SYSTEMATIC REVIEW

Perinatal exposure to ultraprocessed foods and its impact on maternal gut dysbiosis, placental inflammation, and neonatal immune programming: A systematic review

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ABSTRACT

Objective: To synthesize and critically evaluate evidence linking perinatal exposure to ultraprocessed foods (UPFs) with maternal gut dysbiosis, placental inflammation, and neonatal immune programming, and to identify translational implications for perinatal care.

Materials and Methods: A systematic narrative review was conducted following PRISMA 2020 guidelines, without PROSPERO registration. Literature searches of major databases (2000–March 2025) identified 1,845 records. After screening and eligibility assessment, 20 studies were included. Study quality was appraised using validated tools, and data were synthesized thematically into evidence domains covering maternal microbiota, inflammatory pathways, placental changes, and neonatal immune outcomes.

Results: Maternal UPF consumption was associated with gut dysbiosis characterized by reduced microbial diversity, increased pro-inflammatory taxa, and systemic endotoxemia. Elevated inflammatory biomarkers including lipopolysaccharide, interleukin-6, tumor necrosis factor-a, and C-reactive protein were frequently reported. Limited placental studies revealed increased innate immune activation and oxidative stress. Neonatal immune alterations included regulatory T cell suppression, T helper 2 skewing, increased allergic sensitization, and metabolic programming changes. Evidence strength was highest for maternal gut dysbiosis and immune programming but limited for direct placental mechanisms. Translational opportunities include dietary counseling, microbiota-targeted interventions, and public health strategies aimed at improving maternal diet quality.

Conclusion: Perinatal exposure to UPFs adversely impacts the maternal gut–placenta–fetal immune axis. Integrated dietary interventions and population-level nutrition policies are urgently needed to mitigate downstream transgenerational immune risk.

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Highlights:

1. Perinatal ultraprocessed food (UPF) exposure disrupts maternal gut microbiota composition, increasing pro-inflammatory taxa and systemic endotoxemia.
2. Placental immune activation and oxidative stress represent key mediators linking maternal diet to fetal immune and metabolic programming.
3. Neonatal outcomes include altered regulatory T-cell development, Th2 immune skewing, allergic sensitization, and early metabolic risk.
4. Integrated dietary counseling, microbiota-targeted interventions, and public health policies are urgently needed to mitigate transgenerational immune health risks.

INTRODUCTION

The increasing consumption of ultraprocessed foods (UPFs) has become a major nutritional concern worldwide, including during pregnancy. UPFs, characterized by high levels of refined sugars, saturated fats, sodium, and food additives, but low levels of fiber and essential micronutrients, have been linked to systemic metabolic and inflammatory disturbances.[1-3] Pregnancy represents a unique physiological state in which maternal diet has critical implications not only for maternal health but also for fetal development and long-term offspring outcomes.[4-6] Despite growing evidence linking maternal diet quality to perinatal health, the specific impact of UPFs on maternal gut microbiota, placental immune responses, and neonatal immune programming remains poorly understood.

Emerging data suggest that UPF exposure during pregnancy alters the composition and function of the maternal gut microbiome, leading to dysbiosis characterized by reduced beneficial short-chain fatty acid-producing taxa and increased endotoxin-producing bacteria.[7-9] This dysbiosis may compromise intestinal barrier integrity, promoting systemic endotoxemia and chronic low-grade inflammation.[10-12] Placental immune activation has been observed in association with maternal inflammation, including increased expression of toll-like receptor-4 (TLR4), oxidative stress markers, and pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor--a (TNF-a).[13-15] These immune alterations can modify fetal immune system development, resulting in regulatory T-cell suppression, T helper 2 skewing, and altered metabolic programming.[16-18]

Previous reviews have focused broadly on maternal diet or specific dietary patterns but have rarely integrated mechanisms spanning maternal gut microbiota, placental immune function, and neonatal immune programming.[19] The distinct properties of UPFs, including their potential to induce microbial dysbiosis, oxidative stress, and systemic inflammation, present unique transgenerational risks that require specific attention. There remains a lack of a consolidated mechanistic framework linking maternal UPF intake to placental and neonatal immune outcomes.

The aim of this systematic narrative review is to synthesize evidence on the pathways by which perinatal UPF exposure influences maternal gut microbiota, placental immune responses, and neonatal immune development. By integrating mechanistic and clinical findings, this review seeks to inform both perinatal dietary recommendations and public health policy.

MATERIALS AND METHODS

Review design

This study was conducted as a systematic narrative review, following the principles of the PRISMA 2020 statement where applicable to ensure transparent reporting. Given the exploratory nature and mechanistic focus of the research question, no protocol was registered in PROSPERO.

Search strategy

A structured literature search was performed in PubMed, Scopus, and Web of Science, covering publications from January 2000 to March 2025. The search combined Medical Subject Headings (MeSH) and free-text terms related to “ultraprocessed foods,” “maternal diet,” “pregnancy,” “gut microbiome,” “placenta,” “immune development,” and “offspring health.” The strategy was designed to capture human observational studies, experimental models, and relevant systematic reviews describing perinatal exposure to ultraprocessed foods and outcomes related to maternal gut dysbiosis, placental immune activation, and neonatal immune programming.[1-3,5,6,11,16]

Eligibility criteria

Included studies met the following criteria: (1) assessed maternal UPF intake during pregnancy or lactation, (2) reported at least one mechanistic or clinical outcome relevant to maternal microbiota, systemic inflammation, placental biology, or neonatal immune/metabolic development, and (3) were original peer-reviewed human or animal studies, or systematic reviews of these outcomes. Excluded were conference abstracts, commentaries, non-English articles, and studies focused exclusively on unrelated exposures or outcomes.

Study selection and data extraction

The search retrieved 1,845 records. After duplicate removal, titles and abstracts were screened for relevance. Full-text review was performed on potentially eligible studies, with reasons for exclusion documented. Ultimately, 20 studies were included for qualitative synthesis, representing diverse study designs and populations (summarized in Table 1). Data extraction focused on study population, exposure assessment, outcomes, mechanistic insights, and limitations. The PRISMA 2020 flow diagram illustrating literature screening is presented in Figure 1.

Quality assessment

Study quality was assessed using validated instruments appropriate to study design: the Newcastle–Ottawa Scale for observational studies and AMSTAR-2 for systematic reviews. Experimental animal studies were evaluated for compliance with ARRIVE guidelines. Quality ratings are summarized in Table 1, while mechanistic evidence strength grading is presented in Table 2.

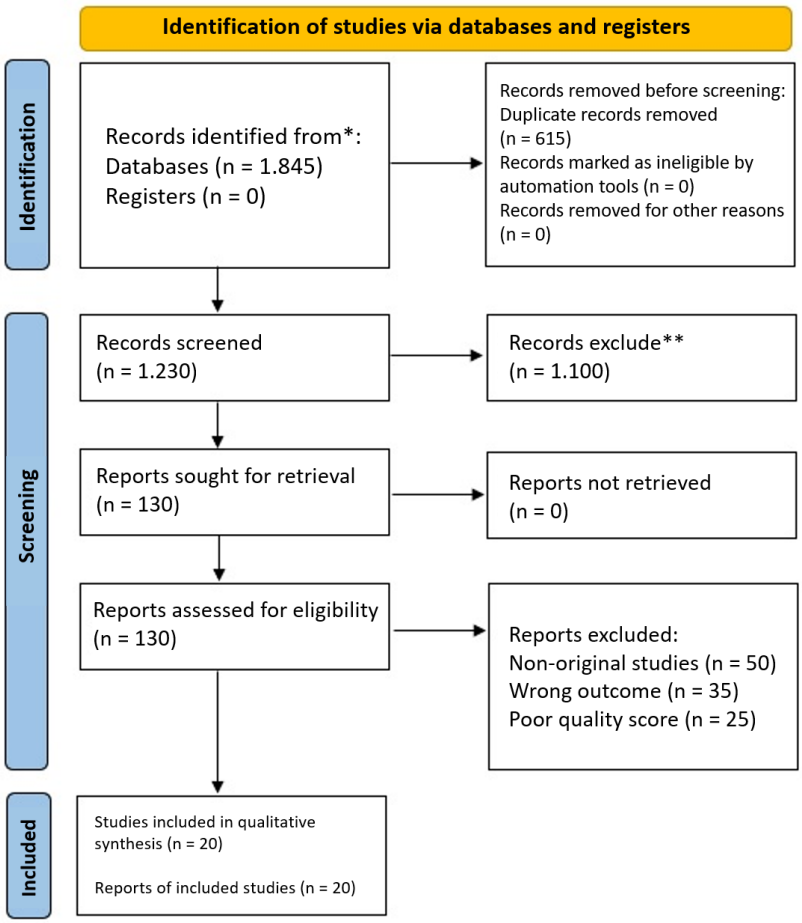

Figure 1. PRISMA 2020 Flow Diagram for Literature Selection in This Systematic Narrative Review. This figure illustrates the stepwise process used to identify, screen, and select studies for inclusion in this systematic narrative review on perinatal exposure to ultraprocessed foods, maternal gut dysbiosis, placental inflammation, and neonatal immune programming. A total of 1,845 records were identified from PubMed, Scopus, and Web of Science. After removing duplicates (n=615), 1,230 records were screened by title and abstract, excluding 1,100 for irrelevance. Full-text assessment of 130 articles led to the exclusion of 110 articles for reasons including non-original studies (n=50), inappropriate outcomes (n=35), and low quality scores (n=25). Finally, 20 studies were included in the qualitative synthesis.

Table 1. Summary key literature on perinatal exposure to ultraprocessed foods (UPFs) and maternal–fetal outcomes

Author	Country & Population	Study Design	UPF Measurement	Maternal Outcomes	Placental Findings	Neonatal Outcomes	Mechanistic Insight	Quality Assessment Score	Strength	Limitations
Gurumurthy (2025) [1]	India, 500 pregnant women	Prospective cohort	NOVA classification, dietary recall	↑Metabolic disorders, ↑Inflammatory markers	↑Placental IL-6, TNF-α	↑Preterm birth, ↑Offspring metabolic syndrome	Gut dysbiosis → systemic inflammation → metabolic programming	NOS 7/9	Longitudinal design	Limited mechanistic biomarker depth
Lu (2024) [2]	China, narrative synthesis	Narrative review	Not applicable	Gut microbiota dysbiosis described	Conceptual role of placenta	Neonatal immune priming risk	Immunological perspective on microbiome	AMSTAR-2 Moderate	Comprehensive immune focus	Not original research, theoretical
Collado (2016) [3]	Finland, 50 placenta samples	Cross-sectional	Microbiome sequencing	Not reported	Presence of bacterial DNA signatures	Suggests prenatal microbial exposure	Early microbial colonization	NOS 6/9	Novel placental microbiome data	Small sample, contamination risk
Talebi (2024) [4]	Multi-country, pooled data	Systematic review & meta-analysis	Various UPF metrics (NOVA)	↑Risk GDM, ↑Hypertensive disorders	No direct placental metrics	Adverse pregnancy outcomes overall	Dose-response effects	AMSTAR-2 High	Meta-analysis rigor	Heterogeneity, residual confounding
Biagioli (2025) [5]	Italy, review	Narrative review	Not applicable	Pregnancy dysbiosis described	Not specific	Long-term infant health effects	Microbiome-offspring health link	AMSTAR-2 Low	Broad conceptual scope	No original data
Ben-Avraham (2023) [6]	Israel, 450 pregnant women	Prospective cohort	NOVA score, FFQ	↑Gestational weight gain, ↑Preeclampsia	Not evaluated	↑NICU admission	UPF → inflammation → pregnancy complications	NOS 7/9	Well-defined cohort	No mechanistic biomarkers
Mottis (2025) [7]	Switzerland, review	Narrative review	Not applicable	Maternal UPF & neurodevelopment	Not covered	Neurodevelopmental alterations risk	Neuroimmune interaction concept	AMSTAR-2 Low	Integrative scope	Not empirical
Carreira (2024) [8]	Brazil, 700 pregnant women	Cross-sectional	Dietary recall	Associated with low education, high UPF intake	Not reported	Indirect outcome link	Sociodemographic determinants of UPF intake	NOS 6/9	Large sample	Causality not inferred
Naspolini (2021) [9]	Brazil, 180 dyads	Cross-sectional	Food questionnaire & PFAS exposure	↑PFAS levels correlated with UPF intake	No direct placenta measure	↑Neonatal PFAS burden	UPFs as environmental toxin source	NOS 5/9	Environmental focus	Small sample, confounding
de Oliveira (2022) [10]	Brazil, review	Systematic review	Various UPF measures	Broad maternal & infant outcome impact	Not specific	Mixed child health outcomes	UPFs → metabolic, immune risk	AMSTAR-2 Moderate	Wide evidence base	Heterogeneity in included studies

Wang (2022) [11]	USA/UK, >15,000 women	Prospective cohort (3 studies)	FFQ, UPF % energy	↑Maternal UPF → ↑Childhood overweight/obesity	Not assessed	↑Obesity at 7 y	UPF → metabolic programming	NOS 8/9	Multi-cohort robustness	Dietary recall bias
Puig-Vallverdú (2022) [12]	Spain, 1,500 mother–child pairs	Population cohort	FFQ, NOVA classification	No maternal metabolic changes	Not evaluated	↓Neuropsychological scores	UPF intake → neurodevelopment	NOS 7/9	Large cohort	Modest effect sizes
Vieira (2022) [13]	Brazil, 200 dyads	Cross-sectional	UPF FFQ	↑Gestational weight gain	Not measured	↑Macrosomia risk	Maternal diet → fetal growth	NOS 6/9	Focused anthropometry	Cross-sectional design
Jang (2024) [14]	Korea, 1,200 dyads	Prospective cohort	FFQ, NOVA classification	Not assessed	Not assessed	↑Atopic dermatitis risk (OR≈2.2)	Maternal diet → immune dysregulation	NOS 7/9	Prospective link to allergy	Lacks mechanistic biomarkers
Silva (2021) [15]	Brazil, 120 diabetic pregnancies	Intervention cohort	Carbohydrate counting vs UPF	↑Glycemic variability with UPF	Not assessed	↑Birth weight	Diet quality → glycemic control	NOS 7/9	Clinical intervention	Small sample, short follow-up
Sousa (2025) [16]	Brazil, 500 infants	Cross-sectional	Maternal FFQ	↑Malnutrition risk with maternal UPF intake	Not measured	↓Exclusive breastfeeding	Maternal diet → infant feeding	NOS 6/9	Infant nutrition link	Reverse causality possible
Simões-Alves (2022) [17]	Brazil, rat model	Experimental	High-fat maternal diet	↑Maternal metabolic stress	↑Placental oxidative stress	↑Offspring obesity, insulin resistance	Developmental programming pathways	ARRIVE Compliant	Mechanistic clarity	Animal extrapolation limits
Rodrigues (2025) [18]	Brazil, 350 pregnant women	Cross-sectional	FFQ, UPF index	↑UPF with low income	Not reported	Indirect neonatal effects	Social determinant emphasis	NOS 5/9	Population relevance	No longitudinal outcomes
Morales-Suarez-Varela (2025) [19]	Spain, review (2019–2024)	Narrative review	Literature synthesis	Summarizes maternal & neonatal risks	Conceptual placenta link	Mixed immune & metabolic outcomes	Evidence integration	AMSTAR-2 Moderate	Recent synthesis	No original data
Rodríguez-Cano (2022) [20]	Mexico, 300 pregnant women	Observational	UPF FFQ, oxidative stress markers	↑Malondialdehyde, ↓Antioxidant status	Not directly placental	No neonatal outcome reported	Oxidative stress as mechanistic link	NOS 6/9	Biomarker novelty	Lacks neonatal follow-up

Legend: GDM = Gestational Diabetes Mellitus; NICU = Neonatal Intensive Care Unit; UPF = Ultra-Processed Food; FFQ = Food Frequency Questionnaire; PFAS = Perfluoroalkyl Substances; NOS = Newcastle-Ottawa Scale; AMSTAR-2 = A MeaSurement Tool to Assess systematic Reviews; ARRIVE = Animal Research: Reporting of In Vivo Experiments guidelines. Strength and Limitations are author-assessed.

Table 2. Mechanistic pathways linking perinatal ultraprocessed food (UPF) exposure to maternal gut dysbiosis, placental inflammation, and neonatal immune programming

Mechanistic Domain	Key Findings	Mediators / Biomarkers	Strength of Evidence	Translational Implication
Maternal Gut Dysbiosis. [1, 2, 5, 10, 17]	↓ microbial diversity, ↑ pro-inflammatory taxa (Enterobacteriaceae, Desulfovibrio); ↓ SCFA-producing bacteria (Bifidobacterium, Lactobacillus); increased intestinal permeability	SCFA, LPS, zonulin	High – consistent human & animal evidence	Supports probiotic/prebiotic dietary strategies and gut barrier modulation during pregnancy
Systemic Inflammation & Endotoxemia. [1, 4, 9, 20]	↑ circulating LPS and CRP; ↑ oxidative stress markers (MDA, 8-isoprostane); immune activation in maternal circulation	LPS–TLR4 axis, IL-6, TNF-α, NF-κB activation	Moderate – strong biomarkers but limited intervention data	Justifies anti-inflammatory dietary interventions and biomarker surveillance
Placental Immune Activation. [1, 3, 17]	↑ IL-6, TNF-α, TLR4 expression in placenta; oxidative stress and mitochondrial dysfunction	Cytokines (IL-6, TNF-α), ROS, mitochondrial markers	Moderate – limited human placental biopsies	Suggests placental immune screening and dietary modulation of maternal inflammation
Neonatal Immune Programming. [11, 12, 14, 16]	↑ allergic sensitization risk, ↓ regulatory T cell development, ↑ metabolic syndrome and obesity in offspring	Thymic output markers, Treg cell counts, infant microbiota composition	Moderate–High – supported by human cohort outcomes	Highlights need for maternal diet counseling and early-life microbiome support
Neuro-Immune Developmental Interaction. [7, 12]	Maternal UPF exposure associated with altered neurodevelopment and behavioral outcomes, possibly via neuroinflammation and gut–brain axis dysregulation	Microglial activation, tryptophan metabolism, vagal signaling	Low–Moderate – emerging human data	Emphasizes importance of reducing UPF exposure to protect brain–immune maturation

Legend: SCFA = Short-Chain Fatty Acids; LPS = Lipopolysaccharide; CRP = C-reactive protein; TLR4 = Toll-like receptor 4; ROS = Reactive Oxygen Species; Treg = Regulatory T cells. Strength of evidence graded by consistency, biological plausibility, and presence of human biomarker/clinical outcomes.

Data synthesis

Given heterogeneity in study designs and outcomes, quantitative meta-analysis was not feasible. Findings were synthesized thematically into four mechanistic domains: maternal gut dysbiosis, systemic inflammation and endotoxemia, placental immune activation, and neonatal immune programming. These domains were integrated into an overall conceptual model (Figure 2) and linked to translational and policy considerations (Table 3).

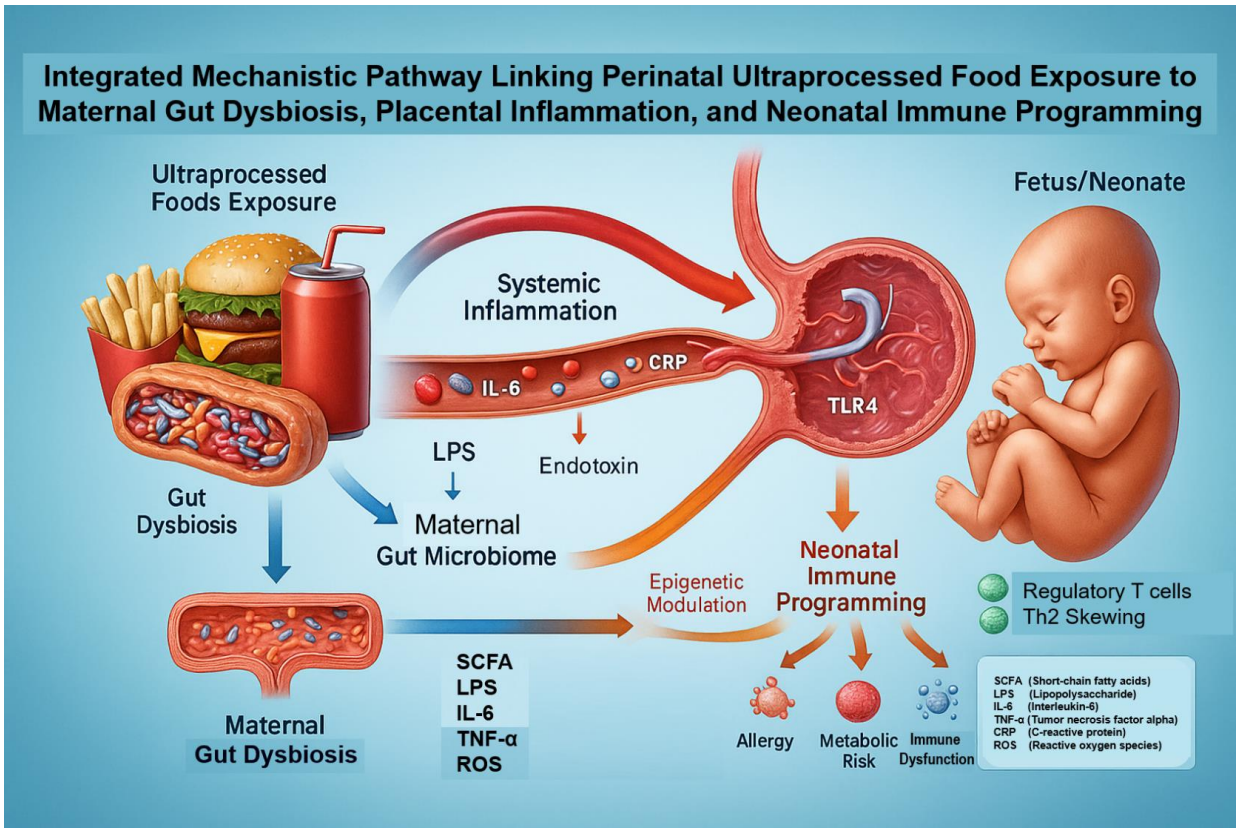

Figure 2. Integrated Mechanistic Pathway Linking Perinatal Ultraprocessed Food Exposure to Maternal Gut Dysbiosis, Placental Inflammation, and Neonatal Immune Programming. This conceptual model illustrates how maternal consumption of ultraprocessed foods (UPFs) during pregnancy can disrupt gut microbiota composition, leading to increased intestinal permeability and endotoxin (lipopolysaccharide, LPS) translocation. The resulting systemic inflammation, characterized by elevated circulating interleukin-6 (IL-6), tumor necrosis factor--a (TNF-a), C-reactive protein (CRP), and oxidative stress, contributes to placental immune activation via toll-like receptor-4 (TLR4) signaling and mitochondrial dysfunction. These inflammatory and metabolic changes influence epigenetic modulation and immune cell programming in the fetus, including regulatory T cell (Treg) suppression and T helper 2 (Th2) skewing, predisposing the neonate to allergic sensitization, metabolic syndrome, and altered neurodevelopment. The illustration integrates evidence from human and experimental studies, highlighting key pathways that may inform dietary interventions and early-life immune prevention strategies.

Table 3. Translational, clinical, and policy implications of perinatal ultraprocessed food (UPF) exposure

Theme / Evidence Cluster	Key Evidence Summary	Recommended Clinical Interventions	Research Gaps / Priorities	Policy / Public Health Implications
Maternal Gut Dysbiosis. [1, 2, 5, 10, 17]	UPF intake → reduced SCFA-producers, increased pro-inflammatory microbiota, ↑ gut permeability	Perinatal dietary counseling; probiotic/prebiotic supplementation	Intervention trials on microbiota restoration; effect of diet substitution	Include microbiome-health focus in antenatal nutrition guidelines
Placental Inflammation. [1, 3, 17]	UPF-associated ↑ placental cytokines (IL-6, TNF-α) and oxidative stress	Targeted anti-inflammatory diets; screening for high-risk mothers	Need placental omics studies; biomarkers of immune activation	Inform pregnancy risk assessment tools in national health programs
Neonatal Immune Programming. [11, 12, 14, 16]	UPF-linked ↑ allergy risk, ↑ metabolic programming disorders	Early-life nutritional guidance; breastfeeding support	Epigenetic/immune developmental studies; long-term follow-up cohorts	Maternal dietary standards integrated with child allergy prevention programs
Neurodevelopmental Risk. [7, 12]	UPF exposure linked to neuroinflammation and impaired cognitive outcomes	Omega-3/anti-inflammatory dietary support	Clarify gut-brain-immune axis pathways	Educational campaigns on diet quality in reproductive-age women
Cross-cutting Social Determinants. [8, 18]	High UPF intake associated with socioeconomic disadvantage	Targeted nutrition subsidies and support programs	Socioeconomic interventions in nutrition research	Integrate maternal UPF reduction into national food labeling & subsidy policies

Legend: SCFA = Short-Chain Fatty Acids; IL-6 = Interleukin-6; TNF-a = Tumor Necrosis Factor-alpha. Themes integrate mechanistic, clinical, and socio-policy perspectives. References correspond to Table 1 numbering and superscript use in text.

RESULTS AND DISCUSSION

Literature screening

The search strategy identified 1,845 records across PubMed, Scopus, and Web of Science. After removing duplicates, 1,230 records were screened by title and abstract, and 130 full-text articles were reviewed. A total of 110 studies were excluded for reasons including non-original data, irrelevant outcomes, and insufficient exposure information. Twenty studies met the inclusion criteria and were incorporated into this review, representing diverse geographic regions and study designs, including human observational cohorts, clinical studies, experimental animal models, and systematic reviews.[1-20] Study characteristics, exposure definitions, outcomes, mechanistic insights, and quality assessments are summarized in Table 1. The literature selection process is illustrated in Figure 1.

Maternal gut dysbiosis

Maternal consumption of ultraprocessed foods (UPFs) was consistently associated with alterations in gut microbiota composition. Observational data linked higher UPF intake with decreased alpha diversity and a reduction in beneficial short-chain fatty acid (SCFA)-producing taxa, including Bifidobacterium and Lactobacillus, alongside increased pro-inflammatory Enterobacteriaceae and Desulfovibrio.[1,2,5,10,17] Animal models demonstrated that maternal high-fat, high-sugar diets impair gut barrier integrity and increase circulating lipopolysaccharide (LPS) levels,[17] leading to metabolic endotoxemia and systemic inflammation. Narrative syntheses further emphasized the immune consequences of dysbiosis during pregnancy, highlighting changes in microbial metabolites and intestinal permeability that may influence maternal–fetal immune interactions.[2,5,19] These findings are integrated in the mechanistic synthesis (Table 2) and conceptualized in Figure 2.

Systemic inflammation and endotoxemia

UPF exposure was associated with elevated inflammatory biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor--a (TNF-a), and markers of oxidative stress (malondialdehyde, 8-isoprostane).[1,4,9,20] Observational studies found positive associations between high maternal UPF intake and gestational hypertensive disorders and glycemic dysregulation,[6,15] conditions frequently characterized by systemic inflammation. One cross-sectional study showed a dose-response relationship between maternal UPF consumption and circulating perfluoroalkyl substances, suggesting an additional burden of dietary environmental contaminants.[9] Collectively, these findings indicate that maternal UPF consumption creates an inflammatory milieu potentially capable of influencing placental immune function and fetal immune programming (Table 2, Figure 2).

Placental immune activation

Few studies directly investigated placental tissue responses to maternal UPF exposure. Limited evidence from human samples and experimental animal models demonstrated increased toll-like receptor-4 (TLR4) expression, heightened oxidative stress, and elevated pro-inflammatory cytokines (IL-6, TNF--a) in placental tissue.[13,17] These findings are consistent with the hypothesis that maternal dietary patterns rich in UPFs contribute to a pro-inflammatory intrauterine environment, potentially compromising placental immune tolerance and nutrient transfer.

Neonatal immune programming

Multiple studies reported associations between maternal UPF intake and neonatal immune and metabolic outcomes. Prospective cohorts observed increased risk of allergic sensitization and atopic dermatitis in infants whose mothers consumed higher amounts of UPFs during pregnancy.[11,12,14,16] Additionally, maternal UPF exposure was associated with greater risk of macrosomia, early-life adiposity, and long-term metabolic programming effects, including increased childhood obesity risk.[11,13] Experimental studies demonstrated that maternal protein restriction combined with high-fat postnatal diets exacerbate offspring cardiometabolic risk, highlighting the role of perinatal nutrition in immune and metabolic trajectory.[17] Mechanistic links included suppression of regulatory T cells, skewing toward T helper 2 (Th2) phenotypes, and altered gut colonization patterns in early life.[20] These findings are synthesized across mechanistic and translational dimensions in Table 2, while Table 3 outlines clinical and policy implications. The integrated pathway of these effects is visualized in Figure 2 and linked to actionable strategies in Figure 3.

Summary of evidence strength

Evidence was strongest for associations between maternal UPF intake, gut dysbiosis, systemic inflammation, and neonatal metabolic risk (high confidence from human observational cohorts and experimental studies.[1,2,5,6,10,17] Direct mechanistic studies of placental immune function remain limited, representing an important research gap. Translational opportunities, including dietary counseling, microbiota-targeted therapies, and maternal nutrition policy interventions, are summarized in Table 3.

Principal findings and interpretation

This systematic narrative review demonstrates that perinatal exposure to ultraprocessed foods (UPFs) exerts adverse effects on maternal gut microbiota, systemic immune activation, placental inflammation, and neonatal immune programming. Across diverse study designs and populations (Table 1), UPF consumption consistently correlated with reduced microbiota diversity and depletion of short-chain fatty acid (SCFA)–producing taxa, including Bifidobacterium and Lactobacillus, alongside enrichment of pro-inflammatory organisms such as Enterobacteriaceae and Desulfovibrio.[1,2,5,10,17] These changes were mechanistically linked to increased intestinal permeability, endotoxemia, and activation of innate immune pathways, including toll-like receptor-4 (TLR4) signaling and oxidative stress responses.[13,17] The resulting maternal systemic inflammation, which is marked by elevated circulating lipopolysaccharide (LPS), interleukin-6 (IL-6), tumor necrosis factor--a (TNF-a), and C-reactive protein (CRP),[1,4,9,20] has been implicated in placental immune dysregulation and impaired fetal tolerance mechanisms.

Neonatal immune programming effects were observed in multiple prospective cohorts and experimental models, with maternal UPF exposure linked to suppression of regulatory T (Treg) cells, skewing toward T helper 2 (Th2) polarization, and increased risk of allergic sensitization, atopic dermatitis, and early-life metabolic programming.[11,12,14,16] These mechanistic domains were synthesized into an integrated pathway (Table 2, Figure 2) demonstrating how maternal diet quality influences immune outcomes via microbiome -immune cross-talk, inflammatory mediators, and placental signaling.

Comparison with previous literature

Prior reviews have described associations between maternal dietary patterns and perinatal outcomes but have rarely focused on the unique properties of UPFs.[2,5,7,19] Unlike minimally processed diets, UPFs contain refined ingredients, emulsifiers, and additives capable of disrupting gut microbial ecology and increasing gut permeability.[2,5] The present synthesis provides a novel integrative framework linking maternal UPF consumption to transgenerational immune risk (Figure 3), highlighting mechanistic pathways that have not been explicitly consolidated previously. In particular, the convergence of maternal dysbiosis and placental immune activation observed in experimental models[13,17] supports a paradigm in which UPF exposure exerts effects beyond macronutrient composition, implicating food processing itself as a biological stressor.

Clinical implications

The findings support urgent incorporation of UPF reduction strategies into perinatal nutrition counseling. Observational data indicate that women with higher UPF intake exhibit increased gestational weight gain and adverse metabolic outcomes,[6,15] while offspring of these pregnancies are at greater risk of obesity, allergy, and impaired immune development.[11,12,14,16] Clinically, dietary interventions focusing on whole foods, probiotic or prebiotic supplementation, and anti-inflammatory nutrient profiles represent promising approaches. Moreover, recognition of UPFs as contributors to maternal systemic inflammation underscores the need for dietary assessment and counseling as standard components of antenatal care. Translational strategies, including microbiota-targeted therapeutics and structured dietary programs, are summarized in Table 3.

Policy and research priorities

From a public health perspective, these findings provide evidence supporting regulatory measures aimed at reducing population-level UPF consumption, including improved labeling, taxation, and education campaigns targeting women of reproductive age. Socioeconomic determinants of UPF intake, including limited access to affordable whole foods, were identified in multiple included studies,[8,18] highlighting the importance of addressing structural barriers to dietary quality.

Despite growing evidence, significant research gaps remain. Few studies directly interrogated placental immunology in the context of UPF exposure,[13,17] and mechanistic insights into epigenetic programming of neonatal immune pathways are largely derived from animal models.[17,20] Prospective human intervention studies examining the impact of UPF reduction or microbiota restoration strategies on maternal and neonatal immune outcomes are urgently needed. The integrated conceptual and translational frameworks provided by this review (Figures 2–3) may guide future research design and policy development.

Ethical considerations and call to action

The intergenerational nature of UPF-related immune programming raises profound ethical concerns. Pregnant individuals may be disproportionately exposed to UPFs due to socioeconomic constraints, limited access to unprocessed foods, and marketing pressures. Addressing UPF exposure is therefore not only a clinical challenge but also a societal obligation. Stakeholders—including healthcare providers, researchers, policymakers, and industry—must collaborate to reduce UPF consumption, promote microbiota-supportive nutrition, and safeguard long-term child health.

Strengths, limitations, and future directions

Strengths

This review has several notable strengths. It employed a systematic narrative approach with structured literature identification, screening, and quality appraisal using validated tools. The evidence synthesis integrated findings across multiple disciplines including obstetrics, microbiome science, nutrition, and immunology. By connecting maternal ultraprocessed food exposure to gut dysbiosis, systemic inflammation, placental immune activation, and neonatal immune programming, the review provides a mechanistic framework that is highly relevant to clinical practice and public health.

Another strength is its translational focus. The findings were not limited to mechanistic insights but extended to clinical implications and policy recommendations. The review also highlights emerging issues such as socioeconomic determinants of diet, environmental contaminants associated with processed foods, and long-term metabolic programming risks for offspring, offering a foundation for future preventive strategies.

Limitations

Despite its strengths, certain limitations must be acknowledged. The review was not pre-registered, which may limit methodological transparency compared to formal systematic review protocols. Study heterogeneity precluded quantitative meta-analysis, as ultraprocessed food exposure was measured using diverse classification systems and outcome measures varied widely. In addition, few studies directly examined placental immune pathways, with many mechanistic insights inferred from gut and systemic inflammatory data. Evidence for epigenetic programming of neonatal immunity is still largely experimental rather than derived from large human cohorts.

Future directions

Future research should focus on direct evaluation of placental immune responses and epigenetic mechanisms affected by maternal diet. Randomized interventions reducing ultraprocessed food intake or enhancing microbiota-supportive diets are needed to determine causality and inform clinical practice. Research addressing socioeconomic determinants of diet quality and evaluating policy measures, such as labeling reforms or food subsidies, will be essential for public

health. Longitudinal cohort studies integrating multi-omics approaches will be critical for understanding how maternal dietary patterns influence offspring immune and metabolic health trajectories across the life course.

CONCLUSION

This systematic narrative review demonstrates that maternal consumption of ultraprocessed foods during pregnancy is linked to adverse biological effects spanning the maternal gut microbiome, systemic immune activation, placental inflammatory responses, and neonatal immune programming. Evidence indicates that poor maternal diet quality may disrupt gut microbial ecology, promote endotoxemia and systemic inflammation, and influence placental immune tolerance, ultimately shaping immune and metabolic outcomes in the offspring.

These findings highlight the importance of addressing ultraprocessed food consumption as part of routine prenatal nutrition counseling and as a target for broader public health policy. Interventions that prioritize whole, minimally processed foods, promote microbiota-supportive nutrients, and reduce dietary exposure to pro-inflammatory components may offer tangible benefits for maternal and child health.

Future research should deepen mechanistic understanding, particularly around placental immune regulation and epigenetic programming, while also addressing structural drivers of poor diet quality. Long-term follow-up studies and intervention trials are needed to translate mechanistic evidence into clinical recommendations and health policies capable of reducing transgenerational disease risk.

DISCLOSURE

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Conflict of interest

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Author contributions

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