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Physiological and Biochemical Impacts of Gestational Diabetes on Maternal and Fetal Health: A Systematic Review

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ABSTRACT

Gestational diabetes mellitus is increasingly recognized as more than a transient elevation of blood glucose during pregnancy. Evidence suggests that GDM represents a broader metabolic disturbance involving chronic low-grade inflammation, dyslipidemia, oxidative stress, endothelial dysfunction, and adipokine imbalance. These alterations appear to influence not only maternal metabolic health but also fetal growth and early developmental outcomes. **Objectives:** To synthesize recent evidence (2017–2024) on physiological and biochemical changes associated with GDM and to examine their implications for maternal and fetal health. **Methods:** A systematic literature search was conducted across PubMed, Scopus, Web of Science, and ScienceDirect in accordance with PRISMA 2020 guidelines. Original human studies comparing GDM and normoglycemic pregnancies were included if they assessed metabolic, inflammatory, oxidative, vascular, or endocrine biomarkers. Study quality was evaluated using the National Institutes of Health quality assessment tools for observational studies and the Cochrane Risk of Bias 2 tool for randomized trials. Due to heterogeneity in study design and outcome measures, findings were synthesized narratively. **Results:** Thirteen studies met the inclusion criteria. GDM was consistently associated with elevated inflammatory markers (hs-CRP, IL-6, IL-18), increased triglycerides, oxidative stress markers such as malondialdehyde, and reduced adiponectin and antioxidant enzymes. Maternal hypertriglyceridemia independently predicted fetal macrosomia, while elevated umbilical cord C-peptide reflected fetal hyperinsulinemia. Nutritional interventions, including DHA supplementation, showed favorable modulation of selected adipokines. **Conclusions:** The evidence supports GDM as a systemic metabolic disorder characterized by interconnected disturbances in glucose, lipid, inflammatory, and oxidative pathways, with important maternal and fetal implications.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a common pregnancy complication, affecting approximately 15% of pregnancies worldwide [1]. It was previously regarded as a transient state of mild hyperglycemia; however, accumulating evidence now characterizes GDM as a complex metabolic disorder involving insulin resistance, adipose tissue dysfunction, oxidative stress, and vascular alterations [2, 3]. This evolving understanding has blurred the distinction between pregnancy-specific metabolic disturbances and the early manifestation of chronic cardiometabolic disease [4]. Despite advances in pathophysiological insight, routine clinical assessment of GDM remains largely centered on glucose tolerance testing, often overlooking the contributory roles of lipid

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dysregulation, inflammation, and oxidative imbalance [5, 6]. Such metabolic disturbances help explain adverse outcomes, including fetal macrosomia, neonatal hypoglycemia, and longer-term cardiometabolic risk, even among pregnancies with apparently adequate glycemic control. This gap highlights a delay in translating mechanistic knowledge into comprehensive clinical evaluation.

While numerous studies have explored glucose dysregulation in GDM, the broader metabolic disturbances such as lipid imbalance, oxidative stress, and inflammation are less consistently evaluated. Existing evidence is fragmented, with limited synthesis of how these factors contribute to complications. This systematic review aims to collate and critically appraise available literature on metabolic alterations in GDM, highlight gaps, and identify potential markers for improved clinical assessment and management.

METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [7]. Gestational diabetes mellitus (GDM) was defined as glucose intolerance with onset or first recognition during pregnancy, irrespective of severity, according to the American Diabetes Association diagnostic criteria [8]. A comprehensive literature search was performed across PubMed, Scopus, Web of Science, and ScienceDirect to identify studies published between 2017 and 2024 that examined physiological and biochemical alterations associated with GDM. The search strategy combined indexed terms and free-text keywords, including gestational diabetes mellitus, biochemical markers, inflammatory cytokines, oxidative stress, adipokines, maternal metabolism, fetal outcomes, and umbilical cord or fetal biomarkers, using Boolean operators (AND/OR) to optimize retrieval. A total of 570 records were identified from PubMed, Scopus, Web of Science, and ScienceDirect. After removal of duplicates and ineligible records (n = 130), 440 records were screened by title and abstract. Out of these, 380 records were excluded due to non-quantitative study design (n = 180), review or case-report format (n = 120), and irrelevant population or outcomes (n = 80). Fifty-eight full-text articles were assessed for eligibility, of which 45 were excluded for predefined reasons. Thirteen studies met the inclusion criteria and were included in the qualitative synthesis (Figure 1). Reference lists of relevant articles were also manually screened to identify additional eligible studies. Only original studies published in English and conducted on human participants were considered. Eligible study designs included cohort, case–control, cross-sectional, and randomized controlled trials that compared pregnancies affected by GDM with normoglycemic controls. Studies were required to report maternal, placental, fetal, or neonatal physiological or biochemical outcomes, including fetal or umbilical cord blood biomarkers (such as C-peptide) reflecting intrauterine metabolic exposure in GDM pregnancies. Reviews, meta-analyses, editorials, animal or in-vitro studies, conference abstracts, and studies lacking primary quantitative data were excluded. A minimum sample size threshold of 50 participants was applied to ensure analytical robustness; however, most included studies exceeded this threshold, with sample sizes generally above 100 participants. Study selection followed a two-stage screening process in accordance with PRISMA 2020. Two reviewers independently screened titles and abstracts, followed by full-text assessment of potentially eligible articles. Any disagreements were resolved through discussion and consensus. For randomized controlled trials, study selection and assessment considered intervention comparison outcome elements consistent with the PICO framework. In such trials, the population comprised pregnant women diagnosed with gestational diabetes mellitus and normoglycemic pregnant controls; the intervention included dietary, nutritional, or glycemic management strategies; comparators consisted of standard care or alternative interventions; and outcomes included maternal, fetal, or neonatal physiological and biochemical measures. For observational studies, eligibility was evaluated using predefined population, exposure, comparator, and outcome criteria. The population was defined as pregnant women diagnosed with gestational diabetes mellitus according to recognized diagnostic criteria, along with appropriate normoglycemic pregnant control groups. Where fetal or neonatal outcomes were assessed, the population also included offspring of mothers with GDM, provided that the reported biomarkers reflected intrauterine metabolic exposure. Exposure referred to the presence of GDM, while comparators were pregnancies without GDM, and outcomes included maternal or fetal physiological and biochemical markers. The PICO framework was not applied as the primary eligibility model because a substantial proportion of included studies were observational and biomarker-based, lacking a clearly defined intervention or interventional comparator. Data extraction was performed using a standardized form capturing study design, country, sample size, diagnostic criteria for GDM, gestational timing of biospecimen collection, measured physiological or biochemical markers, and reported maternal or fetal outcomes. Confounding factors were defined as variables associated with both GDM status and the outcomes of

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interest that could distort observed associations if not adequately controlled. Common confounders included maternal age, pre-pregnancy body mass index, parity, gestational age at sampling, family history of diabetes, and other relevant clinical or lifestyle variables. Information on confounding variables adjusted for in individual studies was extracted and summarized in Table 1. Missing or unclear information was recorded as not reported. Control of confounding was assessed at the individual study level. Multivariable regression modeling, stratification, group matching, and restricted eligibility criteria were considered acceptable methods for confounding control. During data extraction, we specifically recorded whether reported associations were adjusted and which covariates were included. Studies reporting only unadjusted comparisons were interpreted with caution during qualitative synthesis. Quality assessment of observational studies was conducted using the National Institutes of Health (NIH) Quality Assessment Tool [9], for Observational Cohort and Cross-Sectional Studies, which evaluates study objectives, population selection, exposure and outcome measurement, control of confounding, and completeness of follow-up. Randomized controlled trials were assessed using the Cochrane Risk of Bias 2.0 (RoB 2) tool [10]. Risk-of-bias judgments were performed strictly according to the RoB-2 domain-level signaling-question algorithm and overall judgment criteria described in the Cochrane Handbook for Systematic Reviews of Interventions [11]. Studies were classified as low risk of bias when all five RoB-2 domains were judged as low risk; as some concerns when at least one domain raised some concerns but none were high risk; and as high risk when one or more domains were judged as high risk. The five domains assessed were the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported result. Studies were classified as low risk of bias when all key domains were adequately addressed, high risk when one or more critical domains showed methodological weakness, and some concerns when minor limitations were present, in accordance with NIH and Cochrane guidance [9, 10]. Due to substantial heterogeneity in study design, biomarker assays, outcome measures, and analytical approaches, meta-analysis was not undertaken. Instead, findings were synthesized qualitatively and organized into thematic domains encompassing maternal metabolic and inflammatory changes, fetal and neonatal biochemical outcomes, and overall methodological quality.

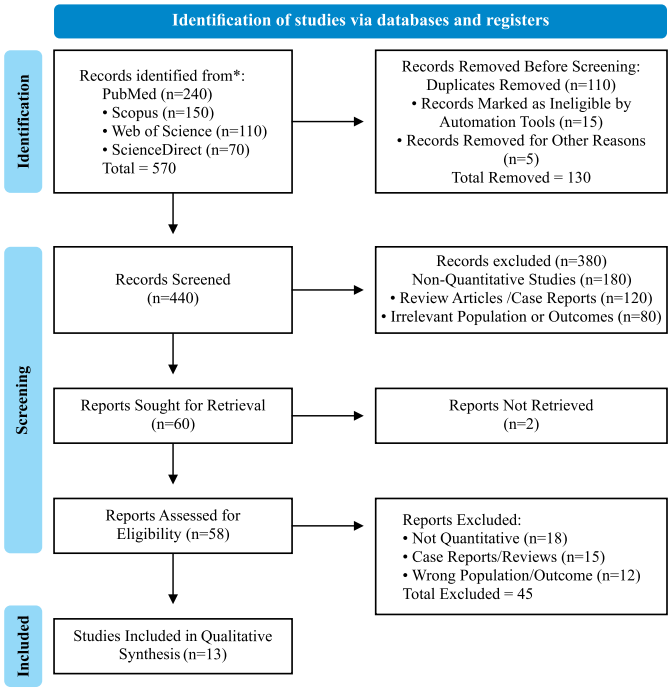

Figure 1: PRISMA flow chart for the study

RESULTS

The relationship between novel adipokines and insulin sensitivity has been evaluated in 18 human studies conducted across diverse populations and metabolic conditions. These studies cover a broad range of clinical contexts, including obesity, polycystic ovary syndrome, gestational diabetes mellitus, type 2 diabetes mellitus, metabolic syndrome, and pediatric populations, facilitating comparative evaluation of adipokine–insulin sensitivity relationships across diverse demographic groups. Omentin-1 and Nesfatin-1 were most frequently evaluated, followed by Chemerin and Visfatin, primarily in relation to HOMA-IR and fasting insulin indices. Across these heterogeneous populations, Omentin-1 showed the most consistent inverse association with insulin resistance, while Chemerin demonstrated the most reproducible positive association with insulin-resistant states, indicating stronger reliability across human studies. A consistent pattern was observed whereby lower levels of Omentin-1 or Nesfatin-1, and higher levels of Chemerin or Visfatin, clustered with obesity, prediabetes, diabetes, and related insulin-resistant conditions. In contrast, Nesfatin-1 and Visfatin showed greater variability across disease states, suggesting population- and stage-dependent effects (Table 1).

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Table 1: Included Primary Studies (2017–2024): Biomarkers/Physiology in GDM and Maternal–Fetal Outcomes

Sr. No.	References	Design	Sample size (GDM / non-GDM)	Gestational Timing of Sampling	Key Biomarkers/ Physiology	Main Maternal–Fetal Outcomes	Covariates Explicitly Adjusted (Confounders)
1	[12]	Prospective Cohort	86 / 273	16–18 weeks	Ficolin-3, adiponectin (FAR)	FAR predicted later GDM	Age, BMI, gestational age
2	[13]	Nested Case–Control (Cohort-Based)	107 / 214	10–39 weeks	Adipokines (FABP4, chemerin, IL-6, leptin, adiponectin, etc.)	Adipokines improved GDM risk prediction	Age, pre-pregnancy BMI, parity, gestational week, family history of diabetes
3	[14]	Case–Control	110 / 100	24–28 weeks	Vitamin D, hs-CRP, Hcy, HOMA-IR	Lower Vit-D; higher inflammation in GDM	Group matching for age, BMI, parity
4	[15]	Cross-Sectional	NR	24–28 weeks	CRP/Albumin ratio	Higher CAR in GDM	NR (comparative analysis only)
5	[16]	Case–Control	NR	Late 2nd–3rd trimester	MDA, SOD, GSH	OS markers linked to adverse neonatal outcomes	NR (ROC-based models)
6	[17]	Case–Control (Cord Blood)	NR	At delivery	Cord C-peptide	Fetal hyperinsulinemia with GDM	NR
7	[18]	Retrospective Cohort	NR	At delivery	Cord C-peptide	Predicts neonatal hypoglycemia	NR
8	[19]	Rct	NR	Mid–late pregnancy; cord	DHA, cord adipokines	Favorable fetal adipokine profile	Maternal BMI, glycemia
9	[20]	Prospective Cohort	NR	24–28 weeks	TG, TG/HDL-C	TG predicts macrosomia	Regression models (limited covariates)
10	[21]	Case–Control	NR	24–28 weeks	hs-CRP, IL-6, IL-18	IL-18 correlated with dysglycemia	Age; BMI in selected models
11	[22]	Cross-Sectional	37 / 33	≥24 months postpartum	Flow-mediated dilation (FMD)	Persistent endothelial dysfunction	Restricted age; exclusion of smokers/ comorbidities
12	[23]	Case–Control	153 / 84	24–29 weeks	Chemerin, lipocalin-2, apelin	Adipokine dysregulation in GDM	NR
13	[24]	RCT	NR	At delivery	Cord leptin/adiponectin; ANGPTL4	Glycemic targets alter fetal profile	NR

NR' indicates that the study did not explicitly report statistical adjustment for confounding variables. Restricted eligibility refers to predefined inclusion/exclusion criteria used to minimize confounding.

Gestational diabetes mellitus was consistently associated with increased insulin resistance, inflammation, oxidative stress, endothelial dysfunction, and dysregulated adipokine profiles, supporting its characterization as a systemic metabolic disorder rather than isolated hyperglycemia. Multiple studies reported significantly elevated fasting glucose and HOMA-IR in women with GDM, alongside increased umbilical cord C-peptide levels, indicating fetal hyperinsulinemia and a close maternal–fetal metabolic link. Maternal hypertriglyceridemia was also identified as an independent predictor of fetal macrosomia, highlighting the role of lipid dysregulation beyond glucose-mediated effects. Inflammatory and oxidative markers, including hs-CRP, IL-6, IL-18, CRP/albumin ratio, and MDA, were consistently elevated, with evidence of persistent vascular impairment extending into the postpartum period. Collectively, these findings depict GDM as a complex metabolic cascade in which insulin resistance, lipid abnormalities, inflammation, oxidative stress, and hormonal disruption converge to influence maternal and fetal outcomes adversely (Table 2).

Table 2: Maternal Physiological and Biochemical Outcomes in Gestational Diabetes Mellitus (GDM)

Outcome Domain	Assay / Time Point	Direction vs Controls	Magnitude Summary	Adjustment Status	Notes On Heterogeneity	References
Glycemic / Insulin (HOMA-IR, fasting / OGTT glucose, insulin, C-peptide)	Fasting glucose, 75 g OGTT indices (24 – 28 w); cord C-peptide at delivery	↑ glycemia & ↑ HOMA -IR in GDM; ↑ cord C- peptide = fetal hyperinsulinemia	Moderate–large group differences; cord C-peptide markedly higher in GDM	Adjusted in Francis and Zhao; others unadjusted	GDM criteria and assay methods vary across studies	[21, 25]
Lipid (TG, HDL-C, LDL-C, NEFA)	Maternal fasting TG / HDL (24–36 w)	↑ maternal TG in GDM	Moderate ↑; TG linked to macrosomia and LGA	Unadjusted in most; Abdullah used regression	Timing and fasting status vary between studies	[20]

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Inflammatory (CRP, IL-6, TNF-α, IL-18)	hs-CRP, IL-6 (24–28 w); CRP/Albumin ratio (1st–2nd trimester)	↑ hs-CRP and ↑ IL-6 / IL-18 in GDM; ↑ CAR in GDM	Small–moderate ↑ for CRP/IL-6; IL-18 strong ↑; CAR distinct difference	Zhao adjusted (age, BMI); Francis multi-adjusted	Inflammatory indices (CAR, NLR) and cytokine panels differ	[13, 25]
Oxidative / Endothelial (MDA, TAC, NO/ADMA, FMD)	MDA, SOD, GSH (late pregnancy); FMD ≥ 24 mo postpartum	↑ MDA; ↓ SOD/GSH in GDM; ↓ FMD in women with prior GDM	Moderate effect sizes; FMD ~3 % lower post-GDM ($p < 0.001$)	Wang used ROC models; Albayrak controlled for age and comorbid	Lab assays vary; FMD measured postpartum (legacy effect)	[16, 22]
Adipokines / Hormones (adiponectin, leptin, chemerin, FABP4, sOB-R, lipocalin-2, apelin, omentin-1, vaspin, RBP-4)	Serial sampling 10–39 w and at delivery (cord)	↓ adiponectin & sOB- R; ↑ leptin, FABP4, chemerin; ↑ lipocalin -2; apelin ↔ / variable	Consistent across cohorts; moderate to large effects for leptin, chemerin, and FABP4	Francis fully adjusted (age, BMI, parity, etc.); Mierzyński correlations;	Different assay kits & sampling windows (10–39 w); cohort vs case-control mix	[13, 23]
Placental Factors (PLGF, sFlt-1, PAPP-A)	Antenatal plasma/placenta	No data within 2017–2024 set	–	–	None of the included studies reported maternal placental angiogenic markers	–
Coagulation (fibrinogen, D-dimer)	Antenatal plasma	No data within 2017–2024 set	–	–	–	–
Dietary lipid intervention signal	Maternal DHA across gestation; cord adipokines at delivery	DHA ↔ / favorable shift in cord leptin/ adiponectin profile despite GDM	Small–moderate improvement in biomarker pattern	Xu adjusted (BMI, glycemia)	Intervention study; mechanistic evidence only	[19]

Fetal and neonatal outcomes closely reflected the maternal metabolic milieu, with dysglycemia, dyslipidemia, and inflammation influencing fetal growth, endocrine function, and early metabolic adaptation. Maternal hypertriglyceridemia showed an independent association with fetal macrosomia, indicating that lipid transfer across the placenta contributes to fetal adiposity beyond glucose-mediated effects. Elevated umbilical cord C-peptide levels in pregnancies complicated by GDM indicated fetal hyperinsulinemia and were predictive of neonatal hypoglycemia, supporting the Pedersen hypothesis. Dysregulated adipokines, characterized by low adiponectin and elevated leptin, FABP4, and chemerin, were associated with increased fetal adiposity and altered cord hormonal profiles, with evidence that looser maternal glycemic control exacerbated these changes. Collectively, oxidative stress, inflammation, and metabolic dysregulation appear to mediate a continuous maternal-fetal metabolic interaction that shapes fetal growth trajectories and may have lasting postnatal consequences (Table 3).

Table 3: Fetal/Neonatal Outcomes and Links to Maternal Biomarkers (Qualitative)

Outcome Category	Maternal Biomarker(S) and Timing	Association Direction (Materna → Fetal/Neonatal)	Effect Summary (Qualitative)	Adjustment Status	Notes on Heterogeneity	References
Fetal Overgrowth (Macrosomia/LGA)	Triglycerides (late 2nd–3rd tri); TG/HDL-C	↑ TG → ↑ macrosomia/LGA	Higher maternal TG independently predicts macrosomia among women with GDM	Adjusted logistic models	Fasting status and lipid panels vary; mostly late -gestation measures	[20]
Birthweight/ Adiposity (Cord Bio-Signatures)	Cord leptin, adiponectin; L/A ratio (at delivery)	↑ maternal glycemia /looser targets → ↑ cord L/A & leptin	Looser glycemic control is associated with higher cord L/A and endothelial gene expression shifts	Trial models (within-trial adjustment)	Intervention context: cord hormones reflec fetal fat mass	[24]
Birthweight/ Adiposity (Maternal Adipokines)	Adiponectin (↓) leptin (↑), FABP4 (↑), chemerin (↑) (10–39 w serial)	Adipokine profile consistent with ↑ fetal growth risk	Early/mid-pregnancy low adiponectin & high leptin/chemerin/ FABP4 associate with later GDM and pro-adiposity milieu	Multivariable models (age, BMI, parity, etc.)	Biomarker panels/ assays differ; multiethnic cohort	[13]

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Neonatal Hypoglycemia	Cord C-peptide (delivery)	↑ C-peptide → ↑ hypoglycemia risk	Cord C-peptide strongly predicts early neonatal hypoglycemia in infants of GDM mothers	Multivariable models	Definitions and glucose thresholds vary by site	[18]
Fetal Hyperinsulinemia (Biochemical)	Maternal glycemia (24–28 w); metabolic control → Cord C-peptide	↑ maternal glycemia → ↑ cord C-peptide	Clear step-up of fetal C-peptide with maternal hyperglycemia/GDM	Regression models/ group comparisons	Cord sampling/assay platforms differ	[17]
Neonatal Neurodevelopment (Early)	Oxidative stress panel: MDA (↑), SOD (↓), GSH (↓)(late gestation)	↑ MDA / ↓ antioxidants → less favorable neurodevelopmental indices	OS markers associated with adverse perinatal outcomes and predicted poorer early neurodevelopment	ROC-based prediction; limited covariates	AMA population; follow-up timeframe is short	[16]
NICU/Perinatal Composite (Signal Via Inflammation)	Inflammatory cytokines: hs-CRP, IL-6, IL-18 (24–28 w)	↑ materna inflammation → adverse perinatal risk signal	Stronger IL-1 elevations track worse glycemic screens; perinatal links are indirect but biologically plausible	Adjusted for age (±BMI)	Cytokine panels and diagnostic thresholds vary	[21]
Placental–Endothelial Milieu (Mechanistic)	Maternal DHA across gestation; cord adipokines (delivery)	↑ maternal DHA → ↓ cord leptin / favorable L/A profile	DHA supplementation shifts cord biomarkers toward a less adipogenic profile	Trial models (BMI, glycemia)	Mechanistic RCT; not standard care	[19]
Fetal Vascular Function (Contextual)	Maternal vascular/ metabolic status (history of GDM)	Prior GDM → persistent maternal endothelial dysfunction	Postpartum ↓FMD suggests endothelial legacy; fetal linkage is indirect but supports milieu of risk	Restricted groups (age, comorbidities)	Postpartum measure (≥24 mo), not antenatal	[22]

Overall, the included studies demonstrated generally acceptable methodological quality, with most exhibiting low to moderate risk of bias based on the NIH Quality Assessment Tool and Cochrane RoB 2 criteria. Participant selection and exposure measurement were clearly described in several large cohort and randomized studies, particularly those by Francis *et al.* and Xu *et al.* which used standardized recruitment procedures and biomarker assays [13, 19]. Some limitations were observed in single-center or retrospective studies, where control for confounding variables such as maternal body mass index, parity, and gestational age was incomplete. Nevertheless, outcome measurements across studies were largely based on validated laboratory methods, with minimal evidence of missing data or selective reporting. Collectively, the low-to-moderate risk of bias supports the credibility of the observed associations between gestational diabetes, metabolic dysregulation, and adverse maternal–fetal outcomes, while underscoring the need for future multicenter studies with standardized adjustment strategies.

DISCUSSION

Gestational diabetes mellitus (GDM) has increasingly been recognized as a complex metabolic disorder rather than a transient disturbance of glucose homeostasis. The findings of this review consistently demonstrate that insulin resistance, dyslipidemia, inflammation, oxidative stress, endothelial dysfunction, and adipokine imbalance form an interconnected pathophysiological network in GDM [26]. These mechanisms appear to operate simultaneously and reinforce one another, supporting the concept that GDM represents a systemic metabolic condition with consequences extending beyond pregnancy [27, 28]. Lipid metabolism emerged as a key determinant of adverse fetal outcomes. Maternal hypertriglyceridemia and elevated triglyceride/HDL-C ratios were independently associated with fetal macrosomia, even after accounting for glycemic indices, highlighting the contribution of non-glucose substrates to fetal overgrowth [29]. These findings align with earlier evidence suggesting that reliance solely on glucose-based screening may underestimate fetal metabolic risk in GDM pregnancies [30, 31]. Placental transfer of lipids likely plays a substantial role in fetal adiposity, reinforcing the importance of dyslipidemia in maternal–fetal fuel dynamics. Inflammation and oxidative stress were also consistently implicated across studies.

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Elevated inflammatory markers, including IL-6, IL-18, and CRP-based indices, reflect immune metabolic activation that may impair placental signaling and fetal metabolic programming [32]. Oxidative stress markers such as malondialdehyde, alongside reduced antioxidant capacity, were associated with endothelial dysfunction and adverse neonatal outcomes, including early neurodevelopmental vulnerability [33, 34]. These findings suggest that inflammatory and redox imbalance may act as mediators linking maternal metabolic stress to both vascular and developmental consequences. Adipokine dysregulation further underscores the systemic nature of GDM. Reduced adiponectin and increased levels of leptin, chemerin, and FABP4 were repeatedly associated with insulin resistance, inflammation, and increased fetal adiposity, independent of maternal body mass index [35, 36]. These alterations highlight the role of adipose tissue inflammation and endocrine dysfunction in shaping maternal and fetal metabolic phenotypes. Collectively, the evidence supports a unified metabolic cascade in which maternal insulin resistance, lipid abnormalities, inflammation, oxidative stress, and hormonal dysregulation converge to influence placental adaptation and fetal programming [37-39].

Most studies included in this review were cross-sectional or single-center, limiting causal inference and generalizability. Variability in biomarker measurement and lack of standardized panels across studies also constrain direct comparisons. Based on the reviewed evidence, future research should prioritize multicenter, longitudinal studies with standardized biomarker panels to clarify the independent and combined roles of glucose, lipids, inflammation, and oxidative stress in gestational diabetes mellitus. Integrating metabolic and inflammatory markers into clinical risk assessment may improve early identification of pregnancies at risk for adverse maternal-fetal outcomes.

CONCLUSIONS

This systematic review demonstrates that gestational diabetes mellitus is a multisystem metabolic disorder involving insulin resistance, dyslipidemia, inflammation, oxidative stress, adipokine imbalance, and vascular dysfunction. These maternal metabolic disturbances are closely linked to fetal consequences, including macrosomia, hyperinsulinemia, altered adipokine profiles, and metabolic vulnerability. Understanding GDM as a complex metabolic condition provides a stronger biological basis for interpreting maternal–fetal outcomes beyond glucose dysregulation alone.

Authors' Contribution

Conceptualization: AM
Methodology: BHI, MK, SZ, QJ
Formal analysis: AM
Writing and Drafting: AM, BHI, MK, SZ, QJ, AI
Review and Editing: AM, BHI, MK, SZ, QJ, AI

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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