ГЕСТАЦИОННЫЙ САХАРНЫЙ ДИАБЕТ И ПРЕЭКЛАМПСИЯ: ОБЩИЕ ПАТОФИЗИОЛОГИЧЕСКИЕ МЕХАНИЗМЫ И ФАКТОРЫ РИСКА

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Аннотация: Гестационный сахарный диабет и преэклампсия являются частыми осложнениями беременности и нередко возникают совместно, усиливая риски для матери и ребёнка. Цель данного обзора — обобщить современные данные о взаимосвязи этих состояний и факторах, повышающих вероятность их сочетанного развития. Анализ опубликованных исследований показывает, что женщины с ГСД имеют более высокий риск преэклампсии по сравнению с общей популяцией, особенно при наличии ожирения, хронического воспаления и выраженной инсулинорезистентности. Представленные данные подчёркивают важность раннего выявления групп риска, оптимизации метаболического контроля и тщательного мониторинга беременных с ГСД для снижения частоты осложнений и улучшения перинатальных исходов.

Ключевые слова: гестационный сахарный диабет, преэклампсия, гипертензивные расстройства беременности, перинатальные исходы, метаболические нарушения, сосудистая дисфункция, факторы риска.

GESTATSION DIABET VA PREEKLAMPSIYA: UMUMIY PATOFIZIOLOGIK MEXANIZMLAR VA XAVF OMILLARI

Annotatsiya: Gestatsion qandli diabet (GQD) va preeklampsiya homiladorlikning eng keng tarqalgan asoratlaridan bo‘lib, ko‘pincha birgalikda uchraydi hamda ona va bola uchun xavflarni oshiradi. Ushbu sharh ushbu holatlar o‘rtasidagi bog‘liqlik va ularning birgalikda rivojlanishiga ta’sir qiluvchi omillar bo‘yicha mavjud ilmiy ma’lumotlarni umumlashtiradi. Dunyo bo'ylab o’tkazilgan tadqiqotlar GQD bo‘lgan ayollarda preeklampsiya rivojlanish ehtimoli yuqoriroq ekanini, ayniqsa semizlik, surunkali yallig‘lanish va kuchli insulinrezistentlik mavjud bo‘lgan hollarda oshishini ko‘rsatadi. Ushbu natijalar xavf guruhlarini erta aniqlash, metabolik nazoratni optimallashtirish va GQD bilan homilador ayollarni sinchiklab kuzatib borishning ahamiyatini ta’kidlaydi. Bu yondashuv asoratlarni kamaytirishga va perinatal natijalarni yaxshilashga yordam beradi.

Kalit so‘zlar: gestatsion qandli diabet, preeklampsiya, homiladorlikdagi gipertenziv buzilishlar, perinatal natijalar, metabolik buzilishlar, tomir disfunksiyasi, xavf omillari.

GESTATIONAL DIABETES AND PREECLAMPSIA: SHARED PATHOPHYSIOLOGICAL MECHANISMS AND RISK FACTORS

Annotation: Gestational diabetes mellitus (GDM) and preeclampsia are among the most common pregnancy complications and frequently coexist, increasing risks for both the mother and the fetus. This review summarizes current evidence on the association between these conditions and the factors contributing to their combined occurrence. Published data indicate that women with GDM have a higher likelihood of developing preeclampsia, particularly in the presence of obesity, chronic inflammation, and marked insulin resistance. These findings highlight the importance of early risk identification, optimization of metabolic control, and careful monitoring of pregnant women with GDM to reduce adverse outcomes and improve perinatal health.

Keywords: gestational diabetes mellitus, preeclampsia, hypertensive disorders of pregnancy, perinatal outcomes, metabolic dysfunction, vascular dysregulation, risk factors.

INTRODUCTION

Gestational diabetes mellitus (GDM) and preeclampsia (PE) are among the leading causes of pregnancy-associated morbidity worldwide, with both conditions demonstrating rising incidence over the past two decades [17]. Although their clinical manifestations differ, contemporary pathophysiological research increasingly highlights substantial overlap between the biological mechanisms driving both disorders. Recent high-quality evidence indicates that chronic low-grade inflammation, systemic endothelial dysfunction, and impaired placental angiogenesis constitute shared early pathways in the development of GDM and PE [18,21].

Growing evidence suggests that metabolic dysregulation plays a pivotal role in linking these two conditions. Hyperglycemia-induced vascular injury, oxidative stress, and angiogenic imbalance—particularly alterations in the sFlt-1/PlGF ratio—are now recognized as central contributors to PE pathogenesis and appear similarly disrupted in women with GDM [19]. Large epidemiological cohorts have further demonstrated that the metabolic vulnerability underlying gestational diabetes mellitus significantly increases the risk of hypertensive disorders of pregnancy, even when confounding factors such as maternal age and obesity are controlled [20].

From a clinical perspective, the coexistence of GDM and PE is associated with markedly increased risks of preterm birth, fetal growth abnormalities, and severe maternal cardiovascular complications. These findings reinforce the need for an integrated mechanistic framework to improve risk stratification, guide antenatal surveillance, and develop targeted strategies for early intervention [18–20].

AIMS

To conduct a comprehensive review of contemporary scientific evidence describing the interrelationship between gestational diabetes mellitus and preeclampsia, with particular focus on

shared mechanistic pathways, risk determinants, and clinical implications, based on data from randomized controlled trials, meta-analyses, and international evidence-based recommendations.

MATERIALS AND METHODS

A targeted literature search was carried out in PubMed/MEDLINE, PubMed Central, and Wiley Online Library. Priority was given to studies addressing pathogenic mechanisms, epidemiological interactions, and clinical outcomes related to the coexistence of GDM and PE. Meta-analyses, large cohort studies, mechanistic papers, and guideline-based publications were included.

RESULTS

A growing body of evidence shows that disturbances characteristic of GDM profoundly affect placental development. Persistent maternal hyperglycemia and insulin resistance impair trophoblast invasion and hinder normal remodeling of spiral arteries, predisposing the placenta to chronic hypoxia and oxidative stress [1]. Hypoxic placental tissue responds by excessive production of antiangiogenic factors—primarily sFlt-1—which neutralizes VEGF and PlGF and provokes widespread endothelial dysfunction leading to hypertension [2,3].

In parallel, heightened activation of neutrophils in GDM results in increased formation of neutrophil extracellular traps (NETs). NET accumulation within the intervillous space disrupts placental perfusion, aggravating hypoxic injury. This phenomenon parallels mechanisms observed in severe PE [1].

Hyperglycemia-induced oxidative stress and the accumulation of advanced glycation end products further reduce nitric oxide bioavailability and promote vasoconstriction, contributing to the systemic vasospastic response that characterizes PE [1]. Recent studies confirm that the combined presence of these metabolic abnormalities in GDM significantly amplifies angiogenic imbalance and endothelial dysfunction, producing a profile closely resembling early PE pathogenesis [9,11].

Taken together, these mechanisms illustrate how the metabolic environment of GDM evolves into a pathological state that reproduces and intensifies the core pathways underlying PE [13].

Epidemiological Evidence

Extensive population-based research demonstrates that GDM acts as an independent predictor of PE. The HAPO study provided strong evidence of a dose–response relationship: rising maternal glucose levels correlate with higher rates of hypertensive disorders of pregnancy [4].

A 2023 meta-analysis published in Hypertension, involving nearly four million women, reported that a history of GDM increases the risk of subsequent hypertension by approximately 80% (RR 1.78; 95% CI 1.47–2.17) [5]. Since PE represents a pregnancy-specific hypertensive disorder, this finding further supports the vascular vulnerability associated with GDM.

Retrospective cohort studies consistently show that gestational diabetes mellitus alone increases the risk of preeclampsia by 50–80%, with the risk potentially doubling in the presence of pronounced hyperglycemia [6]. New large-scale analyses confirm that the coexistence of GDM and PE is associated with significantly worse maternal and neonatal outcomes, including higher rates of preterm delivery and severe hypertensive complications [9].

Importantly, early-onset GDM shows a particularly strong association with PE, reflecting deeper metabolic dysfunction; this relationship has been validated in more recent cohorts published in 2024–2025 [14,16].

The risk escalates substantially when GDM is accompanied by obesity: some studies document up to a threefold increase in PE incidence. Furthermore, early-onset GDM—diagnosed before 20–24 weeks—confers a markedly higher risk (2–8-fold), reflecting more severe underlying metabolic dysfunction.

Role of Diet and Inflammation

A systematic review by Li Hong et al. highlighted the importance of dietary inflammatory load. Women whose diets had the highest inflammatory index demonstrated significantly increased risks of both GDM (35–45%) and PE (30–40%) [7]. Pro-inflammatory dietary habits intensified systemic inflammation and oxidative stress, reinforcing pathogenic pathways shared by both disorders.

Additional recent evidence suggests that inflammatory dietary patterns exacerbate endothelial dysfunction and angiogenic imbalance, thereby increasing susceptibility to PE, especially in metabolically vulnerable women with early GDM [15].

Interaction Between GDM and SARS-CoV-2

The study by Di Martino et al. demonstrated that SARS-CoV-2 infection further amplifies angiogenic imbalance in pregnancies with GDM. Women with both conditions exhibited a markedly elevated sFlt-1/PlGF ratio comparable with that in high-risk PE cases [8]. The combination of hyperglycemia, enhanced inflammation, and viral endothelial injury likely explains increased rates of placental insufficiency in this subgroup.

Later studies have reinforced the prognostic significance of the sFlt-1/PlGF ratio specifically in pregnancies complicated by GDM, proposing this index as a potential screening tool for early detection of impending PE [10,12].

Clinical Significance

Women with simultaneous gestational diabetes mellitus and preeclampsia experience substantially higher risks of:

• preterm delivery,
• fetal growth restriction or macrosomia,
• cesarean delivery,
• postpartum cardiometabolic complications [9,14].

Recent investigations confirm that angiogenic biomarkers (particularly the sFlt-1/PlGF ratio) may help stratify the risk of severe outcomes in this subgroup, offering an opportunity for earlier intervention [10–12].

These observations highlight the importance of early screening for GDM, rigorous glycemic management, proactive blood pressure monitoring, and targeted biomarker assessment in pregnancies at increased risk [15,16].

This underscores the need for:

• early GDM screening,
• stringent glycemic control,
• proactive blood pressure surveillance,
• assessment of placental biomarkers in high-risk pregnancies.

DISCUSSION

The findings summarized in this review reinforce the concept that gestational diabetes mellitus and preeclampsia are interconnected disorders that arise from overlapping metabolic and vascular disturbances. Although traditionally approached as separate clinical entities, the evidence presented across epidemiological, mechanistic, and translational studies indicates that the metabolic environment characteristic of GDM creates conditions that substantially increase susceptibility to PE.

Central to this interaction is the role of maternal hyperglycemia and insulin resistance, which impair trophoblast invasion and spiral artery remodeling, thereby initiating placental hypoxia and oxidative stress — hallmark early mechanisms of preeclampsia. These alterations drive the overproduction of antiangiogenic factors such as sFlt-1, reduce PlGF availability, and precipitate systemic endothelial dysfunction. The reviewed literature consistently demonstrates that this angiogenic imbalance is more pronounced when GDM and PE coexist, underscoring the biological synergy between the two disorders.

Epidemiological data further validate these mechanistic findings. Large population-based cohorts and meta-analyses confirm that GDM acts as an independent predictor of PE, with risk magnitudes remaining significant even after adjusting for confounders such as maternal age and obesity. Early-onset GDM appears to reflect a deeper metabolic derangement and is associated with particularly high rates of hypertensive complications. The consistent dose–response relationship between rising glucose levels and hypertensive outcomes (as shown in HAPO and subsequent large-scale studies) supports the hypothesis that metabolic stress is a primary driver rather than a secondary correlate.

Additional factors may modify this interaction. Diet-induced inflammation, as highlighted in multiple analyses, amplifies oxidative stress and endothelial dysfunction, worsening both GDM and PE risk profiles. Similarly, SARS-CoV-2 infection intensifies angiogenic imbalance, particularly in women with GDM, suggesting that viral endothelial injury and hyperglycemia act synergistically to impair placental function. These insights emphasize that GDM-related metabolic vulnerability can be significantly exacerbated by external inflammatory stimuli.

Clinically, the coexistence of GDM and PE identifies a high-risk phenotype characterized by significantly increased rates of preterm birth, fetal growth abnormalities, cesarean delivery, and postpartum cardiometabolic complications. Importantly, recent studies demonstrate that angiogenic biomarkers — especially the sFlt-1/PlGF ratio — may help refine risk stratification in pregnancies affected by GDM, offering an opportunity for earlier detection of impending PE and more individualized surveillance strategies.

Taken together, the evidence strongly supports a shift toward integrated early-pregnancy risk assessment models that account for metabolic, vascular, and inflammatory factors simultaneously. While traditional glycemic control remains essential, it does not fully mitigate the underlying endothelial vulnerability, explaining why women with well-managed GDM may still progress to PE. Future research should focus on validating biomarker-driven prediction tools and delineating how metabolic interventions can influence angiogenic pathways.

Overall, the convergence of mechanistic and epidemiological findings highlights the need for a unified clinical approach to GDM and PE, recognizing them not as isolated disorders but as interdependent manifestations of broader metabolic–vascular dysfunction during pregnancy.

CONCLUSION

Gestational diabetes mellitus significantly increases the probability of preeclampsia through converging mechanisms involving systemic inflammation, endothelial dysfunction, oxidative stress, and anti-angiogenic imbalance.

The risks are particularly elevated among women with obesity, early-onset GDM, or pronounced glucose-metabolic abnormalities.

Even with effective glycemic management, a considerable residual risk persists, underscoring the need for individualized antenatal surveillance and biomarker-based risk assessment.

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