

# The Influence of Maternal Diet on Gut Microbiota Diversity During Pregnancy: A Mini-Review

Veronica Posse<sup>1</sup>, Pamela Gil Galleguillos<sup>2</sup>, Beatriz Cubilhas<sup>3</sup>, Raissa Carvalho<sup>4,5</sup>, Taciana Baez<sup>6</sup>, Giulia Cenci<sup>7</sup>, Carlos Alberto Vergara Ascenzo<sup>8</sup>, Cristy Tavarez<sup>6,9</sup>, Felipe Martinez<sup>10</sup>, Leo Peña<sup>11</sup>, Diego Saa<sup>12</sup>, Martina Donoso<sup>13</sup>, Andrei Shanchev<sup>14</sup>, Saheed Oyedele<sup>15</sup>, Katherine Amaro<sup>11</sup>, Marcos Barros<sup>16</sup>, Simone Barbosa<sup>17</sup>, Ana Diaz<sup>11</sup>, Sharif Folorunso<sup>15</sup>, Tatiana Gatilova<sup>18</sup>, Patricia Leite<sup>19</sup>, Niurkiss Mallen<sup>20</sup>, Cinthia Minatel<sup>21</sup>, Jinhui Peng<sup>22</sup>, Gabriel Sakaya<sup>23</sup>, Mery Terrero<sup>20</sup>, Carolina Uribe<sup>24</sup>, Adela Yip<sup>25</sup>, Andrés Soto-Rodríguez<sup>26\*</sup>

<sup>1</sup> Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina; <sup>2</sup> Universidad Pontificia de Chile, Santiago, Chile;
 <sup>3</sup> Escola Bahiana de Medicina e Saúde Pública, Salvador, Bahia, Brazil; <sup>4</sup> Hospital Beneficência Portuguesa de São Paulo, São Paulo, Brazil;
 <sup>5</sup> Botucatu Medical School - UNESP, Botucatu, Brazil; <sup>6</sup> Instituto Tecnologico de Santo Domingo, Santo Domingo, Distrito Nacional, Dominican Republic; <sup>7</sup> Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, US; <sup>8</sup> NiuVida, centro especializado de reproducción asistida, Lima, Perú; <sup>9</sup> University of Arizona, Mel and Enid Zuckerman College of Public Health, Tucson, Arizona; <sup>10</sup> Aché Laboratórios Farmacêuticos, São Paulo, Brazil; <sup>11</sup> Pontificia Universidad Católica Madre y Maestra, Santiago, Dominican Republic; <sup>12</sup> Hospital del Trabajador, Santiago, Chile; <sup>13</sup> Centro Oftalmológico Dr Charles, Buenos Aires, Argentina; <sup>14</sup> Kursk State Medical University, Kursk, Russia; <sup>15</sup> Obafemi Awolowo University, Teaching Hospital Complex, Ile-Ife, Osun State, Nigeria; <sup>19</sup> Novo Nordisk, Pharmaceutical Company, Brazil; <sup>20</sup> Universidad Autónoma de Santo Domingo, Santo Domingo, Distrito Nacional, Dominican Republic; <sup>21</sup> Endocrinology Division, Department of Internal Medicine, Faculty of Medical Sciences, University of Campinas, São Paulo, Brazil; <sup>22</sup> CareAlliance, Shanghai, China; <sup>23</sup> Clinica W&S, Sao Paulo, Brazil; <sup>24</sup> Clínica Dávila, Santiago, Chile; <sup>25</sup> Sydney School e fuelta Liniversity of Santo Domingo, Chile; <sup>25</sup> Sydney School

of Public Health, The University of Sydney, Australia; <sup>26</sup> Research Unit, The Regenerative Medicine Institute, San Jose, Costa Rica.

#### Abstract

**Background:** The gut microbiota plays a critical role in maintaining health, influencing nutrient metabolism, immune function, and disease susceptibility. During pregnancy, the maternal diet can significantly alter the composition and diversity of the gut microbiota, potentially impacting maternal and fetal health.

**Objective:** This mini-review aims to answer whether maternal diet during pregnancy is associated with the composition and diversity of maternal gut microbiota.

*Methods:* A comprehensive literature search was conducted in Embase, Scopus, PubMed, Web of Science, and Cochrane databases in May 2024. A risk of bias assessment was performed.

**Results:** Twenty articles were selected, including randomized controlled trials, cohort, cross-sectional, and case-control studies. Increased dietary fiber intake was consistently associated with higher gut microbiota richness and diversity. Conversely, high-fat diets were linked to reduced microbial diversity and pro-inflammatory profiles. Dietary interventions such as vegetarian and Mediterranean diets promoted a more diverse and beneficial gut microbiota composition.

**Conclusion:** Maternal diet during pregnancy is associated with changes in gut microbiota composition and diversity. These findings underscore the importance of dietary interventions to improve the gut microbiota to improve pregnancy health. Future research should focus on personalized nutrition strategies to optimize maternal outcomes.

#### Introduction

Since the advent of sequencing methods and bioinformatic analysis, understanding the microbiome in the human organism has rapidly evolved (Galloway-Peña, 2020). The gut microbiota is involved in nutrient extraction, metabolism, biosynthesis of vitamins, amino acids, and lipids, and/or the development of intestinal mucosa and the immune system (Hou,

<sup>\*</sup>Corresponding author: andres.soto-2024@ppcr.org

Received: July 19, 2024 Accepted: November 19, 2024

**Published:** January 26, 2025 **Editor:** Felipe Fregni

Ealtor: Felipe Fregni

**Reviewers:** Mohamed H. Mahmoud, Khalid Ahmed, Inia Perez, Ygor Junqueira

**Keywords:** microbiome, microbiota, pregnant women, diet, dietary patterns

DOI: https://doi.org/10.21801/ppcrj.2024.103.7

Systematic Review

2022). Numerous studies have demonstrated how a healthy microbiome can reduce the risk of obesity, heart disease, diabetes, and cancer (Noor et al., 2023). Likewise, associations have been established between human intestinal microbiota and a number of diseases, including irritable bowel syndrome, inflammatory bowel disease, systemic metabolic diseases, and atopic eczema (Bull, 2014). During pregnancy, women undergo multiple physiological changes that also affect the microbiome, increasing the risk of diseases linked with altered intestinal flora, such as gestational diabetes, preeclampsia, obesity, and metabolic syndrome (Koren, 2024).

Previous studies found that dietary changes during pregnancy may modify the maternal microbiota in women with pregnancy-related conditions. Fiberrich diets and high consumption of carbohydrates and proteins have been shown to positively affect microbiome variability (Martin, 2023), preventing metabolic disorders and inflammatory diseases (Rinninella, 2023). Conversely, high-sugar and high-fat diets, especially those containing processed foods, can increase harmful bacteria, leading to inflammation and metabolic disorders (Son, 2022). Thus, understanding the correlation between diet, microbiota, and certain conditions is crucial for better clinical practice.

This review aims to explore the effects of dietary patterns and microbiota changes during pregnancy, with a focus on the diversity and predominance of bacterial species, in reducing the incidence of preeclampsia, gestational diabetes, and other metabolic conditions. New research in this area may offer insights into how individualized dietary interventions can foster a healthier maternal microbial environment, which in turn may benefit the newborn by reducing the risk of future health issues.

# Materials and Methods

# Study Design

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The search was conducted in Embase, Scopus, PubMed, Web of Science, and Cochrane databases in May 2024 without the use of any filters in the initial search. The aim was to identify studies that addressed the research question: "Is maternal diet during pregnancy associated with the composition and diversity of maternal microbiota/microbiome?". A protocol for this review was not registered in the International Prospective Register of Systematic Reviews (PROSPERO) because this study is considered an academic exercise.

## Search Strategy

The search was performed in the five selected databases using the terms "pregnancy," "diet," "gut microbiome," and "maternal outcome," and their variations. The research strategy was adapted according to the database. The description of the exact terms used in this review can be found in the supplementary materials.

# Inclusion and Exclusion Criteria

Articles were screened for eligibility based on specific inclusion criteria: pregnant women of any gestational age, over 18 years old, irrespective of ethnicity or health condition. Eligible studies investigated dietary patterns during pregnancy and included dietary interventions to modify the gut microbiota composition and diversity. Some studies also reported maternal outcomes related to gut microbiota changes. The review included randomized controlled trials (RCTs) and observational studies, with publications accepted in English, Portuguese, or Spanish. No limitations were placed on the year of publication.

Excluded articles were animal and in vitro studies, those conducted on postpartum women, or those lacking a description of the dietary pattern or nutritional intervention. Articles providing only general recommendations without specific directions, outcomes unrelated to maternal health or microbiota, and certain study types, including case series, guidelines, reviews, meta-analyses, systematic reviews, editorials, or opinion pieces, were also excluded. Additionally, studies not available in full text were not considered for this review. All excluded articles were assessed individually, without using filters during the search strategy.

## Screening

The screening and data extraction for this review were conducted using Covidence. Initially, selected papers were screened for duplicates and then assessed based on their titles and abstracts by a team of 16 authors. Subsequently, they underwent a full-text review by 23 reviewers. Any discrepancies between reviewers were resolved through discussion among the authors, with a third reviewer consulted when necessary to reach a consensus. Refer to Figure 1 for more details.

## Selection of Studies and Data Extraction

Data from the papers were extracted using a standardized extraction form. After independently



**Figure 1:** PRISMA flow diagram: This diagram provides an overview of the process to ensure the quality and relevance of the included studies.

extracting information, reviewers generated a comparison table to identify any discrepancies. Conflicts were resolved through discussion to reach a consensus, enhancing the accuracy and reliability of the data extraction process. No assumptions were made regarding missing or unclear data in this review.

#### Data Synthesis

Since the primary outcome was the microbiome and its changes, no conventional effect measures, such as risk ratio or mean differences, were used to evaluate this variable. The studies were grouped based on specific characteristics of the population studied in each trial: pregnant women in general, those with gestational diabetes, those with high blood pressure, and those with obesity or overweight. This review aimed to assess the differences in microbiome composition across these groups. As some articles focused on a specific type of population, these subgroups allowed for a more targeted analysis. Data summarized in the text and tables were not adjusted for missing information if an item was omitted in the original study; it was not reported in our results.

#### **Risk of Bias Assessment**

The risk of bias for randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias Tool for Randomized Trials (RoB 2) (Sterne, 2019), which covers domains such as sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other potential biases. Each domain was categorized as low, high, or unclear risk of bias. For observational studies, the Newcastle-Ottawa Scale (NOS) (Wells, 2013) was used to assess selection, comparability, and outcome/exposure with studies rated as good ( $\geq$ 7 stars), fair (2-6 stars), or poor ( $\leq 1$  star). Two independent reviewers conducted the assessments, and any disagreements were resolved through discussion to reach a consensus, ensuring a rigorous and reliable evaluation process.

## Results

#### Description of the Studies

This systematic review includes 20 studies, covering a population of 21,30 pregnant women. The studies' designs varied, including thirteen prospective cohort studies, four cross-sectional studies, two RCTs, and one case-control study. Each addressed the relationship between dietary intake and gut microbiota diversity during pregnancy. The geographic distribution included Asia (27.8%), North America (22.2%), Europe (22.2%), and other regions (27.8%).

Observational studies provided information for understanding how dietary exposures affect the maternal microbiome. For instance, Roytio et al. (2017) correlated the dietary intake of fat and fiber and its relation to gut microbiota richness in overweight pregnant women. This study highlighted significant associations between higher fiber intake and increased microbiota diversity. Moreover, Barret et al. (2018) examined the effects of a vegetarian diet on gut microbiota composition in early pregnancy, demonstrating a significant increase in gut microbiota diversity. The detailed results of each article are described in Table 4: "Summary of Study Designs, Statistical Methods, and Findings."

RCTs provided evidence through controlled dietary interventions. Sugino et al. (2022) conducted a study in Gestational Diabetes Mellitus (GDM), women following a diet that had "60% complex carbohydrate, 25% fat, and 15% protein," concluding that this "CHOICE diet" increased the abundance of Bifidobacterium spp. in adolescent mothers and decreased Prevotella copri, but no significant results were found regarding the diversity of both diets.

#### Population

The summed population varied considerably, encompassing small cohorts of fewer than 50 participants to large groups exceeding 500 individuals. Key demographic variables, such as age, body mass index (BMI), and gestational age at recruitment, were documented to ensure comprehensive demographic representation. Participants' ages ranged from 26 to 37 years, thereby involving a broad spectrum of reproductive ages. The BMI of participants ranged from 21.8 to 34.9 kg/m<sup>2</sup>, with study populations including those with gestational diabetes mellitus, overweight/obesity, and hypertensive diseases. The main characteristics of the studies are displayed in Table 1.

#### Outcomes

Primary outcomes across these studies included changes in gut microbiota diversity, measured using alpha diversity, which addresses diversity within a single microbial community; it is commonly quantified using the Shannon diversity index and species richness. The Shannon index considers both the abundance and evenness of species, providing a nuanced view of community structure; the higher the Shannon index values, the more diverse and resilient gut

Authors	Study design	Sample size	DNA extraction method	Time of Sample Collection	Type of sample	Number of Samples Collected per Participant	Pre-Intervention Sample Collection	Use of 16S rRNA Gene-Base Profiling
Röytiö H et al, 2017	Observational prospective cohort study	100	Sequenced at the Sequencing and Bioinformatics service	$\leq$ 17 gestational weeks	Fecal samples	1 sample	Yes	Yes
Dualib PM et al, 2022	Observational prospective cohort study, longitudinal	115	QIAamp DNA Stool Mini Kit (Qiagen)	First/second trimester and/or third trimester	Fecal samples	2 samples	No	Yes
Kunasegaran, T. et al, 2024	Observational prospective cohort study	105	RNEASY PowerMicrobiome Kit from QIAGEN (QIAGEN, Hilden, Germany)	Second and third (T1) trimesters of pregnancy	Fecal samples	2 samples	Yes	Yes
Tomsett, K.I. et al, 2020	Observational prospective cohort study	174	The Qiagen AllPrep DNA Extraction Kit	16 and 28 weeks gestation	Fecal samples	2 samples	Yes	Yes
Wu N. et al, 2022	Observational prospective cohort study, longitudinal	57	QIAamp DNA Stool Mini Kit protocol (Qiagen, Germany)	24-28 gestational weeks	Fecal samples	2 samples	Yes	No
Houttu N. et al, 2018	Observational prospective cohort study	99	Not described	Mean of 13.2 ± 2.5 gestational weeks	Fecal samples	1 sample	Yes	Yes
Miller C.B. et al, 2021	Observational prospective cohort study, longitudinal	41	AllPrep DNA/RNA Extraction Kit (Qiagen)	11-13 weeks, 18-20 weeks and 34-36 weeks of gestation	Rectal swabs	3 samples	Yes	Yes
Liu Y. et al, 2023	Observational prospective cohort study	57	QIAamp DNA Stool Mini Kit protocol (Qiagen, Germany)	24-28 gestational weeks	Fecal samples	2 samples	Yes	Yes
Haddad E.N. et al, 2023	Observational prospective cohort study	86	MoBio Powesoild DNA Isolation Kit (Qiagen)	36 gestational weeks	Fecal samples	1 sample	No	Yes
Sugino K.Y. et al, 2022	Randomized Controlled Trial. The blinding method isn't stated	34	QIAamp PowerDecal DNA Kit (Qiagen INC, Carlsbad, CA, USA	30-31 and 36-37 gestational weeks	Fecal samples	2 samples	Yes	Yes
Urwin H.J. et al, 2014	Randomized Controlled Trial. Single-blinded	123	Not described	38 gestational weeks	Fecal samples	1 sample	No	Yes
Selma-Royo M. et al, 2020	Observational cross- sectional study (part of the MAMI cohort study)	116	Master-Pure DNA Extraction Kit (Epicentre)	Time of birth	Rectal swabs	1 sample	No	Yes
Wu N. et al, 2022	Observational prospective cohort study	57	QIAamp DNA Stool Mini Kit protocol (Qiagen, Germany)	24-28 gestational weeks	Fecal samples	2 samples	Yes	No
Gow M.L. et al, 2023	Observational prospective cohort study, longitudinal	86	PSP Spin Stool DNA Plus Kit (Stratec, CA, USA).	First trimester and third trimester	Fecal samples	2 samples	Yes	Yes
Ferrocino I. et al, 2018	Observational prospective cohort study	50	RNEASY PowerMicrobiome Kit from QIAGEN (QIAGEN, Milan, Italy)	24-28 gestational weeks	Fecal samples	2 samples	Yes	Yes
Ruebel M.L. et al, 2021	Observational prospective cohort study	320	QIAamp DNA Stool Mini Kit protocol (Qiagen, Hilden, Germany)	12, 24, and 36 gestational weeks	Fecal samples	3 samples	Yes	Yes
Barrett H.L. et al, 2018	Observational cross-cohort study	27	Repeated bead beating and colur	n < 16 gestational weeks	Fecal samples	1 sample	Yes	Yes
Alvernaz S.A. et al, 2024	Observational prospective cohort study, longitudinal	73	Not described	Mean gestational weeks $10.9 \pm 3$	Rectal swabs or stor	1 sample	Yes	Yes
Yu J. et al, 2022	Observational cross- sectional study	170	MagPure Stool DNA KF Kit B (Magen, China)	$\geq$ 28 gestational weeks	Fecal samples	1 Sample	N/A	Yes
Sun Z. et al, 2022	Observational prospective case-control study	241	TIANamp Stool DNA Kit (TIANGEN, Beijing, China)	< 16 gestational weeks; 24 to 28 weeks; ≥ than 29 weeks of gestation	Fecal samples	3 samples	Yes	Yes
N/A: Not Adressed								

Table 1: Characteristics of the included studies.

microbiota, often associated with better health outcomes. Species richness, on the other hand, counts the number of different species present, being another key indicator of gut health. (Gomez-Arango et al., 2018; Knight et al., 2018). Beta diversity is also evaluated in several studies to understand differences in microbial communities across groups, such as those on high-fiber versus high-fat diets. Beta diversity helps to identify how specific dietary patterns shift the gut microbiota's overall composition, often using measures like Bray-Curtis dissimilarity or Principal Component Analysis (PCA) plots (Lozupone & Knight, 2005; Ley et al., 2006). Additionally, shifts in specific microbial taxa and metabolic markers, such as short-chain fatty acids (SCFAs), offer insights into functional changes within the microbiota. SCFAs are key indicators of gut health and metabolic function, as they play a role in reducing inflammation and improving gut barrier function, which is critical during pregnancy (Mokkala et al., 2020). The methods of aggregation and time points for each outcome were clearly stated, ensuring rigorous and reproducible results. Studies measured dietary intake and microbiota composition during the first and third trimesters of pregnancy to assess changes in the microbiota in time and identify significant differences that may arise due to variations in the diet over

#### time. *Main Results*

These studies focused on the impact of dietary intake on gut microbiota diversity during pregnancy., Roytio et al. (2017) explored the relationship between fiber intake and gut microbiota richness in overweight pregnant women. Their findings revealed that adherence to dietary fiber recommendations was associated with a higher microbial diversity. Meanwhile, Barrett et al. (2018) demonstrated that diets high in fat, typical of Western patterns, led to a more pro-inflammatory gut microbiota composition, whereas vegetarian diets were associated with greater microbial diversity, indicating a protective effect of plant-based diets. Kunasegaran et al. (2024) found similar effects, showing that high fiber improves beneficial gut bacteria and reduces inflammation, whereas high fat does the oppositeTomsett et al. (2020) emphasized t that higher fiber intake increases the abundance of bacteria associated with decreased inflammation, such as Veillonella sp. in women with future hypertensive disorders of pregnancy (HDP) and Oscillospira sp. in normotensive women. Additionally, higher fiber intake was associated with a lower increase in gut permeability, reflected in lower serum zonulin levels as pregnancy progressed in nor-

Authors	Study design	Selection	Comparability	Outcome	Total score
Röytiö H et al, 2017	Prospective cohort	**	**	**	6
Dualib PM et al, 2022	Prospective cohort	****	*	***	8
Kunasegaran, T. et al, 2024	Prospective cohort	***	**	**	7
Tomsett, K.I. et al, 2020	Prospective cohort	***	**	***	8
Wu N. et al, 2022	Prospective cohort	****	*	***	8
Houttu N. et al, 2018	Cohort study (nested)	***	*	***	7
Miller C.B. et al, 2021	Longitudinal cohort	***	**	**	7
Liu Y. et al, 2023	Prospective cohort	****	*	***	8
Haddad E.N. et al, 2023	Cross-sectional study	***	**	**	7
Selma-Royo M. et al, 2020	Cross-sectional study	***	**	**	7
Wu N. et al, 2022	Prospective cohort	***	*	***	7
Gow M.L. et al, 2023	Prospective cohort	***	*	***	7
Ferrocino I. et al, 2018	Prospective cohort study	***	*	**	7
Ruebel M.L. et al, 2021	Longitudinal cohort	****	**	***	9
Barrett H.L. et al, 2018	Cross-sectional study	***	*	**	6
Alvernaz S.A. et al, 2023	Prospective cohort	***	*	**	6
Yu J. et al, 2022	Prospective cohort	***	**	**	7
Sun Z. et al, 2022	Case-control study	***	*	***	7

**Table 2:** Patient and arm characteristics.

motensive women. However, this beneficial effect on gut permeability was not observed in women with future HDP, suggesting that dietary fiber's positive impact on gut barrier function may be limited in this population, probably due to other factors influencing gut permeability in women at risk of HDP (Sugnino, 2022).

Ferrocino et al. (2018) investigated the impacts of dietary patterns on gut microbiota diversity in patients with GDM. The study revealed significant changes in microbiota  $\alpha$ -diversity values between enrolment and the end of the study (p<0.001). Specifically, species richness is the number of different species. At the phylum level, there was an increase in Firmicutes and a reduction in Actinobacteria and Bacteroidetes. Further analysis indicated that the microbial diversity of the subjects varied significantly over time. Principal Component Analysis based on microbiota composition showed a significant relationship between genus-level microbiota composition and sampling time (P<0.001). Dualib et al. (2022) illustrated the influence of metabolic conditions on gut flora by comparing normal pregnancies and those with gestational diabetes. Moreover, Ruebel et al. (2021) studied 140 pregnant women and their associations between maternal diet, body composition, and gut microbial ecology during pregnancy. Alpha-diversity measures showed

between women with normal weight (NW) and overweight/obese (OW/OB) status. However, specific microbial taxa such as Actinobacteria, Lachnospiraceae, Akkermansia, Bifidobacterium, Streptococcus, and Anaerotuncus showed significant changes with gestation. Maternal obesity was associated with increased abundance of Lachnospiraceae, Bilophila, Dialister, and Roseburia, while maternal BMI, fat mass, triglyceride, and insulin levels correlated positively with Bilophila abundance. The study highlights the relationships between diet intake and specific bacterial genera. Sun et al. (2023) also conducted a longitudinal case-control study in GDM patients, who were matched with healthy pregnant controls. The study examined the dynamic associations between the gut microbiome and host glucose metabolism. Results showed a decrease in gut microbial diversity and changes in microbial community composition in healthy controls with advancing gestation but not in GDM patients. Specifically, 10 GDM-related microbial species were identified, such as Alistipes putredinis, which had significant associations with glycemic traits and were modulated by habitual intake of fiber-rich plant foods. The study also found that microbial metabolic potentials related to fiber fermentation were linked to GDM status and glycemic traits. Notably, the addition of microbial features to

no significant changes across pregnancy stages or

a predictive model for GDM significantly improved its accuracy.

Alvernaz et al. (2024) conducted a longitudinal cohort study with 49 pregnant women to explore the impact of inflammatory dietary potential on vitamin depletion and gut microbial dysbiosis in early pregnancy. The study found that diets with high inflammatory potential, measured by the Dietary Inflammatory Index (DII), were associated with decreased intake of essential vitamins and minerals, such as vitamins B12, B6, A, iron, magnesium, niacin, and zinc. The gut microbiota of participants with higher DII scores exhibited dysbiotic changes, including a decrease in short-chain fatty acid producers like Faecalibacterium and an increase in bacterial pathways related to vitamin B12 synthesis and methylglyoxal detoxification. The main results indicated that a proinflammatory diet during early pregnancy is linked to nutrient deficiencies and harmful shifts in gut microbiota composition, potentially impacting maternal and fetal health.

Yu et al. (2022) conducted a case-control study with 170 pregnant women, including 72 with hypertensive disorders of pregnancy (HDP) and 98 healthy controls. The study explored dietary nutrient intake and gut microbiota composition in the third trimester. The results showed that daily intakes of vitamins A and C were significantly lower in women with HDP. Gut microbiota analysis revealed increased relative abundances of Bacteroidota and Bacteroides and decreased abundances of Actinobacteriota, Lachnospiraceae, Prevotellaceae, and Bifidobacterium in women with HDP. Notably, a higher abundance of Bifidobacterium was positively correlated with dietary vitamin C intake and was associated with a lower risk of HDP. These findings suggest that diet and gut microbiota composition are significantly linked to HDP, with potential implications for dietary interventions in managing HDP risk.

Selma-Royo et al. (2020) conducted a nested crosssectional study within the longitudinal MAMI birth cohort, including 73 mother-infant dyads, to explore the associations between maternal diet during pregnancy, maternal intestinal markers, and neonatal gut microbiota. The study found that maternal diet significantly influenced maternal and neonatal gut microbiota at birth. Specifically, higher maternal intake of saturated and monounsaturated fatty acids was positively associated with the abundance of Firmicutes in neonatal microbiota and negatively correlated with fiber, vegetable proteins, and vitamin intake. The study also found that maternal intestinal markers, such as zonulin and intestinal alkaline phosphatase, were related to dietary patterns, with higher lipid intake linked to increased zonulin levels, indicating

higher gut permeability. These findings suggest maternal diet, particularly fat intake, affects maternal gut function and microbial transmission to neonates, potentially impacting neonatal health.

Wu et al. (2022) conducted a case-control study involving 57 pregnant women, including 27 with GDM and 30 healthy controls, to analyze the gut microbial composition and the effects of dietary intervention. The study utilized the Illumina HiSeq 2500 platform for microbiome analysis and found that the overall bacterial composition was clustered by diabetes status rather than diet intervention. Notably, the phylum Acidobacteria was significantly increased in the GDM group and positively correlated with blood glucose levels. Additionally, the genera within Firmicutes, Bacteroidetes, Proteobacteria, and Lentisphaerae were distinct in GDM patients. Short-term diet management improved the Firmicutes/Bacteroidetes ratio and increased the abundance of beneficial SCFAs-producing bacteria in GDM subjects. These findings suggest that diet intervention can modulate gut microbiota composition and potentially improve metabolic homeostasis in pregnant women with GDM.

# Assessment of Risk of Bias in Individual Studies

Each study was assessed for risk of bias using standardized tools. Cross-sectional studies and casecontrol studies were evaluated using NOS, as shown in Table 2. Conversely, in randomized controlled trials, the RoB2 assessment was used, as reported in Table 3. Common biases identified included selection bias due to non-randomized designs, performance bias due to lack of blinding, and reporting bias. The overall risk of bias for each study is summarized, providing a clear picture of the quality and reliability of the findings.

# Discussion

The review of 20 studies on gut microbiota and its relationship with pregnancy and diet reveals diverse results. For example, Röytiö et al. (2017) highlighted that high-fiber diets are associated with increased diversity and richness in gut microbiota, while high-fat diets tend to reduce microbial diversity. Kunasegaran et al. (2024) found similar effects, showing that high fiber improves beneficial gut bacteria and reduces inflammation, whereas high fat does the opposite. Dualib et al. (2022) illustrated the influence of metabolic conditions on gut flora by comparing normal pregnancies and those with gestational diabetes. Liu et al. (2023) and Haddad et al. (2023) used various methodologies to explore diet-microbiome interactions, with findings ranging from personalized diet



Green: Low risk. Blue: Unclear. Yellow: Some concerns for bias. Red: H

 Table 3: ROB2 assessment.

Authors	Statistical Methods	Study Population	Outcome	Analysis Summary		
Röytiö et al. (2017)	Correlation analysis	Overweight pregnant women	Increased gut microbiota richness with high fiber diet	Highlighted associations between fiber intake and microbiota diversity		
Barrett et al. (2018)	Alpha diversity (Shannon Index)	Vegetarian pregnant women	Higher gut diversity with vegetarian diet	Examined diet influence on gut microbiota diversity and composition		
Sugino et al. (2022)	T-tests, microbial abundance	Pregnant women with GDM	Increased Bifidobacterium spp. With CHO-rich diet	Explored effects of a complex carbohydrate diet on gut bacteria abundance		
Ferrocino et al. (2018)	Alpha/beta diversity measures	GDM patients	Increase in Firmicutes, decrease in Actinobacteria	Analyzed changes in microbiota diversity over gestation		
Tomsett et al. (2020)	Correlation, zonulin measurement	Pregnant women (normotensive and HDP)	Lower gut permeability in normotensive women with fiber	Investigated dietary fiber impact on gut barrier function by hypertensive risk		
Liu et al. (2023)	Network analysis	Pregnant women with personalized diets	Individualized microbiota changes with diet	Utilized network analysis to assess individualized dietary effects		
Ruebel et al. (2021)	Alpha diversity, regression	Normal and overweight pregnant women	Shift in specific taxa with maternal BMI and diet	Analyzed diet, body composition, and gut microbial ecology		
Alvernaz et al (2024)	Dietary Inflammatory Index (DII)	Pregnant women	Vitamin depletion and dysbiosis with high DII diet	Linked pro-inflammatory diet with nutrient deficiencies and gut dysbiosis		
Yu et al. (2022)	Microbial abundance analysis	Pregnant women with HDP	Altered microbial composition in HDP	Showed associations between diet, gut microbiota, and HDP		
Sun et al. (2022)	Longitudinal analysis	GDM patients and controls	Distinct microbiota composition in GDM	Investigated microbiota changes with gestational progression		
Selma-Royo et al. (2020)	Regression analysis	Pregnant women and neonates	Influence of maternal diet on neonatal microbiota	Explored maternal diet effects on both maternal and neonatal gut microbiota		
Wu et al. (2022)	Microbiome sequencing	Pregnant women with GDM	Higher Firmicutes/Bacteroidetes ratio post diet change	Observed gut microbiota composition clustering by diabetes status		
Kunasegaran et al. (2024)	Cohort analysis	Pregnant women with GDM	Improved gut health with higher-fiber diets	Focused on diet, lifestyle, and microbiome composition in GDM women		
Haddad et al. (2023)	Metabolite analysis	Pregnant women	Metabolite and microbiome shifts with diet	Explored associations between diet, gut microbiota, and metabolic profiles		
Houttu et al. (2018)	Comparative analysis	Overweight/obese pregnant women	Changes in gut microbiota with obesity status	Studied associations between obesity, microbiota, and metabolic profiles		
Miller et al. (2021)	Adherence scoring	Pregnant women on Mediterranean diet	Increased gut diversity with diet adherence	Examined impact of mediterranean diet adherence on microbiota		
Urwin et al. (2014)	Fecal microbiota sequencing	Pregnant women consuming salmon	Increased SCFAs in microbiota with salmon intake	Focused on maternal dietary salmon intake effects on gut microbiota		
Mandal et al. (2016)	Pro-inflammatory index analysis	Pregnant women with high-fat/vitamin D	Pro-inflammatory gut profile with high-fat diet	Examined how fat and vitamin intake affect gut microbiota composition		
GDM: Gestational Diabetes Mellitus. HDP: Hypertensive Disorders of Pregnancy. SCFAs: Short-Chain Fatty Acids. BMI: Body Mass Index. DII: Dietary Inflammatory Index						

**Table 4:** Summary of study designs, statistical methods, and findings.

effects to comprehensive metabolite insights. Houttu et al. (2018) showed alterations in metabolic and inflammatory profiles in obese pregnant women. Miller et al. (2021) linked adherence to the Mediterranean diet to beneficial changes in gut microbiota. Sugino et al. (2022) investigated the effects of a high-complex carbohydrate diet, and Urwin et al. (2014) focused on the influence of salmon consumption during pregnancy.

The studies varied in focus and approach. Röytiö et al. (2017) and Tomsett et al. (2020) emphasized dietary fibers and fats, while Dualib et al. (2022) and Kunasegaran et al. (2024) explored broader lifestyle impacts. Liu et al. (2023) used individualized network analysis, and Haddad et al. (2023) conducted metabolite analyses. Houttu et al. (2018) and Miller et al. (2021) focused on obesity and the Mediterranean diet. Sugino et al. (2022) and Urwin et al. (2014) examined specific dietary components. Their findings suggested that higher dietary quality was associated with greater microbiota diversity (Houttu et al., 2018) (Röytiö et al., 2017). Similarly, the study by Mandal et al. (2016) found that higher intakes of fats and fat-soluble vitamins, particularly vitamin D, were linked to a pro-inflammatory microbiota profile, increasing the abundance of Proteobacteria. Laitinen and Mokkala (2019) demonstrated that higher dietary quality in overweight and obese pregnant women is associated with increased gut microbiota diversity. Conclude that daily consumption of whole grains and vegetables enhances gut microbiota diversity, highlighting the potential benefits of a high-quality diet on maternal metabolic health.

Discrepancies arose concerning the impact of shortterm interventions. Some included studies in this review noted that while immediate changes in microbiota composition occurred, long-term impacts were unclear. These findings contrast with Liu et al. (2023), whose individualized diet network analysis indicated sustained effects on gut microbiota with consistent dietary adherence.

Strengths of this review include several studies with large sample sizes (Gow et al., 2003; Ferrocino et al., 2018; Dualib et al., 2022), enhancing generalizability. The geographic focus also varied, which further increased generalizability. However, differences in study design, sample populations, and methodologies led to diverse findings. Liu et al. (2023) used individualized network analysis, while Haddad et al. (2023) conducted comprehensive metabolite analyses. Wu et al. (2022) and Selma-Royo et al. (2020) focused on specific metabolic conditions and dietary patterns.

Methodological strengths included homogeneous groups in Röytiö et al. (2017), comparable weights in Dualib et al. (2022), and precise microbiome data Limitations included small sample sizes in Röytiö et al. (2017) and Tomsett et al. (2020), regional focus in Houttu et al. (2018), and the short-term nature of Liu et al. (2023). Some studies, like Wu et al. (2022), did not adjust for multiple testing, and reliance on self-reported dietary data (Gow et al., 2023) could lead to inaccuracies. The absence of PROSPERO registration for the review may reduce transparency and replicability. Furthermore, inconsistency in reviewer training for assessing studies may have introduced variability in bias assessment, potentially affecting the objectivity of quality ratings across studies. This review underscores the potential for monitoring and managing the gut microbiota in pregnant women as part of clinical practice due to its impact

from high-throughput sequencing in Wu et al. (2022).

ing and managing the gut microbiota in pregnant women as part of clinical practice due to its impact on overall health. Personalized dietary interventions tailored to individual patient needs are essential for improving health outcomes in pregnancy, especially metabolic disorders.

# Conclusion

This review highlights one of the factors influencing gut microbiota during pregnancy. Dietary patterns affect the diversity of gut microbiota: high-fiber diets enhance diversity, while high-fat diets decrease and promote a pro-inflammatory profile. Besides, studies show that dietary interventions, such as vegetarian and Mediterranean diets, improve gut microbiota composition. These considerations might affect the pregnancy and its outcomes. Consequently, personalized nutritional strategies may be promising for optimal maternal health during pregnancy. Further research is needed to understand these relationships and the long-term effects of maternal diet on health outcomes. In conclusion, improving maternal diet to enhance gut microbiota diversity presents a valuable area for investigation that could inform future clinical practices and improve health outcomes during pregnancy.

# Acknowledgement

The authors would like to acknowledge: Felipe Fregni, Alma Sanchez, Sara Rodrigues de Oliveira Siqueira, Mona Khurana, Ana Lizarranga, Francisco Álvarez Marcos, Joshua R. Dahlben, Kamran Mushtaq, Maria Susanne Simon, Daniela Masoli, Flávia Paiva Proença Lobo Lopes, Fatima Iqbal, Simone Silva Collopy, Erica Victoria Stelmaszewski, Lourdes Grassi, Cecília Lameirinhas Longo, Ketty Wanda Quezada Thormann, Sofia Alexandra Lara Baez, Alaq Haddad, Thaila Pereira Schmidt, Daniela Seelmann Gonzalez, Juan René Delgado Cornejo, Tania Davila, Deborah dos Reis Estrella, Ricardo Bernardo da Silva and Juliana Aparecida Martins do Couto for their valuable contributions and support during this article's development.

# **Supplementary Materials**

Search strategies Domains for the ROB2 assessment Domains of the NOS assessment

# Funding

This research received no external funding.

# **Conflicts of Interest**

The authors declare no conflict of interest.

# References

Alvernaz, S. A., Wenzel, E. S., Nagelli, U., Pezley, L. B., LaBomascus, B., Gilbert, J. A., Maki, P. M., Tussing-Humphreys, L., & Bernabé, B. P. (2024). *The inflammatory dietary potential is associated with vitamin depletion and gut microbial dysbiosis in early pregnancy*. medRxiv. https://doi.org/10.1101/2023.12.02.23299325

Barrett, H. L., Gomez-Arango, L. F., Wilkinson, S. A., McIntyre, H. D., Callaway, L. K., Morrison, M., & Dekker Nitert, M. (2018). *A vegetarian diet is a major determinant of gut microbiota composition in early pregnancy*. Nutrients, 10(7), Article 7. https://doi.org/10.3390/nu10070890

Bellaguarda, E. (2024). What does gut microbiome have to do with your health? Northwestern Medicine. https://www.nm.org/healthbeat/healthytips/what-does-gut-microbiome-have-to-do-withyour-health#: :text=A%20healthy%20microbiome%20 can%20reduce,diet%20and%20limit%20processed%20 foods

Berg, G., Rybakova, D., Fischer, D., et al. (2020). *Microbiome definition re-visited: old concepts and new challenges*. Microbiome, 8, 103. https://doi.org/10.1186/s40168-020-00875-0

Blaser, M. J. (2016). *Antibiotic use and its consequences for the normal microbiome*. Science, 352(6285), 544-545. https://doi.org/10.1126/science.aad9358

Bull, M. J., & Plummer, N. T. (2014). *Part* 1: *The human gut microbiome in health and disease*. Integrative Medicine (Encinitas, Calif.). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC45 66439/ De Filippo, C., Cavalieri, D., Di Paola, M., Ramazzotti, M., Poullet, J. B., Massart, S., et al. (2010). *Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa*. Proceedings of the National Academy of Sciences, 107(33), 14691-14696. https://doi.org/10.1073/pnas.1005963107

Dualib, P. M., Taddei, C. R., Fernandes, G., Carvalho, C. R. S., Sparvoli, L. G., Silva, I. T., Mattar, R., Ferreira, S. R. G., Dib, S. A., & Almeida-Pititto, B. de. (2022). *Gut microbiota across normal gestation and gestational diabetes mellitus: A cohort analysis*. Metabolites, 12(9), Article 9. https://doi.org/10.3390/metabo12090796

Ferrocino, I., Ponzo, V., Gambino, R., Zarovska, A., Leone, F., Monzeglio, C., Goitre, I., Rosato, R., Romano, A., Grassi, G., Broglio, F., Cassader, M., Cocolin, L., & Bo, S. (2018). *Changes in the gut microbiota composition during pregnancy in patients with gestational diabetes mellitus (GDM)*. Scientific Reports, 8(1), 12216. https://doi.org/10.1038/s41598-018-30735-9

Foster, J. A., & Neufeld, K. A. M. (2013). *Gut-brain axis: How the microbiome influences anxiety and depression*. Trends in Neurosciences, 36(5), 305-312. https://doi.org/10.1016/j.tins.2013.01.005

Galloway-Peña, J., & Hanson, B. (2020). *Tools for analysis of the microbiome*. Digestive Diseases and Sciences, 65(3), 674-685. https://doi.org/10.1007/s10620-020-06091-y

Gomez-Arango, L. F., Barrett, H. L., McIntyre, H. D., Callaway, L. K., Morrison, M., & Dekker Nitert, M. (2018). *Connections between the gut microbiome and metabolic hormones in early pregnancy in overweight and obese women*. Diabetes, 67(6), 953–960. https://doi.org/10.2337/db17-1340

Gow, M. L., Chua, X.-Y., El-Omar, E., Susic, D., & Henry, A. (2023). *Relationship between diet quality and maternal stool microbiota in the MUMS Australian Pregnancy Cohort*. Nutrients, 15(3), Article 3. https://doi.org/10.3390/nu15030689

Haddad, E. N., Nel, N. H., Petrick, L. M., Kerver, J. M., & Comstock, S. S. (2023). Associations between the gut microbiota, urinary metabolites, and diet in women during the third trimester of pregnancy. Current Developments in Nutrition, 7(4). https://doi.org/10.1016/j.cdnut.2022.100025

Hou, K., Wu, Z. X., Chen, X. Y., et al. (2022). *Microbiota in health and diseases*. Sig-

nal Transduction and Targeted Therapy, 7, 135. https://doi.org/10.1038/s41392-022-00974-4

Houttu, N., Mokkala, K., & Laitinen, K. (2018). Overweight and obesity status in pregnant women are related to intestinal microbiota and serum metabolic and inflammatory profiles. Clinical Nutrition, 37(6), 1955-1966. https://doi.org/10.1016/j.clnu.2017.12.013

Knight, R., Vrbanac, A., Taylor, B. C., et al. (2018). *Best practices for analyzing microbiomes*. Nature Reviews Microbiology, 16(7), 410–422. https://doi.org/10.1038/s41579-018-0029-9

Koren, O., Konnikova, L., Brodin, P., et al. (2024). *The maternal gut microbiome in pregnancy: Implications for the developing immune system.* Nature Reviews Gastroenterology & Hepatology, 21, 35–45. https://doi.org/10.1038/s41575-023-00864-2

Kunasegaran, T., Balasubramaniam, V. R. M. T., Thirunavuk Arasoo, V. J., Palanisamy, U. D., Tan, Y. K., & Ramadas, A. (2024). *Diet, lifestyle and gut microbiota composition among Malaysian women with gestational diabetes mellitus: A prospective cohort study*. Scientific Reports, 14(1), 6891. https://doi.org/10.1038/s41598-024-57627-5

Laitinen, K., & Mokkala, K. (2019). Overall dietary quality relates to gut microbiota diversity and abundance. International Journal of Molecular Sciences, 20(8), 1835. https://doi.org/10.3390/ijms20081835

Ley, R. E., Turnbaugh, P. J., Klein, S., & Gordon, J. I. (2006). *Microbial ecology: Human gut microbes associated with obesity*. Nature, 444(7122), 1022–1023. https://doi.org/10.1038/4441022a

Liu, Y., Amit, G., Zhao, X., Wu, N., Li, D., & Bashan, A. (2023). Individualized network analysis reveals a link between the gut microbiome, diet intervention, and gestational diabetes mellitus. PLOS Computational Biology, 19(6), e1011193. https://doi.org/10.1371/journal.pcbi.1011193

Lozupone, C. A., & Knight, R. (2005). *UniFrac: A new phylogenetic method for comparing microbial communities*. Applied and Environmental Microbiology, 71(12), 8228–8235. https://doi.org/10.1128/AEM.71.12.8228-8235.2005

Mandal, S., Godfrey, K. M., McDonald, D., Treuren, W. V., Bjørnholt, J. V., Midtvedt, T., Moen, B., Rudi, K., Knight, R., Brantsæter, A. L., Peddada, S. D., & Eggesbø, M. (2016). *Fat and vitamin*  *intakes during pregnancy have stronger relations with pro-inflammatory maternal microbiota than does carbohydrate intake.* Microbiome, 4(1), 55. https://doi.org/10.1186/s40168-016-0200-3

Martin, S. E., Kraft, C. S., Ziegler, T. R., Millson, E. C., Rishishwar, L., & Martin, G. S. (2023). *The role of diet on the gut microbiome, mood, and happiness*. medRxiv, 2023.03.18.23287442. https://doi.org/10.1101/2023.03.18.23287442

Miller, C. B., Benny, P., Riel, J., Boushey, C., Perez, R., Khadka, V., Qin, Y., Maunakea, A. K., & Lee, M.-J. (2021). Adherence to Mediterranean diet impacts gastrointestinal microbial diversity throughout pregnancy. BMC Pregnancy and Childbirth, 21(1), 558. https://doi.org/10.1186/s12884-021-04033-8

Mokkala, K., Houttu, N., Vahlberg, T., Munukka, E., & Laitinen, K. (2020). *Effects of dietary counseling on gut microbiota and cardiometabolic risk markers during pregnancy: A randomized controlled trial*. Gut, 69(1), 183–193. https://doi.org/10.1136/gutjnl-2018-317503

Noor, J., Chaudhry, A., Batool, S., Noor, R., & Fatima, G. (2023). *Exploring the impact of the gut microbiome on obesity and weight loss: A review article*. Cureus, 15(6). https://doi.org/10.7759/CUREUS.40948

Nyangahu, D. D., & Jaspan, H. B. (2019). *Influence* of the maternal microbiota during pregnancy on infant *immunity*. Clinical and Experimental Immunology, 198(1), 47–56. https://doi.org/10.1111/cei.13331

Pathak, N. (2023). *How your gut health affects your whole body*. WebMD. https://www.webmd.com/digestive-disorders/ss/slideshow-how-gut-health-affects-whole-body

Rinninella, E., Tohumcu, E., Raoul, P., Fiorani, M., Cintoni, M., Mele, M. C., Cammarota, G., Gasbarrini, A., & Ianiro, G. (2023). *The role of diet in shaping human gut microbiota*. Best Practice & Research: Clinical Gastroenterology, 62-63, 101828. https://doi.org/10.1016/j.bpg.2023.101828