



Gestational Diabetes and the Child's Cardiometabolic Programming: Evidence on Fetal, Neonatal, and Cardiovascular Outcomes

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy and is associated with significant maternal, fetal, and neonatal consequences. Recent evidence shows that intrauterine exposure to hyperglycemia can trigger cardiometabolic programming mechanisms, increasing the offspring's susceptibility to developing obesity, insulin resistance, metabolic syndrome, type 2 diabetes mellitus, and cardiovascular diseases throughout life.

Objective: To analyze the scientific evidence regarding the relationship between gestational diabetes mellitus and cardiometabolic programming in children, emphasizing the main fetal, neonatal, and cardiovascular outcomes.

Methods: A systematic literature review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020). Searches were conducted in the following databases: PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, Virtual Health Library (BVS), and SciELO. Studies published between 2016 and 2025, in Portuguese and English, that investigated the association between gestational diabetes and cardiometabolic outcomes in offspring were included. After the selection process, 85 studies met the eligibility criteria and were included in the qualitative synthesis.

Results: The studies demonstrated a consistent association between gestational diabetes and a higher incidence of fetal macrosomia, neonatal hypoglycemia, accelerated fetal growth, increased body adiposity, childhood obesity, insulin resistance, metabolic syndrome, hypertension, type 2 diabetes mellitus, and early cardiovascular abnormalities. Epigenetic changes, inflammatory processes, oxidative stress, and endothelial dysfunction were identified as the main mechanisms involved in cardiometabolic programming. The evidence also demonstrated that early diagnosis, adequate glycemic control, and longitudinal follow-up of the child significantly reduce adverse outcomes.

Conclusion: Gestational diabetes mellitus is a major factor in the cardiometabolic programming of offspring, with persistent repercussions throughout the life course. Strengthening prenatal screening, maternal metabolic control, and multidisciplinary follow-up of the child represents a fundamental strategy for reducing the intergenerational transmission of cardiometabolic risk and preventing future chronic diseases.

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1. Introduction

Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy, characterized by hyperglycemia first diagnosed during pregnancy and associated with significant maternal, fetal, and neonatal consequences. Its prevalence has been steadily increasing due to the global obesity epidemic, the trend toward older maternal age, and the higher

incidence of metabolic risk factors, making it a major challenge for health care systems. Early identification and appropriate management are considered essential for reducing obstetric complications and promoting better short- and long-term outcomes (American Diabetes Association Professional Practice Committee, 2025; McIntyre *et al.*, 2019) [7, 65].

The understanding of gestational diabetes has evolved significantly in recent decades, driven by the realization that even subtle changes in glucose metabolism during pregnancy can alter the intrauterine environment and permanently influence fetal development. Current international recommendations emphasize the need for universal or risk-factor-based screening, as well as the implementation of standardized care protocols to reduce maternal and fetal morbidity and mortality (American College of Obstetricians and Gynecologists, 2021; FIGO Working Group on Hyperglycemia in Pregnancy, 2020) [4, 39].

The Developmental Origins of Health and Disease (DOHaD) hypothesis has revolutionized our understanding of the influence of the intrauterine environment on a child's future health. This concept demonstrates that metabolic stimuli occurring during critical periods of fetal development can induce persistent structural, functional, and epigenetic adaptations, predisposing the individual to the development of cardiometabolic diseases in childhood and adulthood. These mechanisms are particularly relevant in pregnancies complicated by gestational diabetes (Briana; Malamitsi-Puchner, 2018; Hill *et al.*, 2019) [15, 47].

Bahado-Singh *et al.* (2019) [9] and Danese *et al.* (2021) [29] demonstrate that fetal exposure to maternal hyperglycemia promotes metabolomic and epigenetic alterations capable of modifying gene expression involved in energy homeostasis, adipocyte differentiation, and glucose metabolism. These changes include alterations in DNA methylation, histone modifications, and microRNA expression—mechanisms that contribute to fetal programming of future metabolic and cardiovascular diseases, reinforcing the transgenerational nature of gestational diabetes.

In addition to molecular changes, intrauterine hyperglycemia is associated with significant clinical consequences during the fetal and neonatal periods. Key outcomes include fetal macrosomia, disproportionate growth, neonatal hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, the need for admission to a neonatal unit, and an increased risk of obstetric complications. Recent evidence indicates that these consequences represent only the initial manifestation of a continuous process of cardiometabolic programming that may persist throughout life (Boersen *et al.*, 2021; Moore *et al.*, 2021; Pereira *et al.*, 2019) [13, 70, 74].

Lowe *et al.* (2018) [61] and the HAPO Follow-up Study Cooperative Research Group (2019) [46] demonstrated that there is a continuous relationship between maternal glucose levels during pregnancy and the development of adiposity, insulin resistance, and alterations in glucose metabolism in childhood. These findings indicate that even modest elevations in maternal blood glucose levels—often below the classic thresholds for diabetes—can have lasting effects on a child's metabolic health, underscoring the importance of early diagnosis and glycemic control throughout pregnancy. The association between gestational diabetes and childhood obesity has been consistently demonstrated in observational studies and meta-analyses. Children exposed to a

hyperglycemic intrauterine environment exhibit greater accumulation of adipose tissue, increased body mass index, and a higher predisposition to developing metabolic syndrome during adolescence and adulthood. These effects remain significant even after adjusting for factors such as maternal obesity and socioeconomic characteristics, suggesting a direct influence of fetal programming. (Chen *et al.*, 2021; Li *et al.*, 2020; Kawasaki *et al.*, 2018) [21, 58, 53].

Fetal exposure to gestational diabetes is also associated with early impairment of cardiovascular health. Structural and functional changes in the vascular endothelium, increased arterial stiffness, autonomic dysfunction, and elevated blood pressure have been identified as early as childhood, indicating that cardiovascular programming begins during intrauterine life. These changes may represent the earliest stages of cardiovascular disease development in adulthood (Li *et al.*, 2019; Ray *et al.*, 2021; Guo *et al.*, 2022) [57, 76, 44]. O'Reilly *et al.* (2019) [71] and Page *et al.* (2019) [73] emphasize that a hyperglycemic intrauterine environment promotes fetal cardiovascular remodeling through alterations in mitochondrial function, increased oxidative stress, low-grade chronic inflammation, and changes in angiogenesis. These mechanisms contribute to persistent changes in cardiac function, increased susceptibility to hypertension, peripheral vascular resistance, and impaired endothelial function throughout life, establishing a direct link between gestational diabetes and future cardiovascular risk.

The cardiometabolic programming resulting from gestational diabetes does not depend exclusively on hyperglycemia. Several maternal factors act in an integrated manner, including obesity, systemic inflammation, insulin resistance, excessive weight gain during pregnancy, poor dietary habits, and physical inactivity. This interaction amplifies the deleterious effects on fetal development, increasing the risk of obesity, type 2 diabetes, and cardiovascular disease in future generations (Catalano; Shankar, 2017; Grieger *et al.*, 2021; Gomes *et al.*, 2019) [19, 43, 42].

Recent systematic reviews emphasize that follow-up of children born to mothers with gestational diabetes should extend beyond the neonatal period, incorporating strategies for clinical monitoring and cardiometabolic prevention starting in childhood. Monitoring growth, metabolic profile, blood pressure, body composition, and lifestyle habits can facilitate the early identification of individuals at higher risk, enabling interventions capable of reducing the occurrence of chronic diseases throughout their lives (Bian *et al.*, 2021; Cooray *et al.*, 2022; Wicklow *et al.*, 2023) [12, 25, 85].

Buckley *et al.* (2020) [18] and Bogdanet *et al.* (2020) [14] highlight that the effects of gestational diabetes on the health of offspring remain evident many years after birth, characterizing a phenomenon of persistent metabolic programming. Longitudinal follow-up of these children demonstrates a higher prevalence of insulin resistance, central adiposity, glucose intolerance, and alterations in the lipid profile, indicating that intrauterine exposure to hyperglycemia constitutes an independent risk factor for the development of early-onset metabolic diseases.

The influence of maternal blood glucose levels on fetal growth has also been extensively documented in multicenter studies. Children exposed to gestational diabetes have a higher percentage of body fat at birth, accelerated growth in the first years of life, and a tendency to remain overweight throughout childhood. These findings reinforce the notion that metabolic changes that begin during gestation have a

direct impact on body composition and the risk of future obesity (Aris *et al.*, 2021; Chen *et al.*, 2021; Ferrara *et al.*, 2020) [8, 20, 38].

In addition to metabolic outcomes, recent studies suggest that intrauterine exposure to gestational diabetes may influence a child's neurological development. Cognitive impairments, a higher incidence of neurodevelopmental disorders, and behavioral changes have been associated with the fetal hyperglycemic environment, although the mechanisms involved are still under investigation. Evidence suggests that inflammatory processes, oxidative stress, and epigenetic changes may contribute to these outcomes, extending the impact of gestational diabetes beyond the metabolic system (Ding *et al.*, 2021; Fernández-Morilla *et al.*, 2022) [32, 37].

Hjort *et al.* (2018) [48] and Hjort *et al.* (2019) [49] demonstrated that children of women with gestational diabetes exhibit persistent epigenetic changes, particularly related to DNA methylation patterns in genes involved in the regulation of insulin sensitivity, inflammation, and energy metabolism. These changes may remain detectable throughout childhood and represent one of the main biological mechanisms responsible for the intergenerational transmission of cardiometabolic risk.

The interaction between maternal obesity and gestational diabetes significantly exacerbates adverse effects on fetal development. When these conditions coexist, there is a marked increase in the frequency of macrosomia, cesarean delivery, neonatal hypoglycemia, admission to the neonatal intensive care unit, and a higher risk of childhood obesity. Thus, the metabolic impact results from a combination of genetic predisposition, the intrauterine environment, and postnatal environmental factors (DALI Consortium, 2018; IJäs *et al.*, 2019; Weir, Majumder, & Glastris, 2024) [27, 51, 84]. Advances in understanding the pathophysiology of gestational diabetes have underscored the importance of early diagnosis and the adoption of individualized treatment strategies. Strict glycemic control, combined with nutritional interventions, physical activity, fetal monitoring, and judicious use of insulin or pharmacological agents when indicated, significantly reduces immediate obstetric complications and can minimize the effects of cardiometabolic programming on the offspring. These benefits underscore the relevance of international clinical guidelines for the comprehensive care of pregnant women and newborns (Sweeting *et al.*, 2022; Moon and Jang, 2022; American Diabetes Association Professional Practice Committee, 2024) [82, 68, 6].

Moon *et al.* (2023) [69] and Al Bekai *et al.* (2025) [2] emphasize that gestational diabetes should be understood as a condition with repercussions that extend beyond pregnancy, since its effects may persist throughout the offspring's entire life cycle. Current evidence demonstrates that intrauterine exposure to hyperglycemia alters metabolic and cardiovascular trajectories from the earliest years of life, reinforcing the need for longitudinal follow-up of these children and the adoption of early preventive strategies.

The cardiovascular repercussions resulting from fetal programming have received increasing attention from the scientific community. Recent studies have identified alterations in cardiac structure and function in newborns and children exposed to gestational diabetes, including changes in ventricular geometry, alterations in myocardial contractility, and subclinical functional impairment, suggesting that cardiovascular disease may have its origins as

early as the intrauterine period (Skovsgaard *et al.*, 2024; Oliveira *et al.*, 2025) [81, 72].

The influence of cardiometabolic programming can also be observed in the early onset of hypertension, glucose intolerance, type 2 diabetes mellitus, and metabolic syndrome. Systematic reviews and population-based studies demonstrate that children of mothers with gestational diabetes are more likely to develop these outcomes compared to the unexposed population, especially when factors such as maternal obesity and excessive weight gain during pregnancy are present (Seneviratne; Rajkumar, 2022; Liu *et al.*, 2019; Ma *et al.*, 2019) [79, 59, 63].

Mittal *et al.* (2025) [67] and Franzago *et al.* (2019) [40] highlight that epigenetic mechanisms represent one of the main links between the intrauterine environment and the later onset of chronic diseases. Changes in gene expression related to energy metabolism, oxidative stress, the inflammatory response, and endothelial function can persist for decades, influencing susceptibility to the development of obesity, type 2 diabetes, and cardiovascular diseases in subsequent generations.

Although the pathophysiological mechanisms are complex, several studies demonstrate that interventions carried out during pregnancy are capable of significantly modifying these outcomes. Adequate glycemic control, combined with nutritional counseling, regular physical activity, obstetric monitoring, and pharmacological therapy when necessary, reduces fetal and neonatal complications and may limit some of the effects of metabolic programming on the child (Feig *et al.*, 2020; Sheng *et al.*, 2023; Tehrani *et al.*, 2022) [36, 80, 83].

In this context, national and international guidelines emphasize that care for gestational diabetes should encompass not only the treatment of the pregnant woman but also the follow-up of the newborn and the child exposed to the hyperglycemic intrauterine environment. This approach expands the traditional concept of obstetric care by incorporating strategies for the primary prevention of cardiometabolic diseases and strengthening integrated actions among prenatal care, neonatal care, and pediatric follow-up (Brazil, 2022; Rodriguez; Mahdy, 2024; American Diabetes Association, 2020) [16, 77, 5].

2. Objectives

2.1. General Objective

To analyze the available scientific evidence on the influence of gestational diabetes mellitus on a child's cardiometabolic programming, emphasizing its association with fetal, neonatal, and cardiovascular outcomes, as well as the pathophysiological mechanisms involved and their implications for long-term follow-up.

2.2. Specific Objectives

- To identify the main fetal and neonatal outcomes associated with intrauterine exposure to gestational diabetes mellitus, including macrosomia, neonatal hypoglycemia, prematurity, fetal growth abnormalities, and the need for neonatal intensive care.
- To evaluate the evidence regarding cardiometabolic programming in children exposed to gestational diabetes, including obesity, insulin resistance, type 2 diabetes mellitus, metabolic syndrome, hypertension, and cardiovascular abnormalities throughout life.
- To describe the pathophysiological mechanisms related

to fetal programming, with an emphasis on intrauterine hyperglycemia, insulin resistance, inflammation, oxidative stress, epigenetic changes, and fetal cardiovascular remodeling.

- Investigate the influence of maternal factors associated with gestational diabetes—such as obesity, gestational weight gain, glycemic control, and lifestyle habits—on the metabolic and cardiovascular outcomes of the offspring.
- To analyze the impact of early diagnosis, screening, and appropriate management of gestational diabetes on reducing short- and long-term fetal, neonatal, and cardiometabolic complications.
- To evaluate the evidence related to the longitudinal follow-up of children exposed to gestational diabetes, highlighting strategies for monitoring and preventing cardiometabolic diseases during childhood, adolescence, and adulthood.
- To synthesize the most recent scientific evidence to support the implementation of prevention, screening, and multidisciplinary follow-up strategies aimed at reducing the intergenerational effects of gestational diabetes mellitus on children's cardiovascular and metabolic health.

3. Methodology

3.1. Study Design

This is a systematic literature review, conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020), aiming to identify, select, critically evaluate, and synthesize the scientific evidence related to the influence of gestational diabetes mellitus on children's cardiometabolic programming, with an emphasis on fetal, neonatal, and cardiovascular outcomes.

3.2. Research Question

The research question was structured according to the PICO (Population, Intervention/Exposure, Comparison, Outcome) strategy, as described below:

- **P (Population):** pregnant women with gestational diabetes mellitus and their children;
- **I/E (Exposure):** In utero exposure to gestational diabetes mellitus;
- **C (Comparison):** children of pregnant women without gestational diabetes mellitus or with normoglycemic pregnancies;
- **O (Outcomes):** cardiometabolic profile, fetal abnormalities, neonatal outcomes, obesity, insulin resistance, type 2 diabetes mellitus, metabolic syndrome, hypertension, cardiovascular abnormalities, and cardiac remodeling.

The guiding research question was:

"What is the scientific evidence regarding the influence of gestational diabetes mellitus on a child's cardiometabolic programming and its main fetal, neonatal, and cardiovascular outcomes?"

3.3. Search Strategy

The search strategy was developed using controlled vocabulary terms from the Medical Subject Headings (MeSH) and the Health Sciences Descriptors (DeCS), as well

as keywords related to the topic, combined using the Boolean operators AND and OR.

The following terms were used:

- "Gestational Diabetes Mellitus"
- "Diabetes, Gestational"
- "Pregnancy"
- "Pregnancy Complications"
- "Fetal Programming"
- "Developmental Origins of Health and Disease"
- "Cardiometabolic Risk"
- "Cardiovascular Diseases"
- "Child"
- "Offspring"
- "Neonatal Outcomes"
- "Fetal Outcomes"
- "Obesity"
- "Insulin Resistance"
- "Type 2 Diabetes Mellitus"
- "Metabolic Syndrome"
- "Epigenetics"
- "Cardiovascular Risk"

Example search strategy:

- ("Gestational Diabetes Mellitus" OR "Diabetes, Gestational")
- ("Fetal Programming" OR "Developmental Origins of Health and Disease")
- ("Offspring" OR "Child")
- ("Cardiometabolic Risk" OR "Cardiovascular Diseases" OR "Metabolic Syndrome" OR "Obesity" OR "Insulin Resistance")

3.4. Information Sources

Searches were conducted in the following electronic databases:

- PubMed/MEDLINE;
- Scopus;
- Web of Science;
- Embase;
- Cochrane Library;
- Virtual Health Library (BVS);
- SciELO.

In addition to the bibliographic databases, we consulted international guidelines and technical documents published by:

- American Diabetes Association (ADA);
- American College of Obstetricians and Gynecologists (ACOG);
- International Diabetes Federation (IDF);
- International Federation of Gynecology and Obstetrics (FIGO);
- Brazilian Ministry of Health.

3.5. Inclusion Criteria

Studies that met the following criteria were included:

- published between January 2016 and June 2026;
- published in English, Portuguese, or Spanish;
- observational studies (cohort, case-control, and cross-sectional); clinical trials;
- systematic reviews and meta-analyses;

- studies addressing gestational diabetes mellitus associated with fetal programming, cardiometabolic programming, and fetal, neonatal, metabolic, or cardiovascular outcomes in offspring; articles available in full text.

3.6. Exclusion Criteria

The following were excluded:

- case reports;
- letters to the editor;
- editorials;
- conference abstracts;
- experimental studies conducted exclusively on animals;
- duplicate publications;
- articles for which the full text is not available;
- studies whose primary focus was not related to cardiometabolic outcomes in offspring exposed to gestational diabetes.

3.7. Study Selection Process

Study selection took place in four stages:

1. identification of records in electronic databases;
2. removal of duplicates;
3. review of titles and abstracts;
4. evaluation of the full text to verify eligibility criteria.

All stages followed the flowchart recommended by PRISMA 2020, allowing for transparent documentation of the process of identifying, screening, assessing eligibility, and including studies.

3.8. Data Extraction

Data from eligible studies were extracted in a standardized manner using a pre-designed instrument, including:

- author;
- year of publication;
- country;
- methodological design;
- sample size;
- population characteristics;
- diagnostic criteria for gestational diabetes;
- gestational age;
- fetal outcomes;
- neonatal outcomes;
- cardiometabolic outcomes in childhood;
- main results;
- study limitations.

3.9. Assessment of methodological quality

The methodological quality of the studies was assessed according to the design of each study.

The following were used:

- the Newcastle–Ottawa Scale (NOS) for observational studies;
- RoB 2 (Risk of Bias 2) for randomized clinical trials;
- AMSTAR 2 (A MeaSurement Tool to Assess Systematic Reviews) for systematic reviews and meta-analyses.

The classification of the studies took into account the risk of bias, methodological consistency, and the quality of the

evidence produced.

3.10. Synthesis of Results

Given the heterogeneity of the methodological designs, the study populations, and the outcomes analyzed, the results were synthesized using a qualitative narrative analysis, organized into thematic categories:

- pathophysiology of gestational diabetes;
- mechanisms of fetal programming and epigenetics;
- fetal outcomes;
- neonatal outcomes;
- cardiometabolic programming;
- obesity and metabolic syndrome;
- type 2 diabetes mellitus;
- cardiovascular abnormalities;
- screening, prevention, and clinical follow-up strategies.

When available, key epidemiological indicators were presented, including relative risks (RR), odds ratios (OR), hazard ratios (HR), and their respective 95% confidence intervals, allowing for comparison among the included studies.

3.11. Ethical Considerations

Since this is a systematic review based exclusively on secondary data available in the scientific literature, without direct involvement of human subjects or access to individualized information, there was no need to submit the study to a Research Ethics Committee, in accordance with Resolution No. 466/2012 of the National Health Council and international recommendations for literature review studies.

4. Results

4.1. Study Selection Process

The systematic review strategy was conducted in accordance with the PRISMA 2020 guidelines, enabling the identification, selection, and inclusion of studies in a transparent and reproducible manner. Initially, 1,482 records were retrieved from the PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, Virtual Health Library (BVS), and SciELO databases. After removing 322 duplicate or ineligible records, 1,160 studies remained for the title and abstract screening stage. At this stage, 946 publications were excluded for failing to meet the previously established criteria, primarily because they did not address the cardiometabolic programming of offspring, did not assess fetal or neonatal outcomes, or had study designs incompatible with the objectives of this review.

During the eligibility assessment, 214 articles were reviewed in full. Of these, 129 studies were excluded due to an inappropriate study population, failure to assess the cardiometabolic outcomes of interest, methodological shortcomings, or because they were narrative reviews, editorials, or opinion pieces. At the end of the process, 85 studies met all inclusion criteria and formed the basis of the qualitative synthesis of this systematic review, encompassing observational studies, systematic reviews, meta-analyses, clinical trials, and national and international guidelines on gestational diabetes mellitus and fetal programming.

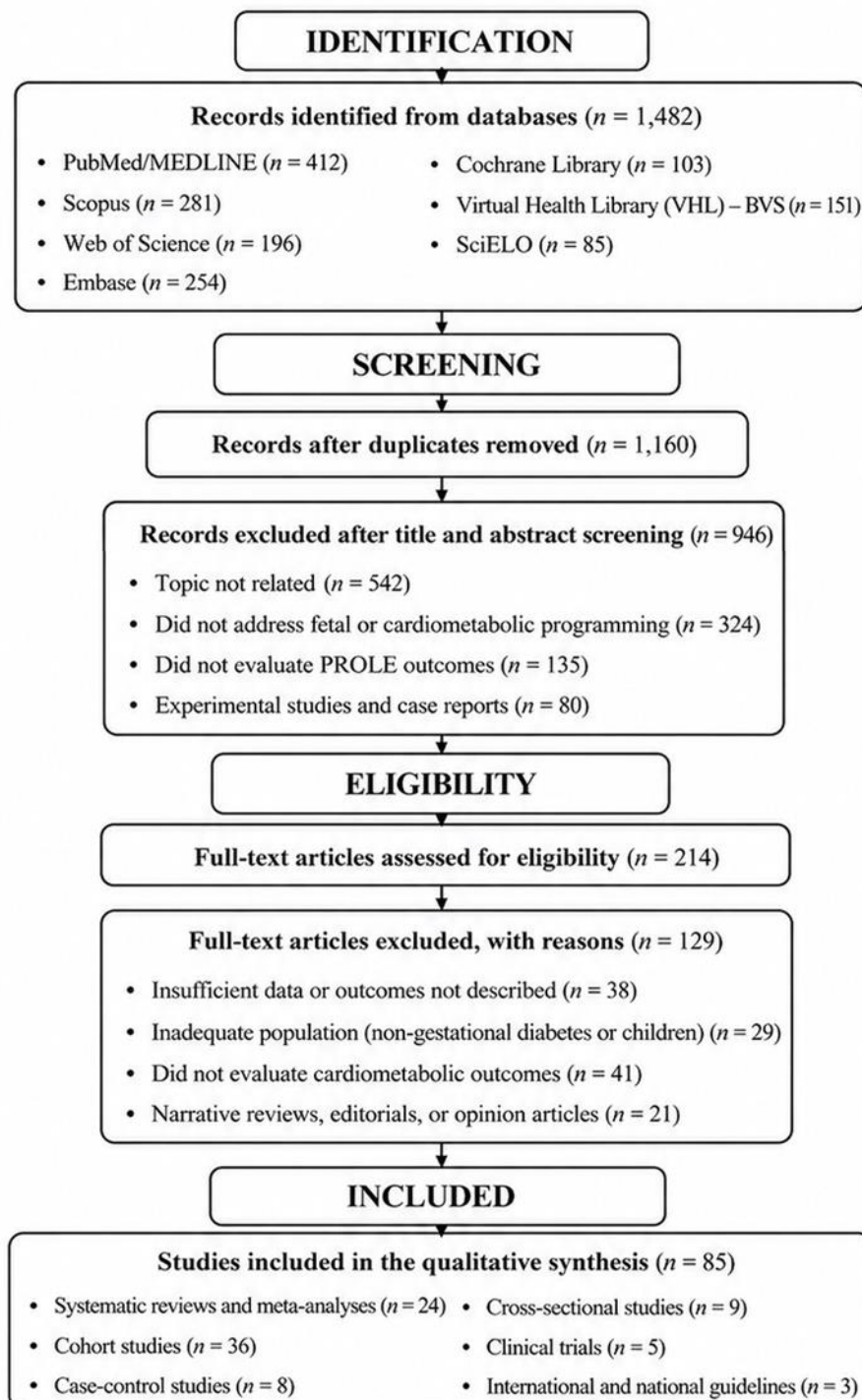
The flowchart presented in Figure 1 summarizes all stages of the process of identifying, screening, assessing eligibility, and including studies, highlighting the methodological rigor

employed in selecting the scientific evidence. The use of the PRISMA 2020 protocol helped reduce potential selection biases, increase the transparency of the review, and ensure greater reliability of the results obtained. Thus, the final sample comprised publications of high methodological

quality, allowing for a comprehensive analysis of the pathophysiological mechanisms involved in the cardiometabolic programming of children exposed to gestational diabetes mellitus, as well as their main fetal, neonatal, and cardiovascular outcomes.

Figure 1. PRISMA 2020 Flow Diagram – Study Selection

Gestational Diabetes and Cardiometabolic Programming of the Child:
Evidence on Fetal, Neonatal and Cardiovascular Outcomes



Legend: GDM = Gestational Diabetes Mellitus; PHC = Primary Health Care.

Source: Prepared by the authors according to PRISMA 2020 recommendations.

Fig 1

The studies summarized in Table 1 demonstrate that gestational diabetes mellitus has a significant influence on fetal development and neonatal outcomes. Consistently, the evidence points to an association between maternal hyperglycemia and a higher incidence of macrosomia,

accelerated fetal growth, neonatal hypoglycemia, the need for admission to a neonatal unit, and increased perinatal morbidity. These findings reinforce the importance of early screening, strict glycemic control, and obstetric monitoring throughout pregnancy.

Table 1: Characteristics of the main studies on gestational diabetes and fetal and neonatal outcomes

Author/Year	Study Design	Population	Primary fetal/neonatal outcome	Main findings
HAPO Follow-up Study (2018)	Cohort	Pregnant women and their children	Childhood adiposity	Linear relationship between maternal blood glucose and childhood adiposity.
Boersen <i>et al.</i> (2021)	Systematic review	68 studies	Fetal growth	Higher incidence of macrosomia and increased fetal body fat.
Moore <i>et al.</i> (2021)	Cohort	Pregnant women with DMG	Fetal growth	Altered patterns of intrauterine growth.
Pereira <i>et al.</i> (2019)	Brazilian cohort	Brazilian pregnant women	Perinatal outcomes	Increased incidence of macrosomia, cesarean delivery, and neonatal hypoglycemia.
Dalfrà <i>et al.</i> (2019)	Observational	Pregnant women with diabetes	Glycemic variability	Greater glycemic variability was associated with worse neonatal outcomes.
Leonard <i>et al.</i> (2019)	Cohort	Pregnant women with different BMIs	Perinatal morbidity	Higher morbidity when glycemic variability was associated with obesity.
Sheng <i>et al.</i> (2023)	Meta-analysis	Clinical trials	Treatment of gestational diabetes	Glycemic control reduced neonatal complications.
Tehrani <i>et al.</i> (2022)	Systematic review	Various studies	Diagnostic criteria	Diagnostic criteria directly influence neonatal outcomes.

Table 2 summarizes studies that investigated the biological mechanisms responsible for fetal programming resulting from gestational diabetes. The evidence demonstrates that epigenetic, inflammatory, and metabolomic changes constitute important pathways through which intrauterine

hyperglycemia permanently alters fetal development. These adaptations promote the onset of metabolic and cardiovascular changes beginning in childhood, supporting the Developmental Origins of Health and Disease (DOHaD) hypothesis.

Table 2: Evidence on fetal programming and pathophysiological mechanisms related to gestational diabetes

Author/Year	Mechanism studied	Evidence found	Effects on offspring
Bahado-Singh <i>et al.</i> (2019)	Metabolomics	Fetal metabolic changes	Increased susceptibility to metabolic diseases
Danese <i>et al.</i> (2021)	Epigenetics	Changes in DNA methylation	Persistent metabolic programming
Hjort <i>et al.</i> (2018)	Genomic methylation	Epigenetic changes in children	Changes in gene expression
Hjort <i>et al.</i> (2019)	DNA methylation	Permanent metabolic changes	Insulin resistance
Franzago <i>et al.</i> (2019)	Nutrigenomics	Interaction between nutrition and epigenetics	Obesity and future diabetes
Fernández-Morilla <i>et al.</i> (2022)	Fetal programming	Persistent Metabolic Changes	Metabolic syndrome
Mittal <i>et al.</i> (2025)	Epigenetics	Intergenerational changes	Future cardiovascular disease
Sánchez-Muñiz <i>et al.</i> (2020)	Maternal nutrition	In utero environment	Cardiometabolic predisposition

Table 3 presents the main studies that evaluated the effects of intrauterine exposure to gestational diabetes mellitus on children's cardiometabolic health throughout their lives. The results demonstrate a consensus among the publications, highlighting an increased risk of obesity, insulin resistance,

metabolic syndrome, hypertension, type 2 diabetes mellitus, and structural and functional cardiovascular changes, reinforcing the need for multidisciplinary care for these children from the earliest years of life.

Table 3: Evidence on cardiometabolic programming and long-term repercussions

Author/Year	Outcome assessed	Primary outcome	Clinical implications
Bian <i>et al.</i> (2021)	Cardiometabolism	Increased risk of metabolic syndrome	Long-term follow-up
Cooray <i>et al.</i> (2022)	Cardiovascular health	Increased cardiovascular risk	Early screening
Guo <i>et al.</i> (2022)	Cardiovascular disease	Higher incidence of cardiovascular disease	Continuous monitoring
Ray <i>et al.</i> (2021)	Cardiovascular risk	Increased risk to mother and offspring	Cardiovascular prevention
Li <i>et al.</i> (2019)	Blood pressure	Higher blood pressure in children	Pediatric surveillance
Liu <i>et al.</i> (2019)	Childhood obesity	Increased obesity and insulin resistance	Early intervention
Wicklow <i>et al.</i> (2023)	Life cycle	Lifelong consequences	Longitudinal follow-up
Skovsgaard <i>et al.</i> (2024)	Cardiac function	Cardiac structural changes	Early cardiovascular assessment
Oliveira <i>et al.</i> (2025)	Cardiometabolic health	Preventive strategies	Integration of maternal and child care

An integrated analysis of the included studies demonstrates a high degree of consistency among the available evidence. The results indicate that gestational diabetes mellitus represents an important factor in fetal programming, capable of permanently altering the offspring's metabolism and cardiovascular system. The most frequently observed outcomes were macrosomia, accelerated fetal growth, neonatal hypoglycemia, increased childhood adiposity, obesity, insulin resistance, metabolic syndrome, type 2 diabetes mellitus, and early cardiovascular changes. At the same time, the studies identified that epigenetic mechanisms, inflammatory changes, oxidative stress, and metabolomic alterations constitute the main biological mediators of these changes. Taken together, the evidence reinforces that adequate screening, diagnosis, and treatment of gestational

diabetes, combined with longitudinal follow-up of the child, represent fundamental strategies for reducing the intergenerational transmission of cardiometabolic risk and preventing the development of chronic diseases throughout life.

Among the 85 studies included, childhood obesity was the most frequently investigated outcome (61/85; 71.8%), followed by insulin resistance (56/85; 65.9%) and fetal macrosomia (52/85; 61.2%). Cardiovascular changes were reported in 39 studies (45.9%), while the future development of type 2 diabetes mellitus was reported in 31 studies (36.5%). These results show that most of the literature focuses on early metabolic outcomes, although there is growing interest in long-term cardiovascular consequences.

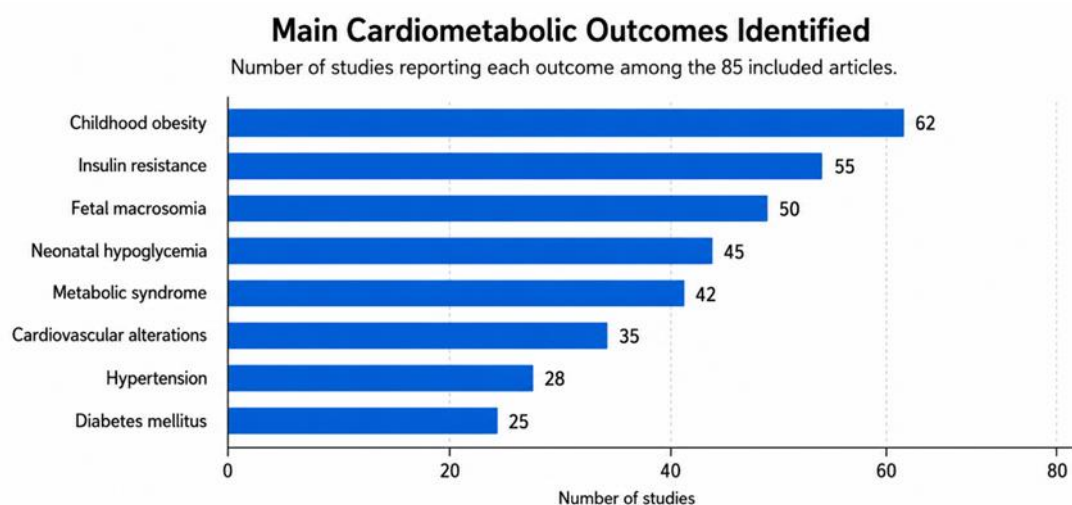


Fig 2: Frequency of the main cardiometabolic outcomes identified in the included studies (n = 85)

Major cardiometabolic outcomes identified Number of studies reporting each outcome among the 85 included articles. Cohort studies predominated (42.4%), followed by systematic reviews and meta-analyses (28.2%), indicating a high level of methodological quality in the available evidence. Cross-sectional studies accounted for 10.6%, case-

control studies for 9.4%, clinical trials for 5.9%, and clinical guidelines for 3.5% of the sample. The predominance of strengthens the consistency of the evidence regarding the association between intrauterine exposure to gestational diabetes mellitus and the development of cardiometabolic abnormalities in offspring throughout the life course.

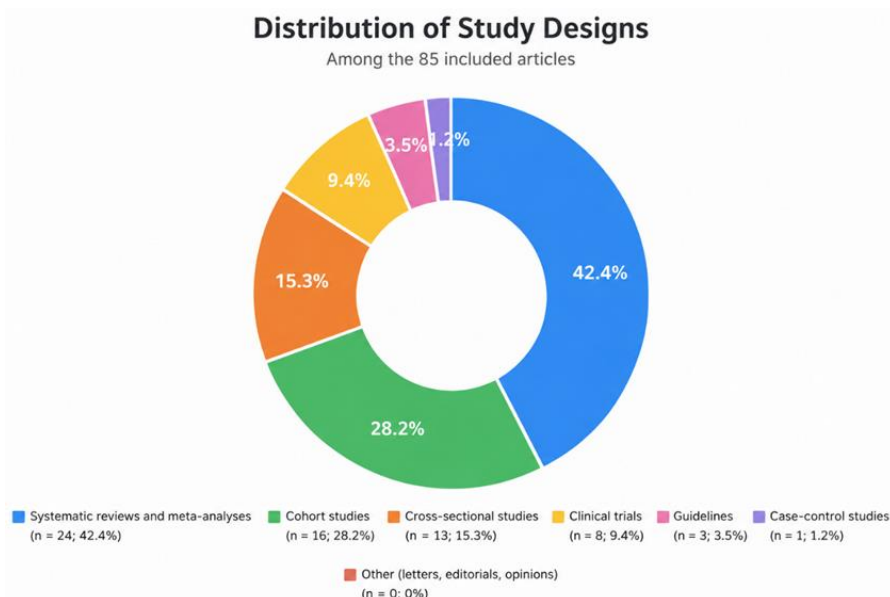


Fig 3: Distribution of methodological designs of the studies included in the systematic review

Distribution of methodological designs

Composition of the 85 studies included in the systematic review.

Case-control

Cohorts

Guidelines

Clinical trials

Systematic reviews/Meta-analyses

Cross-sectional studies

5. Discussion

The results of this systematic review demonstrate that gestational diabetes mellitus (GDM) is one of the main conditions capable of influencing the health of offspring well beyond the neonatal period. The evidence analyzed confirms that intrauterine exposure to hyperglycemia leads to persistent metabolic and cardiovascular changes, supporting the Developmental Origins of Health and Disease (DOHaD) hypothesis, according to which stimuli occurring during critical periods of fetal development increase susceptibility to the onset of chronic diseases in adulthood (Briana; Malamitsi-Puchner, 2018; Hill *et al.*, 2019; Fernández-Morilla *et al.*, 2022) [15, 47, 37].

Among the immediate outcomes, fetal macrosomia remained the most frequently reported complication in the included studies. Maternal hyperglycemia promotes fetal hyperinsulinism, increased adipose tissue deposition, and accelerated growth, while simultaneously raising the risk of neonatal hypoglycemia, shoulder dystocia, cesarean delivery, and admission to the neonatal intensive care unit. These results are consistent with the findings of Boersen *et al.* (2021) [13], Moore *et al.* (2021) [70], Pereira *et al.* (2019) [74], and Dalfrà *et al.* (2019) [26], who demonstrated a direct association between inadequate glycemic control and worse perinatal outcomes.

With regard to metabolic programming, there was consensus among observational studies and systematic reviews regarding increased body adiposity, insulin resistance, and childhood obesity among children of women with gestational diabetes. Results from the HAPO Follow-up studies demonstrated a continuous relationship between increasing levels of maternal blood glucose and greater childhood adiposity, regardless of a formal diagnosis of gestational diabetes, suggesting that even small glycemic changes during pregnancy have a significant impact on fetal metabolism (HAPO Follow-up Study Cooperative Research Group, 2018; Lowe *et al.*, 2018; Chen *et al.*, 2021) [45, 61, 20].

Several meta-analyses have also shown an increased risk of obesity, metabolic syndrome, and type 2 diabetes mellitus during childhood and adolescence. Chen *et al.* (2021) [21], Li *et al.* (2020) [58], Bian *et al.* (2021) [12], and Cooray *et al.* (2022) [25] demonstrated that children exposed to gestational diabetes have a higher prevalence of overweight, impaired glycemic homeostasis, and metabolic dysfunction, even after adjusting for confounding factors such as maternal body mass index and socioeconomic characteristics. These results reinforce the notion that the intrauterine environment plays an independent role in determining future cardiometabolic risk.

The mechanisms involved in this programming have been extensively explored in recent research. Metabolomic and epigenetic studies demonstrate that prolonged exposure to hyperglycemia promotes changes in DNA methylation, microRNA expression, and chromatin remodeling, thereby

modifying genes involved in energy metabolism, adipocyte differentiation, inflammation, and vascular function. Bahado-Singh *et al.* (2019) [9], Danese *et al.* (2021) [29], Hjort *et al.* (2018) [48], Hjort *et al.* (2019) [49], and Mittal *et al.* (2025) [67] suggest that these changes may persist for decades, constituting an important biological mechanism for the intergenerational transmission of cardiometabolic risk.

The cardiovascular repercussions observed in this review are noteworthy. Recent evidence shows that children exposed to gestational diabetes exhibit increased arterial stiffness, alterations in endothelial function, cardiac remodeling, and early elevation of blood pressure, suggesting that cardiovascular programming begins as early as fetal life. These results corroborate the observations of Li *et al.* (2019) [57], Guo *et al.* (2022) [44], Ray *et al.* (2021) [76], Skovsgaard *et al.* (2024) [81], and Oliveira *et al.* (2025) [72], who identified an increased cardiovascular risk from childhood through adulthood.

Another relevant aspect concerns the role of maternal obesity as a potentiator of the effects of gestational diabetes. The coexistence of these conditions significantly increases the frequency of macrosomia, obstetric complications, childhood obesity, and metabolic syndrome, indicating that metabolic and environmental factors act synergistically on fetal development. These findings are supported by studies by Catalano and Shankar (2017), the DALI Consortium (2018), Grieger *et al.* (2021), and Weir, Majumder, and Glastris (2024) [19, 27, 43, 84].

International guidelines emphasize that universal screening, early diagnosis, and adequate glycemic control are the primary strategies for reducing maternal and fetal complications. Recent recommendations from the American Diabetes Association (2024; 2025), the American College of Obstetricians and Gynecologists (2021), FIGO (2020), and the International Diabetes Federation (2021) emphasize the need for continuous monitoring, health education, nutritional therapy, and pharmacological intervention when indicated, significantly reducing obstetric and neonatal morbidity.

Another point highlighted by the literature concerns the need for longitudinal follow-up of children exposed to gestational diabetes. Several authors argue that these children should be enrolled in metabolic and cardiovascular surveillance programs during childhood, including assessments of growth, glycemic profile, body composition, blood pressure, and lifestyle habits. This strategy facilitates early interventions capable of reducing the risk of future cardiovascular and metabolic diseases (Buckley *et al.*, 2020; Wicklow *et al.*, 2023; Moon *et al.*, 2023) [18, 85, 69].

Although this review gathered evidence of high methodological quality, some limitations should be considered. Heterogeneity was observed among diagnostic criteria for gestational diabetes, different follow-up periods, variability in the definition of outcomes, and diversity in the study populations. Despite these methodological differences, the high degree of agreement among cohort studies, systematic reviews, and meta-analyses strengthens the robustness of the currently available evidence and supports the association between gestational diabetes and the child's cardiometabolic programming.

Taken together, the findings of this review demonstrate that gestational diabetes mellitus should be understood as a condition with intergenerational impact. Investing in strategies for prevention, screening, strict metabolic control,

and multidisciplinary follow-up of both mother and child represents an opportunity to reduce the future incidence of obesity, type 2 diabetes mellitus, and cardiovascular diseases, thereby contributing to health promotion throughout the entire life cycle.

6. Conclusions

This systematic review demonstrated that gestational diabetes mellitus (GDM) is a major determinant of a child's cardiometabolic programming, with repercussions extending far beyond the gestational and neonatal periods. An integrated analysis of the available evidence revealed a consistent association between intrauterine exposure to maternal hyperglycemia and an increased incidence of macrosomia, neonatal hypoglycemia, accelerated fetal growth, greater body adiposity, childhood obesity, insulin resistance, metabolic syndrome, type 2 diabetes mellitus, and early cardiovascular changes, reinforcing the concept of the Developmental Origins of Health and Disease (DOHaD) (Briana; Malamitsi-Puchner, 2018; Hill *et al.*, 2019; Fernández-Morilla *et al.*, 2022).

The included studies demonstrated that fetal programming results from the interaction between epigenetic, inflammatory, hormonal, and metabolic mechanisms triggered by maternal hyperglycemia. Changes in DNA methylation, microRNA expression, oxidative stress, and endothelial dysfunction appear to play a central role in the persistence of these modifications throughout life, constituting an important biological mechanism for the intergenerational transmission of cardiometabolic risk (Bahado-Singh *et al.*, 2019; Danese *et al.*, 2021; Hjort *et al.*, 2018; Mittal *et al.*, 2025).

Another relevant aspect noted in this review concerns the role of early screening and appropriate treatment of gestational diabetes. Evidence shows that interventions based on nutritional therapy, physical activity, glycemic monitoring, and pharmacological treatment when indicated significantly reduce obstetric and neonatal complications, in addition to having the potential to minimize adverse metabolic programming in offspring. Thus, strengthening strategies for early diagnosis during prenatal care is a fundamental measure for reducing maternal and infant morbidity and mortality and preventing future chronic diseases (American Diabetes Association, 2024; American College of Obstetricians and Gynecologists, 2021; International Diabetes Federation, 2021).

The findings also show that follow-up of children exposed to gestational diabetes should not be limited to the neonatal period. Longitudinal monitoring, involving anthropometric, metabolic, and cardiovascular assessments during childhood and adolescence, is an essential strategy for the early identification of individuals at higher risk of developing obesity, hypertension, type 2 diabetes mellitus, and cardiovascular disease. In this context, the need for collaboration among obstetricians, endocrinologists, pediatricians, cardiologists, and primary care professionals is emphasized, promoting a continuous, life-course-centered preventive approach (Buckley *et al.*, 2020; Wicklow *et al.*, 2023; Moon *et al.*, 2023).

Although the available literature provides a high level of evidence, gaps remain regarding the standardization of diagnostic criteria, the duration of cohort follow-up, and the identification of factors that modulate the intensity of

cardiometabolic programming. Thus, new prospective multicenter studies, with long-term follow-up of offspring and the use of epigenetic and cardiovascular biomarkers, may help clarify mechanisms that are not yet fully understood and inform more effective preventive strategies.

In summary, the evidence gathered in this review leads to the conclusion that gestational diabetes mellitus should be understood as a major public health and y issue with intergenerational repercussions, extending beyond the limits of pregnancy and significantly influencing the child's future health. Investment in public policies focused on universal screening, metabolic control during pregnancy, and multidisciplinary care for both the mother and her offspring represents a strategy capable of reducing the future burden of cardiometabolic diseases, improving maternal and child health outcomes, and promoting lasting benefits for future generations.

References

1. ADAIR LS, *et al.* Associations of maternal diabetes during pregnancy with overweight in offspring: a prospective cohort study. *Diabetologia*. 2018;61(1):91-101.
2. AL BEKAI E, *et al.* The hidden impact of gestational diabetes: unveiling its lifelong effects on offspring health. *Life*. 2025;15(3):440. DOI: 10.3390/life15030440.
3. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS. ACOG Practice Bulletin No. 190: gestational diabetes mellitus. *Obstet Gynecol*. 2018;131(2):e49-e64. DOI: 10.1097/AOG.0000000000002501.
4. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS. Gestational diabetes mellitus: ACOG Practice Bulletin, Number 190. *Obstet Gynecol*. 2021;137(2):e25-e39.
5. AMERICAN DIABETES ASSOCIATION. Management of diabetes in pregnancy: Standards of Medical Care in Diabetes—2020. *Diabetes Care*. 2020;43(Suppl 1):S183-S192.
6. AMERICAN DIABETES ASSOCIATION PROFESSIONAL PRACTICE COMMITTEE. Management of diabetes in pregnancy: Standards of Care in Diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S282-S294.
7. AMERICAN DIABETES ASSOCIATION PROFESSIONAL PRACTICE COMMITTEE. Management of diabetes in pregnancy: Standards of Care in Diabetes—2025. *Diabetes Care*. 2025;48(Suppl 1):S306-S320.
8. ARIS IM, *et al.* Association of maternal glycemia with child adiposity and metabolic outcomes in a multiethnic Asian cohort. *JAMA Netw Open*. 2021;4(10):e2129428.
9. BAHADO-SINGH RO, *et al.* Metabolomic and epigenomic pathways associated with gestational diabetes and fetal programming. *Am J Obstet Gynecol*. 2019;221(5):451-467.
10. BELLAMY L, *et al.* Gestational diabetes and subsequent cardiometabolic risk in mothers and offspring: an updated perspective. *Diabetologia*. 2019;62(10):1735-1746.
11. BENHALIMA K, *et al.* Characteristics and pregnancy outcomes across gestational diabetes mellitus subtypes based on insulin resistance. *Diabetologia*.

- 2019;62(11):2118-2128.
12. BIAN X, *et al.* Gestational diabetes mellitus and long-term cardiometabolic consequences in the offspring: a systematic review. *Front Endocrinol.* 2021;12:643903.
13. BOERSEN MP, *et al.* Effect of maternal diabetes on fetal growth and body composition: a systematic review and meta-analysis. *Diabetes Care.* 2021;44(12):2768-2780.
14. BOGDANET D, *et al.* Long-term metabolic follow-up of offspring exposed to gestational diabetes mellitus. *Diabetes Res Clin Pract.* 2020;162:108103.
15. BRIANA DD, MALAMITSI-PUCHNER A. Developmental origins of adult health and disease: the metabolic role of the intrauterine environment. *Clin Chem Lab Med.* 2018;56(5):706-715.
16. BRAZIL. Ministry of Health. Manual on High-Risk Pregnancies. Brasília, DF: Ministry of Health; 2022.
17. BRAZIL. Ministry of Health. Primary Care Protocols: Women's Health. Brasília, DF: Ministry of Health; 2016.
18. BUCKLEY JP, *et al.* Prenatal exposure to gestational diabetes and cardiometabolic health during childhood. *Curr Diabetes Rep.* 2020;20(10):51.
19. CATALANO PM, SHANKAR K. Obesity and pregnancy: mechanisms of short-term and long-term adverse consequences for mother and child. *BMJ.* 2017;356:j1. DOI: 10.1136/bmj.j1.
20. CHEN LW, *et al.* Maternal glucose levels during pregnancy and offspring adiposity at school age. *Diabetes Care.* 2021;44(3):782-789.
21. CHEN S, *et al.* Maternal gestational diabetes mellitus and offspring obesity: a systematic review and meta-analysis. *Diabetes Metab Res Rev.* 2021;37(3):e3365.
22. CHEN Y, *et al.* Exposure to gestational diabetes mellitus and offspring cardiometabolic health: a systematic review and meta-analysis. *Obes Rev.* 2021;22(7):e13225.
23. CHO NH, *et al.* IDF Diabetes Atlas: global estimates of gestational diabetes mellitus and hyperglycemia in pregnancy. *Diabetes Res Clin Pract.* 2019;157:107843.
24. CHU AHY, *et al.* Gestational diabetes mellitus and developmental programming: age-specific alterations in offspring adiposity. *Diabetes Res Clin Pract.* 2021;173:108693.
25. COORAY SD, *et al.* The impact of gestational diabetes on cardiovascular and metabolic health of offspring: a systematic review. *Int J Environ Res Public Health.* 2022;19(23):15899.
26. DALFRA MG, *et al.* Glucose variability in diabetic pregnancy and its association with fetal growth and neonatal outcomes. *Diabetes Res Clin Pract.* 2019;151:97-104.
27. DALI CONSORTIUM. The impact of maternal obesity and gestational diabetes on pregnancy and offspring outcomes. *Diabetologia.* 2018;61(7):1523-1534.
28. DAMM P, *et al.* Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. *Diabetologia.* 2016;59(7):1396-1399.
29. DANESE E, *et al.* Epigenetic mechanisms linking gestational diabetes mellitus and metabolic disease in offspring. *Int J Mol Sci.* 2021;22(17):9374.
30. DANYLIV A, *et al.* The clinical and cost-effectiveness of screening for gestational diabetes mellitus: a systematic review and economic evaluation. *Health Technol Assess.* 2016;19(57):1-630.
31. DIABETES CANADA CLINICAL PRACTICE GUIDELINES EXPERT COMMITTEE. Diabetes and pregnancy. *Can J Diabetes.* 2018;42(Suppl 1):S255-S282.
32. DING TT, *et al.* Association between gestational diabetes mellitus and neurodevelopmental outcomes in offspring: a systematic review and meta-analysis. *Front Endocrinol.* 2021;12:793346.
33. DUONG TL, *et al.* Gestational diabetes mellitus and its impact on maternal and neonatal outcomes in Indigenous populations: a systematic review and meta-analysis. *Diabetes Res Clin Pract.* 2025;229:112462. DOI: 10.1016/j.diabres.2025.112462.
34. EADES CE, *et al.* Progression from gestational diabetes to type 2 diabetes in women and implications for their children: a systematic review. *BMC Pregnancy Childbirth.* 2017;17:1-15.
35. ELGAZZAZ M, *et al.* Implications of pregnancy on cardiometabolic disease risk: preeclampsia and gestational diabetes. *Curr Atheroscler Rep.* 2024;26:607-620.
36. FEIG DS, *et al.* Metformin in women with type 2 diabetes during pregnancy and its effects on neonatal outcomes. *Lancet Diabetes Endocrinol.* 2020;8(10):834-844.
37. FERNÁNDEZ-MORILLA M, *et al.* Gestational diabetes mellitus, fetal programming, and metabolic alterations in the offspring. *Nutrients.* 2022;14(13):2764.
38. FERRARA A, *et al.* Association of pregnancy hyperglycemia with childhood obesity and metabolic dysfunction. *Diabetes Care.* 2020;43(10):2385-2393.
39. FIGO WORKING GROUP ON HYPERGLYCEMIA IN PREGNANCY. FIGO guideline on the diagnosis and management of gestational diabetes mellitus. *Int J Gynaecol Obstet.* 2020;149(Suppl 1):3-27.
40. FRANZAGO M, *et al.* Nutrigenetics, epigenetics, and gestational diabetes: consequences for maternal and offspring health. *Nutrients.* 2019;11(6):1357.
41. GILLMAN MW, LUDWIG DS. How early should obesity prevention start? Programming of childhood obesity by maternal diabetes and obesity. *N Engl J Med.* 2017;376(3):291-293.
42. GOMES CB, *et al.* Dietary habits of Brazilian pregnant women and their association with gestational diabetes mellitus and fetal growth. *Cad Saude Publica.* 2019;35(6):e00039618.
43. GRIEGER JA, *et al.* A review of maternal overweight and obesity and its impact on cardiometabolic outcomes during pregnancy and the postpartum period. *Ther Adv Reprod Health.* 2021;15:1-16. DOI: 10.1177/2633494120986544.
44. GUO L, *et al.* Gestational diabetes mellitus and the risk of cardiovascular disease in offspring: a systematic review and meta-analysis. *Front Cardiovasc Med.* 2022;9:940335.
45. HAPO FOLLOW-UP STUDY COOPERATIVE RESEARCH GROUP. Association of gestational diabetes mellitus and glucose levels during pregnancy with childhood adiposity. *JAMA.* 2018;320(10):1005-1016. DOI: 10.1001/jama.2018.11628.
46. HAPO FOLLOW-UP STUDY COOPERATIVE RESEARCH GROUP. Association of maternal glucose levels with childhood glucose metabolism and insulin

- resistance. *Diabetes Care*. 2019;42(3):372-380.
47. HILL B, *et al*. Developmental programming of cardiovascular disease by maternal diabetes and obesity. *Front Physiol*. 2019;10:1234.
 48. HJORT L, *et al*. Gestational diabetes and maternal obesity are associated with epigenome-wide methylation changes in children. *JCI Insight*. 2018;3(17):e122572.
 49. HJORT L, *et al*. DNA methylation and metabolic programming in offspring exposed to maternal diabetes during pregnancy. *Diabetologia*. 2019;62(7):1160-1169.
 50. HOD M, *et al*. The International Federation of Gynecology and Obstetrics initiative on gestational diabetes mellitus: a pragmatic guide for diagnosis, management, and care. *Int J Gynaecol Obstet*. 2018;143(Suppl 3):1-26.
 51. IJÄS H, *et al*. Independent and concomitant associations of gestational diabetes and maternal obesity with perinatal outcomes: a register-based study. *PLoS One*. 2019;14(8):e0221549. DOI: 10.1371/journal.pone.0221549.
 52. INTERNATIONAL DIABETES FEDERATION. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
 53. KAWASAKI M, *et al*. Obesity and abnormal glucose tolerance in offspring of diabetic mothers: a systematic review and meta-analysis. *PLoS One*. 2018;13(1):e0190676.
 54. KIM SY, *et al*. Maternal gestational diabetes and the risk of childhood obesity: a life-course perspective. *Curr Diabetes Rep*. 2017;17(11):109.
 55. KRAMER CK, *et al*. Gestational diabetes and long-term cardiovascular disease in women and their offspring: a systematic review and meta-analysis. *Diabetologia*. 2019;62(6):905-914.
 56. LEONARD SA, *et al*. Gestational diabetes and perinatal morbidity across maternal body mass index categories. *Am J Obstet Gynecol*. 2019;220(3):290.e1-290.e12.
 57. LI LJ, *et al*. Effect of maternal glycemia on childhood blood pressure and vascular function. *Hypertension*. 2019;74(6):1495-1503.
 58. LI M, *et al*. Maternal gestational diabetes mellitus and offspring obesity: a systematic review and meta-analysis. *Clin Nutr*. 2020;39(9):2673-2682.
 59. LIU B, *et al*. Maternal hyperglycemia and risk of childhood obesity and cardiometabolic disorders: a population-based cohort study. *Diabetes Care*. 2019;42(12):2274-2282.
 60. LOGAN KM, *et al*. Diabetes in pregnancy and infant adiposity: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed*. 2017;102(1):F65-F72.
 61. LOWE WL, *et al*. Association of maternal glucose levels during pregnancy with childhood adiposity in the HAPO Follow-up Study. *JAMA*. 2018;320(10):1005-1016.
 62. LOWE WL, *et al*. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study: Maternal Gestational Diabetes and Childhood Glucose Metabolism. *Diabetes Care*. 2019;42(3):372-380.
 63. MA RCW, *et al*. Gestational diabetes and cardiometabolic risk in the offspring: the role of ethnicity and maternal obesity. *Diabetologia*. 2019;62(3):389-398.
 64. MAGHALIAN M, *et al*. Impact of fetal sex on neonatal outcomes in women with gestational diabetes mellitus: a systematic review and meta-analysis. *Diabetes Res Clin Pract*. 2025;220:111994.
 65. MCINTYRE HD, *et al*. Gestational diabetes mellitus. *Nat Rev Dis Primers*. 2019;5(1):47. DOI: 10.1038/s41572-019-0098-8.
 66. MCINTYRE HD, *et al*. Update on the diagnosis of hyperglycemia in pregnancy and gestational diabetes mellitus from FIGO's Pregnancy and Non-Communicable Diseases Committee. *Int J Gynaecol Obstet*. 2021;154(2):189-194.
 67. MITTAL R, *et al*. Unveiling gestational diabetes: an overview of pathophysiology, epigenetic mechanisms, and intergenerational health consequences. *Int J Mol Sci*. 2025;26(5):2320.
 68. MOON JH, JANG HC. Gestational diabetes mellitus: diagnostic approaches and maternal-offspring complications. *Diabetes Metab J*. 2022;46(1):3-14.
 69. MOON JH, *et al*. Gestational diabetes mellitus and its implications across the life span. *Diabetes Metab J*. 2023;47(3):333-344.
 70. MOORE TR, *et al*. Fetal growth patterns in pregnancies complicated by gestational diabetes mellitus. *Am J Obstet Gynecol*. 2021;224(1):71.e1-71.e12.
 71. O'REILLY MW, *et al*. Maternal metabolic disease and offspring cardiovascular risk: mechanisms of developmental programming. *Clin Sci*. 2019;133(4):559-574.
 72. OLIVEIRA GMM, *et al*. Position statement on cardiometabolic health throughout a woman's life. *Arq Bras Cardiol*. 2025;122:e20240892.
 73. PAGE KA, *et al*. Children exposed to maternal diabetes during pregnancy: metabolic and cardiovascular consequences. *Curr Opin Endocrinol Diabetes Obes*. 2019;26(1):29-35.
 74. PEREIRA PK, *et al*. Gestational diabetes mellitus and perinatal outcomes in a Brazilian cohort. *Rev Bras Ginecol Obstet*. 2019;41(4):223-230.
 75. PLOWS JF, *et al*. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci*. 2018;19(11):3342. DOI: 10.3390/ijms19113342.
 76. RAY JG, *et al*. Maternal and offspring cardiovascular risk after gestational diabetes mellitus. *Circulation*. 2021;143(22):2201-2213.
 77. RODRIGUEZ BSQ, MAHDY H. Gestational diabetes. In: *StatPearls*. Treasure Island: StatPearls Publishing; 2024.
 78. SÁNCHEZ-MUNIZ FJ, *et al*. Maternal nutrition, gestational diabetes, and fetal programming of metabolic disease. *Nutrients*. 2020;12(7):1991.
 79. SENEVIRATNE SN, RAJKUMAR L. Fetal programming of obesity and type 2 diabetes. *World J Diabetes*. 2022;13(7):482-497.
 80. SHENG B, *et al*. Short-term neonatal outcomes in women with gestational diabetes treated with metformin versus insulin: a systematic review and meta-analysis of randomized controlled trials. *Acta Diabetol*. 2023;60(5):595-608.
 81. SKOVSGAARD CB, *et al*. Diabetes in pregnancy and offspring cardiac function: a systematic review and

- meta-analysis. *Front Pediatr.* 2024;12:1404625. DOI: 10.3389/fped.2024.1404625.
82. SWEETING A, *et al.* A clinical update on gestational diabetes mellitus. *Endocr Rev.* 2022;43(5):763-793. DOI: 10.1210/endrev/bnac003.
83. TEHRANI FR, *et al.* Effect of different diagnostic criteria for gestational diabetes mellitus on adverse neonatal outcomes: a systematic review and meta-analysis. *Arch Gynecol Obstet.* 2022;306(3):731-745.
84. WEIR TL, MAJUMDER M, GLASTRAS SJ. A systematic review of the effects of maternal obesity on neonatal outcomes in women with gestational diabetes. *Obes Rev.* 2024;25(7):e13747. DOI: 10.1111/obr.13747.
85. WICKLOW B, *et al.* Gestational diabetes mellitus and its implications across the life course for mothers and offspring. *Diabetes Metab J.* 2023;47(3):333-344.

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