However, meta-analyses suggest a potential increased risk of preeclampsia, emphasizing the need for individualized assessment to balance benefits and risks [14,38].

The efficacy of probiotics, prebiotics, and synbiotics depends on microbial strain, dosage, indication, and host-specific factors such as health status, age, and baseline microbiome composition [43]. Supplementation in cesarean-born

neonates promotes gut microbiota development resembling that of vaginally born infants, especially increasing Bifidobacterium colonization [34,52,53]. However, data remain limited regarding optimal probiotic regimens to correct microbiota deficits in cesarean-born infants [34]. Probiotic use in women at high risk of preterm birth increased gestational length, reduced chorioamnionitis, and improved birth weight, with some evidence supporting reduced early neonatal sepsis, although data on NEC remain inconclusive [6,12,39,54,55]. Prebiotics containing GOS demonstrate immunomodulatory effects by reducing pro-inflammatory cytokines and increasing anti-inflammatory IL-10 [52]. Probiotics also contribute to immune regulation [14]. Supplementation with probiotics has been shown to reduce total and LDL cholesterol levels during pregnancy, independent of normal gestational increases [29].

Studies included in this review did not find significant improvements in GDM outcomes with probiotic supplementation in mothers or offspring [29,40,42]. However, other literature shows mixed results, with some evidence supporting improved glycemic control in non-pregnant diabetic women, raising questions about potential therapeutic roles in GDM [29]. For example, probiotic supplementation combined with dietary interventions improved glucose regulation and reduced GDM incidence in healthy pregnant women compared to placebo [40]. Yogurt enriched with probiotics helped maintain insulin concentrations, possibly preventing insulin resistance [40]. Probiotic intake during pregnancy decreased plasma glucose levels in the third trimester, lowered GDM risk, improved insulin sensitivity, and reduced incidence of insulin resistance, particularly with strains like L. rhamnosus and Bifidobacterium, without adverse effects reported in mothers or fetuses [40,42].

Meta-analyses indicate probiotic supplementation significantly lowers glucose, insulin, triglycerides, total cholesterol, and very low-density lipoproteins, with some evidence of reduced neonatal birth weight when L. acidophilus is included [42]. Multi-strain probiotics showed the greatest effect, reducing GDM incidence by approximately 33% [14]. Nonetheless, heterogeneity in strains, dosages, and duration complicates consensus on efficacy [40,52]. The World Allergy Organization recommends probiotics for pregnant and lactating women with children at high risk of allergies to prevent atopic dermatitis, although evidence is mixed regarding other allergic conditions [14,33]. Variability in probiotic strains and protocols likely underlies inconsistent findings [14].

Psychobiotics represent a novel class targeting the microbiota-gut-brain axis, with evidence suggesting they alleviate anxiety and depression symptoms by modulating immune, chemical, nervous, and metabolic pathways [18]. Despite increasing availability of probiotic strains, significant gaps remain concerning their comparative effectiveness and mechanisms, underscoring the need for more rigorous research and clear clinical guidelines [7].

Suggestions for Future Research

Future research should focus on conducting more human studies aimed at the precise identification of microbial species, strains, molecules, and metabolites within the gut microbiome that significantly impact health, either positively or negatively. Furthermore, it is essential to define the specific properties of each microbial species, strain, molecule, and metabolite. A notable gap in the literature exists concerning the relationship between the gut microbiome and the intrauterine microbiota. In general, further investigation in humans is recommended, particularly during pregnancy, as there is a significant lack of information regarding the interaction between the gut microbiota and the endocrine system.

Current knowledge about the neonatal gut microbiome and its influence on health during the neonatal period and later life mainly derives from studies of the adult gut microbiota [21]. Therefore, understanding a wide range of disorders will likely be enhanced through a deeper assessment of the neonatal gut microbiome. This, in turn, will contribute to the development of more targeted microbiome-based therapies aimed at improving neonatal health.

5. Conclusion

The maternal gut microbiome plays a critical role in regulating endocrine and metabolic functions during pregnancy, with significant implications for neonatal health. While emerging evidence supports the potential of microbiome-targeted interventions, further research is needed to clarify mechanisms, optimize supplementation strategies, and inform clinical practice.

Compliance with ethical standards

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