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Gestational Diabetes Mellitus and Adverse Maternal and Neonatal Health Outcomes: an Umbrella review of Meta-Analyses

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Received: 4 April 2025 | **Revised:** 1 October 2025 | **Accepted:** 14 January 2026

Keywords: gestational diabetes mellitus | health outcomes | umbrella review

ABSTRACT

Introduction: This study systematically synthesized evidence on adverse health outcomes related to gestational diabetes mellitus (GDM) via an umbrella review with integrated meta-analyses.

Methods: The search covered publications from the database (PubMed/MEDLINE, Google Scholar, Embase, and CINAHL) inception to August 12, 2024. Meta-analyses of observational studies examining the impact of GDM on maternal and neonatal health outcomes were included. Two independent researchers screened and extracted data. Associations were reanalyzed and presented as equivalent odds ratios (eORs) with 95% confidence intervals (CI). The quality of meta-analyses was assessed using AMSTAR 2, and the credibility of associations was categorized into five levels: convincing (Class I), highly suggestive (Class II), suggestive (Class III), weak (Class IV), or nonsignificant (NS).

Results: A total of 27 meta-analyses encompassing 85 associations were included. Among 28 significant maternal outcomes, 11 (subclinical atherosclerosis, angina, hypertension, overall cardiovascular diseases, ischemic stroke, overall stroke, combined cardiovascular/cerebrovascular diseases, subclinical left ventricle systolic dysfunction, type 2 diabetes, postpartum

Jiseung Kang, Hyeon Jin Kim, and Yeona Jo contributed equally to this work as the first authors.

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metabolic syndrome, and infections) were supported by convincing or highly suggestive evidence. Of 13 significant neonatal outcomes, three (atrial septal defect, congenital heart disease, and ventricular septal defect) were highly suggestive, while four of eight significant delivery outcomes (hypertensive disorders, cesarean delivery, admission to neonatal intensive care unit admission, and preterm birth) reached this level. Notably, no outcomes previously deemed nonsignificant turned significant upon reanalysis.

Conclusions: These findings underscore the need for targeted prevention and management, and further research is needed to clarify causality and refine guidelines.

Study registration: PROSPERO CRD42024590322

1 | Introduction

Gestational diabetes mellitus (GDM) has emerged as a significant worldwide health burden among millions of pregnant women as one of the common chronic diseases during pregnancy [1, 2]. GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [3]. The increasing prevalence of overall obesity and advanced maternal age, both of which are associated with increased insulin resistance, has contributed to an increase in the diagnosis of GDM, placing pregnant women with GDM at higher risk for pregnancy complications [1]. Previous research suggests that GDM disrupts maternal metabolism, with potential adverse impacts extending to their children [3]. According to the International Diabetes Federation, GDM complicates approximately 16% of pregnancies worldwide [4]. Patients with GDM experience hyperglycemia due to impaired glucose regulation, which may occur even in the first trimester [5]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends screening for GDM between 24 and 28 weeks of gestation [6].

Previous studies have shown that GDM is associated with various pregnancy complications and postnatal morbidities, including increased risks of cesarean delivery, preterm birth, low Apgar scores, macrosomia, large-for-gestational-age infants, respiratory distress, neonatal jaundice, and neonatal intensive care unit (NICU) admission [1, 7, 8]. In addition to these adverse complications at delivery, GDM has been associated with long-term health risks for both mothers and their children [7–9]. Therefore, quantifying and synthesizing these risks of GDM are essential for prevention, risk assessment, and patient education.

This umbrella review aimed to synthesize and provide empirical evidence on currently reported health outcomes associated with GDM, reflecting an awareness of the importance of providing information for clinical practice and policy-making. While previous reviews focused on specific complications, assessed maternal and neonatal outcomes separately, or limited meta-analysis levels, this study is the first to conduct an umbrella review systematically summarizing the full spectrum of adverse health outcomes associated with GDM among both pregnant women and their children. Based on extensive existing meta-analyses, we present a comprehensive overview of key findings, applying quantitative criteria to assess the credibility of the evidence for each association.

2 | Methods

2.1 | Literature Search Strategy and Selection Criteria

This umbrella review was conducted following the PRISMA 2020 guidelines and registered with PROSPERO (registration number, CRD42024590322) [10]. Two independent investigators (JK and YJ) screened papers, extracted data, and assessed methodological quality. We systematically searched the literature databases PubMed/MEDLINE, Embase, CINAHL, and Google Scholar from inception up to August 12, 2024, to identify eligible articles. In addition, we manually reviewed the reference lists of relevant studies to ensure the inclusion of all eligible papers. Systematic review articles were included, including meta-analyses of observational studies such as case–control and cross-sectional studies [11]. The search strategy employed was as follows: (gestational diabetes [title/abstract]) AND (meta [title/abstract]), along with variations of these search terms. During the selection process, the titles, abstracts, and full texts of the selected articles were reviewed, and the reference lists were manually checked for additional relevant studies [12].

Duplicate studies, studies with repeated outcomes, or articles not published in English were excluded (Table S1). In this study, we evaluated the impact of GDM on various health outcomes by analyzing subgroups of mothers diagnosed with GDM, their children, patients with GDM at delivery, and fetuses of patients with GDM at delivery.

Health outcomes for pregnant women with GDM included the following: hypertension, overall cardiovascular and cerebrovascular diseases, overall cardiovascular diseases, overall cerebrovascular diseases, coronary artery disease, myocardial infarction, heart failure, angina pectoris, overall stroke, ischemic stroke, hemorrhagic stroke, venous thromboembolism, metabolic syndrome during pregnancy, postpartum metabolic syndrome, postpartum depression, breast cancer, thyroid cancer, stomach cancer, liver cancer, colon cancer, colorectal cancer, ovarian cancer, uterine cervical cancer, pancreatic cancer, brain cancer, blood cancer, specifically leukemia, endometrial cancer, skin cancer, and urological cancer.

Health outcomes for the children of pregnant women with GDM included atopic dermatitis or eczema, asthma, nonalcoholic fatty liver disease (NAFLD), GDM, systolic blood pressure (mmHg), body mass index (BMI) *z*-score, fasting glucose level, autism spectrum disorder, attention-deficit hyperactivity disorder, congenital

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heart disease, atrial septal defect, ventricular septal defect, tetralogy of Fallot, general developmental defects of enamel, hypoplasia, molar incisor hypomineralization, hypomineralized primary second molars, developmental defects of enamel in deciduous dentition, and major congenital malformations.

Health outcomes for pregnant women with GDM at delivery were selected as follows: shoulder dystocia, emergent cesarean delivery, polyhydramnios, hypertensive disorders of pregnancy, induction of labor, cesarean delivery, gestational hypertension, preeclampsia, instrumental delivery, and postpartum bleeding.

Health outcomes for fetuses of pregnant women with GDM at delivery included neonatal respiratory distress syndrome, neonatal hypoglycemia, neonatal hyperbilirubinemia, small for gestational age, large for gestational age, preterm birth, low Apgar score, admission to NICU, neonatal death, perinatal mortality, macrosomia, low birth weight, neonatal jaundice, and stillbirth.

To avoid duplication, if multiple meta-analyses covered the same topic, only one was selected. If two or more meta-analyses received the same evaluation score, the meta-analysis with the most included studies was chosen, as in previous umbrella reviews with integrated meta-analyses [13, 14].

2.2 | Data Extraction

For each meta-analysis, we extracted the first author's name, publication years, the total number of participants, the number of included original studies, reported estimates for associations, and their corresponding 95% confidence intervals (CIs) [15]. In addition, we recorded the indicators used in the analysis, such as standardized mean difference (SMD), mean difference (MD), odds ratio (OR), and relative risk (RR). We also summarized whether each study followed a cohort or case–control study design [11].

2.3 | Data Analysis

The objective of this study was to reassess the strength and consistency of the health outcomes associated with GDM based on the reported estimates of each association derived from existing meta-analyses. Two independent researchers (JK and YJ) initially screened the titles and abstracts, followed by an in-depth analysis of full texts aligned with the research objectives. Key data extracted from the selected studies included publication year, number of studies, key findings, country of study, number of cases, and total participants, study design, effect estimation method (random or fixed effects model), level of heterogeneity, the maximum adjusted effect, and the 95% CIs [16]. The methodological quality of the included studies was assessed using the AMSTAR 2 systematic review evaluation tool [17]. In case of disagreement, a third researcher (DKY) was involved in the discussion to reach a consensus.

We calculated pooled effect estimates and p-values using both fixed effects and random effects models, with statistical significance set at $p < 0.05$. To assess the potential influence of small studies, we performed Egger's test for funnel plot asymmetry, considering a p-value of less than 0.1 as indicative of small-study effects. For statistically significant results, we evaluated publication bias using p-curve analysis, where a right-skewed p-curve suggests a true effect, while a flat or left-skewed p-curve indicates selective reporting or publication bias [18]. The analysis was conducted according to a pre-specified protocol to ensure transparency, and multiple statistical approaches were used to guarantee the consistency and reliability of the results [19].

The meta-analyses were reanalyzed using DerSimonian and Laird's method, and heterogeneity was evaluated using the I^2 statistic, with a value exceeding 50% indicating substantial heterogeneity. Additionally, we assessed the possibility of p-hacking through p-curve analysis and evaluated uncertainty in the estimates using 95% prediction intervals (PIs). Bayesian statistics were employed to predict future observations and to reduce Type I errors. The Knapp–Sidik–Jonkman random effects model was applied. If the p-value in Egger's test was ≤ 0.1, we further assessed the potential for publication bias [12]. Effect size indicators such as SMD, MD, OR, and RR were transformed into equivalent OR (eOR) following the latest guidelines, and pooled effect sizes were recalculated. All statistical tests were two-sided, with $p \leq 0.05$ considered statistically significant.

2.4 | Strength of Evidence

The strength of the evidence was categorized into five levels based on several established criteria, including the p-value from the random effects model, the number of GDM cases, the statistical significance of the largest study, the I^2 value, the presence of small-study effects, the presence of excess significance bias, the random effects summary estimate at the 10% confidence limit, and the 95% PI [20]. The levels were classified as follows: Class I (convincing), Class II (highly suggestive), Class III (suggestive), Class IV (weak), and NS (nonsignificant) [11].

The classification criteria were as follows:

- Class I (convincing): p-value from the random effects model < 0.000001, at least 1000 GDM cases, p-value < 0.05 for the largest study, $I^2 < 50\%$, no small-study effects, no excess significance bias, and a 95% PI excluding 0.
- Class II (highly suggestive): p-value < 0.000001, at least 1000 GDM cases, p-value < 0.05 for the largest study, with no additional criteria required regarding heterogeneity, small-study effects, or PIs.
- Class III (suggestive): p-value < 0.001, at least 1000 GDM cases, with no further requirements regarding the largest study's significance or additional criteria.
- Class IV (weak): p-value < 0.05, with no restrictions on the number of GDM cases, and no criteria applied for heterogeneity, small-study effects, or excess significance bias.
- NS (nonsignificant): p-value ≥ 0.05, indicating no statistical significance, regardless of the number of GDM cases or other criteria.

These evidence classification and quality evaluation standards play a crucial role in enhancing the reliability and accuracy of the health outcomes associated with GDM.

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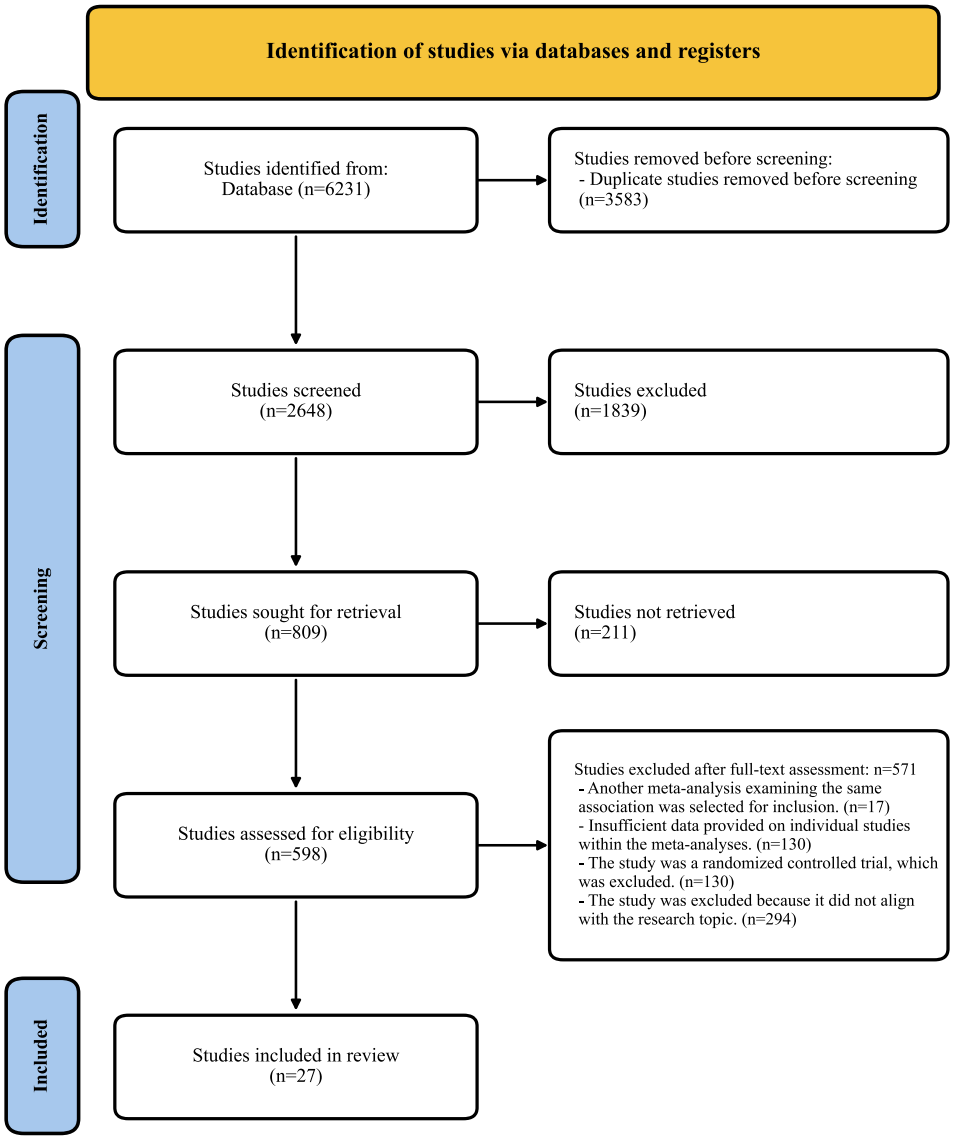


FIGURE 1 | PRISMA 2020 flow diagram.

2.5 | Patient and Public Involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for the design or implementation of the study. No patients were asked to advise on the interpretation or writing up of results. However, we plan on disseminating the results of this study to study participants on request and plan to disseminate to the wider relevant communities via email distribution and social media outlets.

3 | Results

3.1 | Characteristics of Included Studies

From the inception of databases to Aug 12, 2024, we identified 6231 articles. After removing duplicates and screening titles, abstracts, and full texts, 27 studies met the inclusion criteria (Figure 1). Details of the excluded studies are shown in Table S1. The eligible meta-analyses were published between 2012 and 2024. A total of 1010 original articles across 46 countries (Denmark, Egypt, Ethiopia, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Iran, Iraq, Ireland, Israel, Italy, Japan, South Korea, Lebanon, Mexico, Morocco, Netherlands, New Zealand, Nigeria, Norway, Peru, Poland, Portugal, Qatar, Saudi Arabia, Slovenia, Spain, Sweden, Taiwan, Thailand, Turkey, Uganda, United Kingdom, United States, and Vietnam) and six continents (Africa, Asia, Europe, North America, Oceania, and South America) were included (Table 1) [1, 8, 9, 21–44].

The 27 eligible articles provided 85 unique meta-analyses examining the association between maternal GDM and adverse health outcomes. These analyses covered 42 maternal health outcomes, 19 neonatal outcomes, 10 maternal adverse outcomes at delivery, and 14 neonatal adverse outcomes at delivery, involving over 363 million participants. Among the 27 original publications on health outcomes of maternal GDM, 17 (62.96%) were categorized as high quality, while 10 (37.04%) were graded

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TABLE 1 | Characteristics of a meta-analysis investigating the association between maternal gestational diabetes mellitus and health outcomes.

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
1. Maternal outcomes					
1.1 Cardiovascular outcome					
Hypertension	Liu X et al. [21]	Canada, China, Denmark, Finland, France, Hong Kong, China, Ireland, Multinational, Netherlands, Singapore, Sweden, the UK, and the US	GDM (GDM laboratory results, self-report, report from medical professionals, medical records, or birth certificates)	Hypertension (i.e., measured blood pressures, self-report, report from medical professionals, or medical records) subsequent to the index pregnancy and after the 12-week postpartum period)	High
Subclinical left ventricle systolic dysfunction	Sonaglioni A et al. [22]	China, Italy, Spain, the UK, and the US	GDM (NR)	Echocardiographic assessments (conventional echoDoppler parameters and LV-GLS)	High
Subclinical atherosclerosis	Sonaglioni A et al. [23]	Brazil, Germany, Hungary, India, Iran, Italy, Korea, Turkey, and the US	GDM and PGDM (NR)	Subclinical atherosclerosis (CCA-IMT)	High
Overall cardiovascular and cerebrovascular diseases	Xie W et al. [24]	Canada, Denmark, France, Iran, Israel, Korea, Sweden, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Overall cardiovascular diseases	Xie W et al. [24]	Canada, Denmark, France, Iran, Israel, Korea, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Overall cerebrovascular diseases	Xie W et al. [24]	Canada, Denmark, France, Korea, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Coronary artery diseases	Xie W et al. [24]	Canada, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Myocardial infarction	Xie W et al. [24]	Canada, Denmark, Korea, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Heart failure	Xie W et al. [24]	Canada, Denmark, Korea, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Angina pectoris	Xie W et al. [24]	Canada, France, and Israel	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Overall stroke	Xie W et al. [24]	Canada, Denmark, France, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Ischemic stroke	Xie W et al. [24]	Canada, Denmark, France, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Hemorrhagic stroke	Xie W et al. [24]	Canada and US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
Venous thromboembolism	Xie W et al. [24]	Canada, Denmark, the UK, and the US	GDM (self-report, ICD code, diagnostic codes, oral glucose tolerance test, or laboratory tests)	Cardiovascular and cerebrovascular diseases (self-report, ICD code, diagnostic codes, medical records, electrodiogram, or biomarkers)	High
1.2. Metabolic outcome					
Postpartum NAFLD	Foo RX et al. [25]	Denmark, India, South Korea, Taiwan, the UK, and the US	GDM (oral glucose tolerance test, or ICD code)	NAFLD (abdominal ultrasonography and transient elastography, medical records, imaging diagnoses)	High
Type 2 diabetes mellitus	Dennison RA et al. [26]	Australia, Brazil, Canada, China, Denmark, Finland, France, Germany, Hong Kong, India, Iran, Ireland, Israel, Italy, Multiple, Norway, Poland, South Korea, Spain, Sri Lanka, Sweden, Turkey, the UK, and the US	GDM (medical records or glycemic test)	Type 2 diabetes mellitus (medical records or glycemic test)	Low
Metabolic syndrome during pregnancy	Pathirana MM et al. [27]	Brazil, Italy, and Turkey	GDM (medical records or oral glucose tolerance test)	Metabolic syndrome (medical records or diagnoses based on IDF)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Postpartum metabolic syndrome	Pathirana MM et al. [27]	Canada, China, Denmark, Finland, Hong Kong, Hungary, India, Iran, Ireland, Italy, Poland, Singapore, Spain, Sri Lanka, Thailand, Turkey, the UK, and the US	GDM (medical records or oral glucose tolerance test)	Metabolic syndrome (medical records or diagnoses based on IDF)	High
1.3. Psychiatric outcome					
Perinatal depression	Jin Y et al. [28]	Bangladesh, China, Ethiopia, India, Iraq, Peru, and Turkey	GDM (medical records, oral glucose tolerance test, or blood test)	Depression (EPDS, MINI structured interview, PHQ-9, BDI, MADRS, or self-reported)	Low
Antenatal depressive symptoms at the time of GDM diagnosis	Wilson CA et al. [29]	Austria, Bangladesh, and Peru	GDM (medical records, oral glucose tolerance test, or blood test)	Depression (EPDS, MHI-5, BDI, PHQ-9, or MADRS)	High
Antenatal depressive symptoms after a diagnosis of GDM	Wilson CA et al. [29]	China, Greece, Israel, and Turkey	GDM (medical records, oral glucose tolerance test, or blood test)	Depression (EPDS, MHI-5, BDI, PHQ-9, or MADRS)	High
Postnatal depressive symptoms	Wilson CA et al. [29]	Austria, Bangladesh, Finland, Greece, Iran, Israel, Poland, and Sweden	GDM (medical records, oral glucose tolerance test, or blood test)	Depression (EPDS, MHI-5, BDI, PHQ-9, or MADRS)	High
Postpartum depression	Azami M et al. [30]	Arab, Finland, Greece, Iran, Italy, Poland, Qatar, Sweden, and the US	GDM (medical records or oral glucose tolerance test)	Depression (ICD, EPDS, CES-D, PHQ-9, OR HADS)	High
1.4 Oncological outcome					
Breast cancer	Wang Y et al. [31]	Canada, China, Israel, South Korea, the UK, and the US	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Thyroid cancer	Wang Y et al. [31]	Canada, China, Israel, and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Stomach cancer	Wang Y et al. [31]	China, Israel, and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Liver cancer	Wang Y et al. [31]	China and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Colon cancer	Wang Y et al. [31]	Israel and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Colorectum cancer	Wang Y et al. [31]	Canada and China	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Ovary cancer	Wang Y et al. [31]	Canada, China, Israel, and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Uterine cervix cancer	Wang Y et al. [31]	Canada, China, and Israel	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Pancreas cancer	Wang Y et al. [31]	China and Israel	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Brain cancer	Wang Y et al. [31]	China and Israel	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Blood cancer	Wang Y et al. [31]	Canada, Israel, and South Korea	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High

(Continues)

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Leukemia cancer	Wang Y et al. [31]	Canada and China	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Endometrium cancer	Wang Y et al. [31]	Canada and the US	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Skin cancer	Wang Y et al. [31]	Canada, China, and Israel	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
Urological organs cancer	Wang Y et al. [31]	Canada, China, and Israel	GDM (ICD code, medical records, self-administered questionnaire, or self-reported)	Cancer (ICD code, cancer registry, medical records, interview, or surgeon's and oncologist's reports)	High
1.5. Infectious outcome					
Infections during pregnancy	Yefet E et al. [32]	Bangladesh, Brazil, France, Italy, Poland, South Korea, Switzerland, Thailand, Turkey, the US, Uganda, and the UAE	GDM (ICD code, medical records, IADPSG criteria, Carpenter and Coustan criteria, NDDG criteria, WHO criteria, blood test, or oral glucose tolerance test)	Infection (NR)	Low
Chronic hepatitis B infection during pregnancy	Kong D et al. [33]	China, Germany, Hong Kong, China, Iran, Thailand, and the US	GDM (ICD code, medical records, or computer database)	Chronic hepatitis B infection during pregnancy (NR)	Low
1.6. Other outcomes					
Maternal rectovaginal colonization by group B Streptococcus	Mercado-Evans V et al. [34]	Australia, China, Finland, Lebanon, Mexico, Morocco, Nigeria, Spain, and the US	GDM (oral glucose tolerance test or abnormal glucose tolerance test, interview, ICD code, or medical records)	Group B Streptococcus maternal rectovaginal colonization (laboratory, medical records, or self-reported)	High
Delayed onset of lactogenesis	Wu JL et al. [35]	Brazil, China, India, Israel, and the US	GDM (NR)	Delayed onset of lactogenesis (NR)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
2. Neonatal outcomes					
2.1 Allergic outcomes					
Atopic dermatitis or eczema	Pan L et al. [36]	China, Finland, Taiwan, and the US	GDM, HDP (ICD code, oral glucose tolerance test, or medical records)	Atopic dermatitis or eczema (ICD code, parent-reported, or clinical diagnosis)	High
Asthma	Huang X et al. [9]	Canada, China, Greece, Israel, and the US	GDM (medical records or questionnaire)	Asthma (medical records, ICD code, or questionnaire)	High
2.2. Metabolic outcomes					
NAFLD	Foo RX et al. [25]	Canada, China, the Netherlands, and the UK	GDM (oral glucose tolerance test, or ICD code)	NAFLD (abdominal ultrasonography and transient elastography, medical records, imaging diagnoses)	High
GDM	Pathirana MM et al. [27]	Denmark and the US	GDM (medical records or oral glucose tolerance test)	Metabolic syndrome (medical records or diagnoses based on IDF)	High
2.3. Cardiovascular outcomes					
Systolic blood pressure (mmHg)	Pathirana MM et al. [37]	Brazil, China, England, Finland, Hong Kong, India, and the US	GDM (ICD code, medical records, IADPSG criteria, hospital records, WHO criteria, ADA criteria, self-reported or oral glucose tolerance test)	Systolic blood pressure (laboratory)	High
BMI *z*-score	Pathirana MM et al. [37]	China, England, and the US	GDM (ICD code, medical records, IADPSG criteria, hospital records, WHO criteria, ADA criteria, self-reported or oral glucose tolerance test)	BMI (laboratory)	High
Fasting glucose level	Pathirana MM et al. [37]	Brazil, Denmark, England, Hong Kong, India, Poland, and the US	GDM (ICD code, medical records, IADPSG criteria, hospital records, WHO criteria, ADA criteria, self-reported or oral glucose tolerance test)	Fasting glucose level (laboratory)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
2.4. Psychiatric outcomes					
Autism spectrum disorder	Rowland J et al. [38]	Canada, Israel, and the US	GDM (medical records, interviews, or self-reported)	Autism spectrum disorder (medical records, interviews, or self-reported)	Low
Attention-deficit hyperactivity disorder	Rowland J et al. [38]	Eight European countries, France, Turkey, and the US	GDM (medical records, interviews, or self-reported)	Attention deficit hyperactivity disorder (medical records, interviews, or self-reported)	Low
2.5. Other outcomes					
Congenital heart disease	Liu Y et al. [39]	Australia, Canada, China, Colombia, Denmark, France, Hungary, Norway, SAU, Sweden, the UK, and the US	GDM (medical records, database codes, or clinically diagnosed)	Congenital heart disease (medical records, database codes, or clinically diagnosed)	High
Atrial septal defect	Liu Y et al. [39]	Norway, SAU, and the US	GDM (medical records, database codes, or clinically diagnosed)	Congenital heart disease (medical records, database codes, or clinically diagnosed)	High
Ventricular septal defect	Liu Y et al. [39]	Norway, SAU, and the US	GDM (medical records, database codes, or clinically diagnosed)	Congenital heart disease (medical records, database codes, or clinically diagnosed)	High
Tetralogy of Fallot	Liu Y et al. [39]	The US	GDM (medical records, database codes, or clinically diagnosed)	Congenital heart disease (medical records, database codes, or clinically diagnosed)	High
General developmental defects of enamel	Tolomeu JSO et al. [40]	Brazil, India, Iran, Italy, Sweden, Turkey, and the UK	GDM (self-report, hospital records, adapted Pedersen's method, or questionnaire)	Developmental defects of enamel (EAPD criteria or modified DDE index)	Low
Hypoplasia	Tolomeu JSO et al. [40]	Iran and Sweden	GDM (self-report, hospital records, adapted Pedersen's method, or questionnaire)	Developmental defects of enamel (EAPD criteria or modified DDE index)	Low

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Molar incisor hypomineralization	Tolomeu JSO et al. [40]	Brazil, India, Italy, Turkey, and the UK	GDM (self-report, hospital records, adapted Pedersen's method, or questionnaire)	Developmental defects of enamel (EAPD criteria or modified DDE index)	Low
Hypomineralized primary second molars	Tolomeu JSO et al. [40]	Brazil	GDM (self-report, hospital records, adapted Pedersen's method, or questionnaire)	Developmental defects of enamel (EAPD criteria or modified DDE index)	Low
Developmental defects of enamel in the deciduous dentition	Tolomeu JSO et al. [40]	Brazil	GDM (self-report, hospital records, adapted Pedersen's method, or questionnaire)	Developmental defects of enamel (EAPD criteria or modified DDE index)	Low
Major congenital malformations	Balsells M et al. [41]	Australia, Canada, Croatia, Germany, India, Israel, Italy, Malta, Mexico, Spain, Sudan, and the US	GDM, PGDM (WHO criteria or NDDG criteria)	Major congenital malformations (NR)	Critically Low
3. Maternal adverse outcomes at delivery					
Shoulder dystocia	Sgayer I et al. [42]	Israel, Japan, Korea, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Shoulder dystocia (NR)	High
Emergent cesarean delivery	Sgayer I et al. [42]	France, India, Israel, Japan, the Netherlands, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Emergent cesarean delivery (NR)	High
Polyhydramnios	Sgayer I et al. [42]	France, Israel, Korea, the Netherlands, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Polyhydramnios (NR)	High
Hypertensive disorders of pregnancy	Greco E et al. [8]	Australia, Canada, Chile, China, Denmark, France, India, Israel, Italy, Japan, Korea, Malaysia, Mexico, Qatar, Saudi Arabia, Slovenia, South Korea, Spain, Sweden, Taiwan, Thailand, the UK, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Hypertensive disorders of pregnancy (NR)	High
Induction of labor	Greco E et al. [8]	Australia, Canada, Finland, France, India, Iran, Israel, Qatar, South Korea, Sweden, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Induction of labor (NR)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Cesarean delivery	Greco E et al. [8]	Australia, Canada, Chile, China, Denmark, Finland, France, Germany, India, Iran, Israel, Italy, Japan, Korea, Malaysia, Mexico, Qatar, Saudi Arabia, Slovenia, Slovenia, South Korea, Spain, Sweden, Taiwan, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Cesarean delivery (NR)	High
Gestational hypertension	Tu F et al. [43]	Canada and Spain	GDM (NR)	Gestational hypertension (NR)	Critically Low
Preeclampsia	Ye W et al. [1]	9 countries, Canada, Ireland, Japan, Korea, Thailand, the UK, and Vietnam	GDM (diagnostic code, medical records, or hospital records)	Pre-eclampsia (NR)	Critically Low
Instrumental delivery	Ye W et al. [1]	Thailand and the UK	GDM (diagnostic code, medical records, or hospital records)	Instrumental delivery (NR)	Critically Low
Postpartum bleeding	Ye W et al. [1]	China, Thailand, the UK, and Vietnam	GDM (diagnostic code, medical records, or hospital records)	Postpartum bleeding (NR)	Critically Low
4. Neonatal adverse outcomes at delivery					
Neonatal respiratory distress syndrome	Sgayer I et al. [42]	France, India, Israel, Japan, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Neonatal respiratory distress syndrome (NR)	High
Neonatal hypoglycemia	Sgayer I et al. [42]	France, Israel, Japan, Korea, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Neonatal hypoglycemia (NR)	High
Neonatal hyperbilirubinemia	Sgayer I et al. [42]	France, India, Israel, Japan, and Portugal	GDM (oral glucose tolerance test, WHO criteria, or IADPSG criteria)	Neonatal hyperbilirubinemia (NR)	High
Small for gestational age	Greco E et al. [8]	Brazil, Canada, Chile, China, Finland, France, Israel, Italy, Japan, Qatar, Saudi Arabia, Slovenia, South Korea, Spain, Sweden, Taiwan, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Small for gestational age (NR)	High
Large for gestational age	Greco E et al. [8]	Australia, Brazil, Canada, China, Denmark, Finland, France, India, Israel, Japan, Korea, Slovenia, Slovenia, Spain, Sweden, Taiwan, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Large for gestational age (NR)	High

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Preterm birth	Greco E et al. [8]	Australia, Canada, China, Finland, France, India, Israel, Italy, Japan, Korea, Malaysia, Mexico, Qatar, Slovenia, Slovenia, South Korea, Spain, Sweden, Taiwan, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Preterm birth (NR)	High
Low Apgar score	Greco E et al. [8]	Australia, Brazil, Canada, China, Denmark, Finland, France, India, Israel, Japan, Korea, Slovenia, Slovenia, Spain, Sweden, Taiwan, Thailand, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Low Apgar score (NR)	High
Admission to NICU	Greco E et al. [8]	Australia, Canada, China, Finland, France, Germany, India, Iran, Israel, Japan, Korea, Malaysia, Qatar, Saudi Arabia, Slovenia, South Korea, Sweden, Taiwan, Thailand, the UK, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Admission to NICU (NR)	High
Neonatal death	Greco E et al. [8]	Australia, Canada, India, Iran, Israel, Japan, Qatar, Slovenia, Sweden, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Neonatal death (NR)	High
Perinatal mortality	Greco E et al. [8]	Australia, Canada, Finland, Israel, Qatar, Spain, Sweden, and the US	GDM (CDA criteria, JSOG criteria, SCOG criteria, SDS criteria, Carpenter and Coustan, NDDG criteria, WHO criteria, or IADPSG criteria)	Perinatal mortality (NR)	High
Macrosomia	Ye W et al. [1]	Australia, China, Denmark, Ireland, Japan, Korea, New Zealand, Spain, Thailand, the UK, and the US	GDM (diagnostic code, medical records, or hospital records)	Marcosomia (NR)	Critically Low
Low body weight	Ye W et al. [1]	China and Thailand	GDM (diagnostic code, medical records, or hospital records)	Low body weight (NR)	Critically Low
Neonatal jaundice	Ye W et al. [1]	Denmark, Japan, Korea, and Vietnam	GDM (diagnostic code, medical records, or hospital records)	Neonatal jaundice (NR)	Critically Low

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TABLE 1 | (Continued)

Outcome	Author	Included countries	Inclusion criteria for exposures	Inclusion criteria for outcomes	AMSTAR2
Stillbirth	Lemieux P et al. [44]	Australia, Bangladesh, Brazil, Canada, China, Croatia, Denmark, Egypt, Finland, France, Ghana, India, Iran, Ireland, Israel, Italy, Japan, Kuwait, Netherlands, Oman, Qatar, Saudi Arabia, Sweden, Taiwan, Thailand, the US, Uganda, Vietnam, and Zimbabwe	GDM (Sweden criteria, CDA criteria, ADA criteria, WHO criteria, ADIPS criteria, Carpenter and Coustan criteria, O'Sullivan and Mahan criteria, NDDG criteria, or IADPSG criteria)	Stillbirth (NR)	Critically Low

Abbreviations: ADA, American Diabetes Association; ADIPS, Australasian Diabetes in Pregnancy Society; AMSTAR2, a measurement tool to assess systematic reviews 2; BDI, Beck Depression Inventory; BMI, body mass index; CCA-IMT, common carotid artery-intima-media thickness; CDA, Canadian Diabetes Association; CES-D, center for epidemiologic studies depression scale; DDE, developmental defects of enamel; EAPD, European Academy of Paediatric Dentistry; EPDS, Edinburgh Postnatal Depression Scale; GDM, gestational diabetes mellitus; HADS, hospital anxiety and depression scale; HDP, hypertensive disorders of pregnancy; IADPSG, International Association of Diabetes and Pregnancy Study Groups; ICD, International Classification of Diseases; IDF, International Diabetes Federation; JSOG, Japan Society of Obstetrics and Gynaecology; LV-GLS, left ventricular-global longitudinal strain; MADRS, Montgomery–Åsberg Depression Rating Scale; MHI-5, Mental Health Inventory-5; NAFLD, nonalcoholic fatty liver disease; NDDG, National Diabetes Data Group; NICU, neonatal intensive care unit; NR, not reported; PGDM, pregestational diabetes mellitus; PHQ-9, Patient Health Questionnaire-9; SCOG, Spanish Society of Obstetricians and Gynaecologists; SDS, Spanish Diabetes Society; UK, United Kingdom; US, United States.

as low or critically low quality, primarily due to insufficient assessment or reporting of bias in individual studies (Tables 1 and S2). The number of original studies included in the pooled analyses had a median of 6, with a range of 2 to 67 (Table S3). Effect sizes were reported using metrics such as MD, SMD, OR, and RR, all of which were converted to eOR.

Our reanalyses showed that 57.6% (49/85) of associations were statistically significant under the random effects model. Of these significant associations, 97.96% (48/49) included more than 1000 participants. Additionally, 51.02% (25/49) of the significant associations exhibited substantial heterogeneity ($I^2 > 50$). Egger's regression test indicated no evidence of small-study effects or publication bias in 79.59% (39/49) of the reported associations.

Based on the evaluated CE levels of each association, 1.2% (1/85) of meta-analytical effects were categorized as having convincing evidence (Class I), 20.0% (17/85) as highly suggestive evidence (Class II), 23.5% (20/85) as suggestive evidence (Class III), 20.0% (17/85) as weak evidence (Class IV), and 35.3% (30/85) of effects were categorized as having nonsignificant evidence. The detailed classification of the certainty of evidence is shown in Table S4. The forest plot, Funnel plot, and *P*-curve for each health outcome are presented in Figures S1–85.

3.2 | Associations Between GDM and Adverse Maternal Outcomes

For maternal outcomes, patients with GDM had significant associations with several cardiovascular outcomes, including subclinical atherosclerosis (eOR, 5.10 [95% CI, 2.77 to 9.38]; CE = II), angina pectoris (2.26 [1.25 to 4.08]; CE = II), hypertension (1.78 [1.45 to 2.20]; CE = II), myocardial infarction (1.74 [1.30 to 2.32]; CE = III), overall cardiovascular diseases (1.72 [1.44 to 2.05]; CE = II), heart failure (1.62 [1.27 to 2.07]; CE = III), ischemic stroke (1.49 [1.24 to 1.79]; CE = II), overall stroke (1.45 [1.25 to 1.69]; CE = II), overall cardiovascular and cerebrovascular disease (1.45 [1.36 to 1.54]; CE = II), hemorrhagic stroke (1.44 [1.22 to 1.68]; CE = IV), overall cerebrovascular diseases (1.40 [1.29 to 1.51]; CE = III), coronary artery disease (1.40 [1.14 to 1.71]; CE = III), venous thromboembolism (1.28 [1.04 to 1.58]; CE = III), and subclinical left ventricle systolic dysfunction (0.17 [0.08 to 0.33]; CE = II; Figure 2 and Table 2).

Patients with GDM also showed an increased OR of various metabolic outcomes, including metabolic syndrome during pregnancy (eOR, 20.45 [10.19 to 41.03]; CE = IV), Type 2 diabetes mellitus (8.57 [6.28 to 11.71]; CE = II), postpartum metabolic syndrome (2.36 [1.82 to 3.07]; CE = II), and postpartum NAFLD (1.45 [1.12 to 1.87]; CE = III). In addition, there are significant associations between GDM and several psychiatric outcomes among patients with GDM: antenatal depressive symptoms at the time of GDM diagnosis (eOR, 2.21 [1.23 to 3.96]; CE = III), perinatal depression (1.98 [1.21 to 3.23]; CE = IV), postpartum depression (1.64 [1.16 to 2.32]; CE = III), and postnatal depressive symptoms (1.62 [1.24 to 2.11]; CE = III). Among 15 previously reported oncological outcomes, the results from reanalysis showed significantly increased odds of blood cancer (1.48 [1.05

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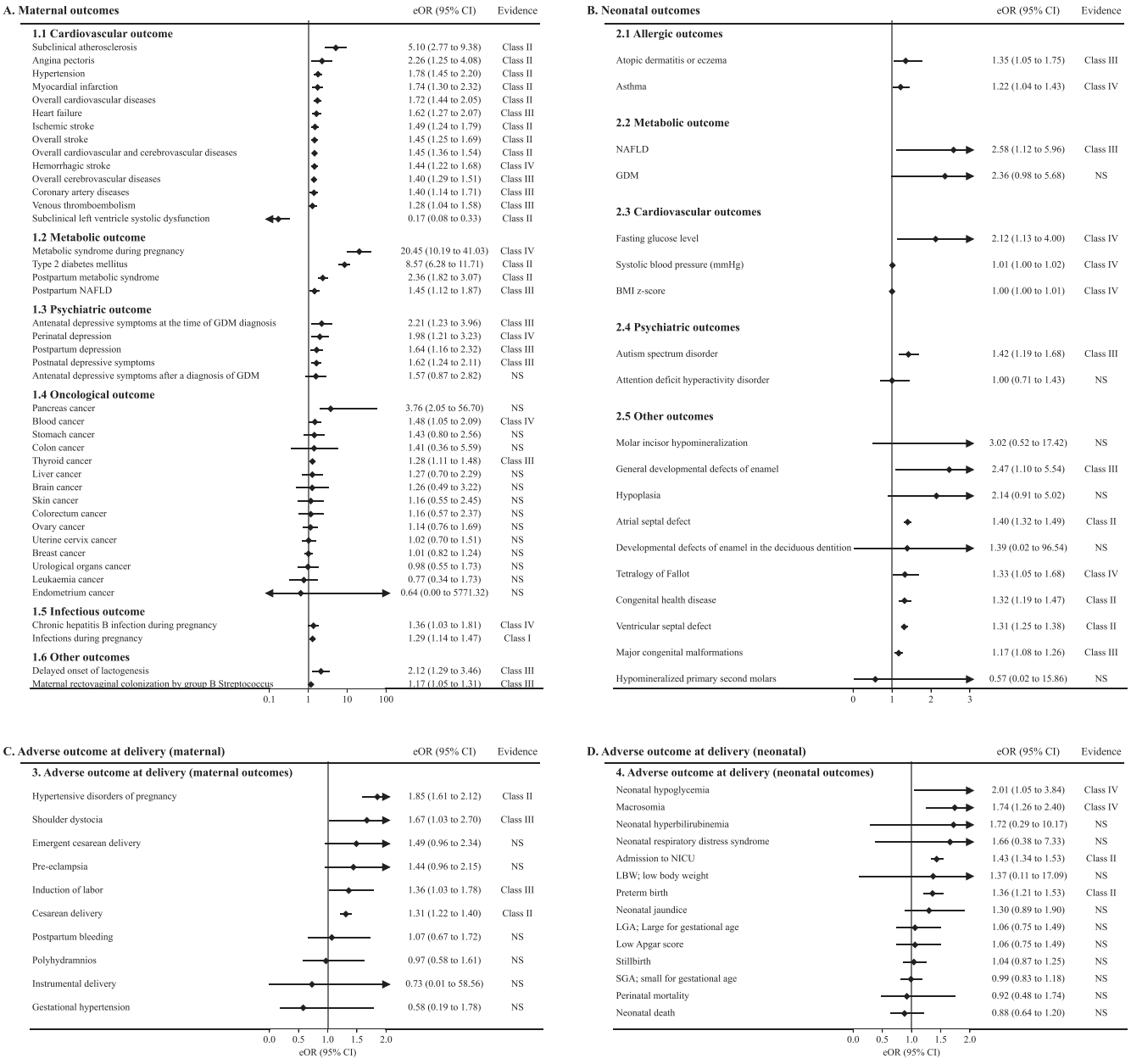


FIGURE 2 | Findings of meta-analysis of the association between maternal gestational diabetes mellitus and health outcomes. (A) Maternal outcomes, (B) neonatal outcomes, (C) maternal adverse outcomes at delivery, and (D) neonatal adverse outcomes at delivery. Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; MD, mean differences; N, no; NAFLD, nonalcoholic fatty liver disease; NICU, neonatal intensive care unit; OR, odds ratio; RR, risk ratio; SMD, standardized mean differences.

to 2.09]; CE = IV) and thyroid cancer (1.28 [1.11 to 1.48]; CE = III) among patients with GDM.

After reanalysis, two infectious outcomes showed statistical significance and were graded as convincing or weak evidence, respectively: infections during pregnancy (1.29 [1.14 to 1.47]; CE = I) and chronic hepatitis B infection during pregnancy (1.36 [1.03 to 1.81]; CE = IV). Moreover, patients with GDM had a significantly increased likelihood of delayed onset of lactogenesis (2.12 [1.29 to 3.46]; CE = III) and maternal rectovaginal colonization by group B Streptococcus (1.17 [1.05 to 1.31]; CE = III).

3.3 | Associations Between GDM and Adverse Neonatal Outcomes

Maternal GDM is significantly associated with increased odds of neonatal allergic outcomes, including atopic dermatitis or eczema (eOR, 1.35 [1.05 to 1.75]; CE = III) and asthma (1.22 [1.04 to 1.43]; CE = IV). Children exposed to maternal GDM during fetal development exhibit increased ORs for developing NAFLD (2.58 [1.12 to 5.96]; CE = III) later in life. Other adverse cardiovascular outcomes among children included elevated fasting glucose level (2.12 [1.13 to 4.00]; CE = IV), higher systolic blood pressure

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TABLE 2 | Evidence maps of umbrella review on the association between maternal gestational diabetes mellitus and health outcomes.

Outcomes	eOR	Direction	Class
1. Maternal outcomes			
1.1 Cardiovascular outcome			
Subclinical atherosclerosis	**5.10 (2.77 to 9.38)**	Association	II
Angina pectoris	**2.26 (1.25 to 4.08)**	Association	II
Hypertension	**1.78 (1.45 to 2.20)**	Association	II
Myocardial infarction	**1.74 (1.30 to 2.32)**	Association	III
Overall cardiovascular diseases	**1.72 (1.44 to 2.05)**	Association	II
Heart failure	**1.62 (1.27 to 2.07)**	Association	III
Ischemic stroke	**1.49 (1.24 to 1.79)**	Association	II
Overall stroke	**1.45 (1.25 to 1.69)**	Association	II
Overall cardiovascular and cerebrovascular diseases	**1.45 (1.36 to 1.54)**	Association	II
Hemorrhagic stroke	**1.44 (1.22 to 1.68)**	Association	IV
Overall cerebrovascular diseases	**1.40 (1.29 to 1.51)**	Association	III
Coronary artery diseases	**1.40 (1.14 to 1.71)**	Association	III
Venous thromboembolism	**1.28 (1.04 to 1.58)**	Association	III
Subclinical left ventricle systolic dysfunction	**0.17 (0.08 to 0.33)**	Association	II
1.2 Metabolic outcome			
Metabolic syndrome during pregnancy	**20.45 (10.19 to 41.03)**	Association	IV
Type 2 diabetes mellitus	**8.57 (6.28 to 11.71)**	Association	II
Postpartum metabolic syndrome	**2.36 (1.82 to 3.07)**	Association	II
Postpartum NAFLD	**1.45 (1.12 to 1.87)**	Association	III
1.3 Psychiatric outcome			
Antenatal depressive symptoms at the time of GDM diagnosis	**2.21 (1.23 to 3.96)**	Association	III
Perinatal depression	**1.98 (1.21 to 3.23)**	Association	IV
Postpartum depression	**1.64 (1.16 to 2.32)**	Association	III
Postnatal depressive symptoms	**1.62 (1.24 to 2.11)**	Association	III
Antenatal depressive symptoms after a diagnosis of GDM	1.57 (0.87 to 2.82)	No association	NS
1.4 Oncological outcome			
Pancreas cancer	3.76 (0.25 to 56.70)	No association	NS
Blood cancer	**1.48 (1.05 to 2.09)**	Association	IV
Stomach cancer	1.43 (0.80 to 2.56)	No association	NS
Colon cancer	1.41 (0.36 to 5.59)	No association	NS
Thyroid cancer	**1.28 (1.11 to 1.48)**	Association	III
Liver cancer	1.27 (0.70 to 2.29)	No association	NS
Brain cancer	1.26 (0.49 to 3.22)	No association	NS
Skin cancer	1.16 (0.55 to 2.45)	No association	NS
Colorectum cancer	1.16 (0.57 to 2.37)	No association	NS
Ovary cancer	1.14 (0.76 to 1.69)	No association	NS

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TABLE 2 | (Continued)

Outcomes	eOR	Direction	Class
Uterine cervix cancer	1.02 (0.70 to 1.51)	No association	NS
Breast cancer	1.01 (0.82 to 1.24)	No association	NS
Urological organs cancer	0.98 (0.55 to 1.73)	No association	NS
Leukemia cancer	0.77 (0.34 to 1.73)	No association	NS
Endometrium cancer	0.64 (0.00 to 5771.32)	No association	NS
1.5 Infectious outcome			
Chronic hepatitis B infection during pregnancy	**1.36 (1.03 to 1.81)**	Association	IV
Infections during pregnancy	**1.29 (1.14 to 1.47)**	Association	I
1.6 Other outcomes			
Delayed onset of lactogenesis	**2.12 (1.29 to 3.46)**	Association	III
Maternal rectovaginal colonization by group B Streptococcus	**1.17 (1.05 to 1.31)**	Association	III
2. Neonatal outcomes			
2.1 Allergic outcomes			
Atopic dermatitis or eczema	**1.35 (1.05 to 1.75)**	Association	III
Asthma	**1.22 (1.04 to 1.43)**	Association	IV
2.2 Metabolic outcome			
NAFLD	**2.58 (1.12 to 5.96)**	Association	III
GDM	2.36 (0.98 to 5.68)	No association	NS
2.3 Cardiovascular outcomes			
Fasting glucose level	**2.12 (1.13 to 4.00)**	Association	IV
Systolic blood pressure (mmHg)	**1.01 (1.00 to 1.02)**	Association	IV
BMI z-score	**1.00 (1.00 to 1.01)**	Association	IV
2.4 Psychiatric outcomes			
Autism spectrum disorder	**1.42 (1.19 to 1.68)**	Association	III
Attention deficit hyperactivity disorder	1.00 (0.71 to 1.43)	No association	NS
2.5 Other outcomes			
Molar incisor hypomineralization	3.02 (0.52 to 17.42)	No association	NS
General developmental defects of enamel	**2.47 (1.10 to 5.54)**	Association	III
Hypoplasia	2.14 (0.91 to 5.02)	No association	NS
Atrial septal defect	**1.40 (1.32 to 1.49)**	Association	II
Developmental defects of enamel in the deciduous dentition	1.39 (0.02 to 96.54)	No association	NS
Tetralogy of Fallot	**1.33 (1.05 to 1.68)**	Association	IV
Congenital heart disease	**1.32 (1.19 to 1.47)**	Association	II
Ventricular septal defect	**1.31 (1.25 to 1.38)**	Association	II
Major congenital malformations	**1.17 (1.08 to 1.26)**	Association	III
Hypomineralized primary second molars	0.57 (0.02 to 15.86)	No association	NS
3. Adverse outcome at delivery (maternal outcomes)			
Hypertensive disorders of pregnancy	**1.85 (1.61 to 2.12)**	Association	II

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TABLE 2 | (Continued)

Outcomes	eOR	Direction	Class
Shoulder dystocia	**1.67 (1.03 to 2.70)**	Association	III
Emergent cesarean delivery	1.49 (0.96 to 2.34)	No association	NS
Pre-eclampsia	1.44 (0.96 to 2.15)	No association	NS
Induction of labor	**1.36 (1.03 to 1.78)**	Association	III
Cesarean delivery	**1.31 (1.22 to 1.40)**	Association	II
Postpartum bleeding	1.07 (0.67 to 1.72)	No association	NS
Polyhydramnios	0.97 (0.58 to 1.61)	No association	NS
Instrumental delivery	0.73 (0.01 to 58.56)	No association	NS
Gestational hypertension	0.58 (0.19 to 1.78)	No association	NS
4. Adverse outcome at delivery (neonatal outcomes)			
Neonatal hypoglycemia	**2.01 (1.05 to 3.84)**	Association	IV
Macrosomia	**1.74 (1.26 to 2.40)**	Association	IV
Neonatal hyperbilirubinemia	1.72 (0.29 to 10.17)	No association	NS
Neonatal respiratory distress syndrome	1.66 (0.38 to 7.33)	No association	NS
Admission to NICU	**1.43 (1.34 to 1.53)**	Association	II
Low body weight	1.37 (0.11 to 17.09)	No association	NS
Preterm birth	**1.36 (1.21 to 1.53)**	Association	II
Neonatal jaundice	1.30 (0.89 to 1.90)	No association	NS
Large for gestational age	1.06 (0.75 to 1.49)	No association	NS
Low Apgar score	1.06 (0.75 to 1.49)	No association	NS
Stillbirth	1.04 (0.87 to 1.25)	No association	NS
Small for gestational age	0.99 (0.83 to 1.18)	No association	NS
Perinatal mortality	0.92 (0.48 to 1.74)	No association	NS
Neonatal death	0.88 (0.64 to 1.20)	No association	NS

Note: The bold indicates statistical significance ($p < 0.05$). Color represents the magnitude of the estimated eORs, with darker red indicating larger eOR values and lighter shading indicating smaller values.
[a]Class and quality of evidence:
- Class I (convincing evidence): > 1000 cases and statistical significance at $p < 10^{-6}$ (random effects); no evidence of small study effects and excess significance bias; 95% prediction interval excluded null value; no large heterogeneity ($I^2 < 50\%$).
- Class II (highly suggestive evidence): > 1000 cases and statistical significance at $p < 0.001$ (random effects); no evidence of small study effects and excess significance bias; 95% prediction interval excluded null value; no large heterogeneity ($I^2 < 50\%$).
- Class III (suggestive evidence): > 1000 cases and statistical significance at $p < 0.001$.
- Class IV (weak evidence): remaining significant associations with $p < 0.05$.
- NS (nonsignificant): $p \geq 0.05$.
Abbreviations: BMI, body mass index; eOR, equivalent odds ratio; GDM, gestational diabetes mellitus; NAFLD, nonalcoholic fatty liver disease; NICU, neonatal intensive care unit.

(1.01 [1.00 to 1.02]; CE = IV), and increased BMI *z*-score (1.00 [1.00 to 1.01]; CE = IV).

After reanalysis, autism spectrum disorder in children showed statistical significance and was graded as suggestive evidence, as neonatal psychiatric outcomes related to maternal GDM (1.42 [1.19 to 1.68]; CE = III). GDM was also observed to be associated with general developmental defects of enamel (2.47 [1.10 to 5.54]; CE = III), atrial septal defect (1.40 [1.32 to 1.49]; CE = II), tetralogy of Fallot (1.33 [1.05 to 1.68]; CE = IV), congenital heart disease (1.32 [1.19 to 1.47]; CE = II), ventricular septal defect (1.31 [1.25 to 1.38]; CE = II), and major congenital malformations (1.17 [1.08 to 1.26]; CE = III).

3.4 | Associations Between GDM and Adverse Maternal Outcomes at Delivery

Women with GDM had increased odds of hypertensive disorders (eOR, 1.85 [1.61 to 2.12]; CE = II), shoulder dystocia (1.67 [1.03 to 2.70]; CE = III), induction of labor (1.36 [1.03 to 1.78]; CE = III), and cesarean delivery (1.31 [1.22 to 1.40]; CE = II).

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3.5 | Associations Between GDM and Adverse Neonatal Outcomes at Delivery

GDM was significantly associated with several adverse neonatal outcomes at delivery, including neonatal hypoglycemia (eOR, 2.01 [1.05 to 3.84]; CE = IV), macrosomia (1.74 [1.26 to 2.40]; CE = IV), admission to the NICU (1.43 [1.34 to 1.53]; CE = II), and preterm birth (1.36 [1.21 to 1.53]; CE = II).

4 | Discussion

4.1 | Key Findings

This study is a novel umbrella review with integrated meta-analyses to systematically quantitatively collect and assess the hierarchy of evidence for providing quantitative estimates for the association between maternal GDM and health outcomes among pregnant women and their children. From 27 meta-analyses covering over 363 million participants, we identified 85 unique associations relevant to maternal GDM. These 85 unique associations between GDM and health outcomes included 42 maternal health outcomes, 19 neonatal outcomes, 10 maternal adverse outcomes at delivery, and 14 neonatal adverse outcomes at delivery. After reanalysis, among 85 associations, we identified a total of 49 statistically significant health outcomes. As for maternal outcomes, patients with GDM had significant associations with 14 cardiovascular outcomes, four metabolic outcomes, four psychiatric outcomes, two oncological outcomes, two infectious outcomes, and two other outcomes, with various evidence levels from weak (Class IV) to convincing (Class I). For the neonatal adverse outcomes, children exposed to maternal GDM showed higher odds of developing two allergic outcomes, two metabolic outcomes, three cardiovascular outcomes, one psychiatric outcome, and six other outcomes, with various evidence levels from weak (class IV) to highly suggestive (class II). In addition, reanalysis found that GDM was also associated with several adverse health outcomes at delivery, including four maternal outcomes and four neonatal outcomes. None of the health outcomes that were nonsignificant in previous studies have been identified to have an association through reanalysis.

4.2 | Comparisons With Previous Studies

Recent reviews and original clinical trials have enhanced our understanding of the adverse health outcomes associated with GDM during pregnancy [1, 8, 25]. However, most previous reviews narrowly focused on specific complications, such as macrosomia, congenital malformation, asthma, metabolic syndrome, ADHD, or preterm birth [7, 9, 27, 38, 39]. Furthermore, many studies exclusively addressed either maternal or neonatal outcomes or primarily focused on adverse outcomes occurring at delivery [1, 8, 9, 21–44]. To the best of our knowledge, this study is the first to perform an umbrella review systematically summarizing the full spectrum of adverse health outcomes associated with GDM among both pregnant women and their children. Our study provided a comprehensive overview by summarizing and categorizing health outcomes into four domains: maternal outcomes, neonatal outcomes, adverse outcomes at delivery (maternal and neonatal), and systematically evaluating the hierarchy of evidence supporting these associations.

4.3 | Plausible Mechanisms

Our study identified 49 statistically significant associations between GDM and health outcomes among pregnant women and their children, systematically quantified and assessed the hierarchy of credibility of existing evidence. This umbrella review aims to provide an overview and summary of potential health outcomes associated with GDM. We seek to provide plausible mechanisms for each association based on previous studies. A complex interplay of metabolic, hormonal, and inflammatory pathways likely drives observed associations between GDM and adverse maternal and neonatal outcomes [45]. GDM is characterized by glucose intolerance and insulin resistance, which frequently leads to maternal hyperglycemia [46]. Chronic hyperglycemia during pregnancy can disrupt normal fetal development, neocortical neurogenesis, and maternal physiology, contributing to adverse health outcomes for both mother and child [47, 48].

Maternal GDM increases the production of oxidative stress and triggers inflammatory responses, which are known to impair vascular function, predisposing mothers to cardiovascular conditions such as hypertension, myocardial infarction, and stroke [49]. GDM also disrupts maternal immunity and vaginal microbiota and elevates insulin resistance, increasing the risk of metabolic disorders like Type 2 diabetes mellitus, metabolic syndrome, and postpartum NAFLD [50, 51]. Likewise, GDM is well known as a comorbidity with various metabolic diseases [48]. Furthermore, GDM hinders maternal hormonal regulations or disrupts neural circuits, potentially contributing to psychiatric conditions, including antenatal and postpartum depression [52].

For neonates, maternal GDM can result in excessive fetal insulin production, resulting in macrosomia and hypoglycemia after birth [46]. Impaired metabolism in utero increases the risk of developing cardiovascular or metabolic diseases, including childhood obesity, NAFLD, and hypertension [46]. Exposure to maternal GDM may also disrupt neurodevelopment, fetal neurogenesis, differentiation, migration, and aggregation, increasing the risk of psychiatric disorders such as autism spectrum disorder [52]. In addition, maternal GDM altered fetal development, induced disruptions in immunity, which are associated with higher odds of allergic outcomes such as atopic dermatitis and asthma among children [53].

At delivery, GDM increases the risk of complications, including induction of labor, cesarean delivery, shoulder dystocia, and hypertensive disorders due to the physiological burdens imposed by altered glucose metabolism [8, 42]. Neonatal complications, such as preterm birth and admission to NICU, could be caused by compromised placental function and fetal overgrowth [42]. In summary, the adverse outcomes associated with GDM are likely mediated through multiple biological mechanisms, including elevated oxidative stress, dysregulated immunity, insulin resistance, altered hormonal regulation, and disrupted fetal

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development. These alterations collectively contribute to both short- and long-term risks for developing adverse health outcomes in both pregnant women and their children, suggesting the need for early screening and interventions to ameliorate the impact of GDM.

4.4 | Clinical Policy Implications

These findings highlight the need for comprehensive clinical policies aimed at early detection, effective management, and long-term monitoring of GDM to reduce its adverse health outcomes for both pregnant women and their children. Given the extensive adverse health outcomes associated with GDM among both pregnant women and their children, early detection and universal screening during pregnancy are imperative. Universal screening, as recommended by the US Preventive Services Task Force after 24 weeks of gestation, is essential [54]. Also, future studies are needed to develop effective biomarkers or criteria for enabling earlier detection of GDM. Healthcare systems should promote the introduction of standardized diagnostic criteria, such as those recommended by the International Association of Diabetes and Pregnancy Study Groups, to ensure consistent identification and management of GDM [1].

Given the diversity of adverse outcomes, care models for pregnant women and neonates should incorporate individualized management strategies, including nutritional counseling, physical activity, and pharmacological interventions when needed [55]. Multidisciplinary teams consisting of obstetricians, endocrinologists, cardiologists, pediatricians, and mental health professionals are essential to addressing the diverse health outcomes associated with GDM. Postpartum monitoring is essential, given the strong associations between GDM and metabolic disorders such as Type 2 diabetes and NAFLD [25]. Routine glucose assessments, lifestyle interventions, and mental health evaluations can reduce long-term risks [56]. Pediatric follow-up should focus on early identification of obesity, hypertension, and developmental delays to improve long-term outcomes.

4.5 | Limitations

While this umbrella review provides valuable evidence on adverse health outcomes associated with GDM, several limitations should be acknowledged. First, the umbrella review is based entirely on existing meta-analyses, which may restrict the breadth of evidence considered [57]. Most included studies investigated GDM during pregnancy rather than pregestational diabetes mellitus (PGDM), although a few included both GDM and PGDM within their inclusion criteria [23, 41]. Consequently, due to heterogeneity in GDM definitions across the included meta-analyses and the inherent limitations of the umbrella review design, it was not possible to conduct a direct comparison between PGDM and GDM. Second, until the IADPSG introduced new diagnostic criteria in 2010, overt diabetes was not clearly distinguished from GDM [1]. As a result, studies conducted before 2010 or those adopting earlier diagnostic standards may have included individuals with pre-existing diabetes within the GDM group. Consequently, some neonatal complications might be attributable to prolonged maternal hyperglycemia rather than GDM specifically. Third, given the observational nature of the included studies, the identified associations do not explain causality. Although consistent associations were observed across multiple studies, the potential impact of confounders cannot be entirely ruled out, necessitating future studies to explore the underlying mechanisms and causality of each association [12, 57]. Fourth, while we aimed to focus on pregnant women with GDM or children exposed to maternal GDM compared to healthy controls, heterogeneity in group definitions across included meta-analyses and original studies must be recognized [18]. We only evaluated associations reported in published meta-analyses, which implies we might have missed or underestimated associations not assessed in other meta-analyses [11]. Lastly, the quality of the included meta-analyses was not directly evaluated, which may affect the reliability of our results [58]. Although well-established methodologies were employed, alternative statistical approaches could yield different results and certainty of the evidence, introducing potential bias [59].

5 | Conclusion

In this umbrella review with integrated meta-analyses, we investigated and mapped the hierarchy of evidence among 85 potential health outcomes associated with GDM in more than 363 million participants. Out of these, 49 were identified as significant health outcomes comorbid with GDM, and GDM was significantly associated with a range of maternal outcomes, neonatal outcomes, and pregnancy complications. Our findings provide a comprehensive overview and evidence for understanding adverse health outcomes related to GDM among pregnant women and their children and can help update guidelines or management of GDM. However, these associations do not necessarily imply causality, and future high-quality primary studies are needed to confirm these findings.

Funding

This work was supported by the United States of America National Institutes of Health National Institute on Aging (R01AG076704 to CJN) and the Ministry of Science and ICT (RS-2024-00509257 and IITP-2024-RS-2024-00438239 to DKY).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that supports the findings of this study are available in the supplementary material of this article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Studies excluded, with reason for exclusion. **Table S2:** AMSTAR 2 quality assessment of meta-analyses. **Table S3:** Reanalysis of estimated effect using Hartung–Knapp–Sidik–Jonkman (HS) method, and CE on association between gestational diabetes mellitus and its health outcomes. **Table S4:** Grading of recommendations assessment, development, and evaluation assessment of each association. **Figure S1:** Association between gestational diabetes mellitus and hypertension as a maternal outcome. **Figure S2:** Association between gestational diabetes mellitus and subclinical left ventricle systolic dysfunction as a maternal outcome. **Figure S3:** Association between gestational diabetes mellitus and overall subclinical atherosclerosis as a maternal outcome. **Figure S4:** Association between gestational diabetes mellitus and overall cardiovascular and cerebrovascular diseases as a maternal outcome. **Figure S5:** Association between gestational diabetes mellitus and overall cardiovascular diseases as a maternal outcome. **Figure S6:** Association between gestational diabetes mellitus and overall cerebrovascular diseases as a maternal outcome. **Figure S7:** Association between gestational diabetes mellitus and coronary artery diseases as a maternal outcome. **Figure S8:** Association between gestational diabetes mellitus and myocardial infarction as a maternal outcome. **Figure S9:** Association between gestational diabetes mellitus and heart failure as a maternal outcome. **Figure S10:** Association between gestational diabetes mellitus and angina pectoris as a maternal outcome. **Figure S11:** Association between gestational diabetes mellitus and overall stroke as a maternal outcome. **Figure S12:** Association between gestational diabetes mellitus and ischemic stroke as a maternal outcome. **Figure S13:** Association between gestational diabetes mellitus and hemorrhagic stroke as a maternal outcome. **Figure S14:** Association between gestational diabetes mellitus and venous thromboembolism as a maternal outcome. **Figure S15:** Association between gestational diabetes mellitus and postpartum NAFLD as a maternal outcome. NAFLD,

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nonalcoholic fatty liver disease. **Figure S16:** Association between gestational diabetes mellitus and type 2 diabetes mellitus as a maternal outcome. **Figure S17:** Association between gestational diabetes mellitus and metabolic syndrome during pregnancy as a maternal outcome. **Figure S18:** Association between gestational diabetes mellitus and postpartum metabolic syndrome as a maternal outcome. **Figure S19:** Association between gestational diabetes mellitus and perinatal depression as a maternal outcome. **Figure S20:** Association between gestational diabetes mellitus and antenatal depressive symptoms after a diagnosis of gestational diabetes mellitus as a maternal outcome. **Figure S21:** Association between gestational diabetes mellitus and antenatal depressive symptoms after a diagnosis of gestational diabetes mellitus as a maternal outcome. **Figure S22:** Association between gestational diabetes mellitus and postnatal depressive symptoms a maternal outcome. **Figure S23:** Association between gestational diabetes mellitus and postpartum depression a maternal outcome. **Figure S24:** Association between gestational diabetes mellitus and breast cancer a maternal outcome. **Figure S25:** Association between gestational diabetes mellitus and thyroid cancer a maternal outcome. **Figure S26:** Association between gestational diabetes mellitus and stomach cancer a maternal outcome. **Figure S27:** Association between gestational diabetes mellitus and liver cancer a maternal outcome. **Figure S28:** Association between gestational diabetes mellitus and colon cancer a maternal outcome. **Figure S29:** Association between gestational diabetes mellitus and colorectum cancer a maternal outcome. **Figure S30:** Association between gestational diabetes mellitus and ovary cancer a maternal outcome. **Figure S31:** Association between gestational diabetes mellitus and uterine cervix cancer as a maternal outcome. **Figure S32:** Association between gestational diabetes mellitus and pancreas cancer a maternal outcome. **Figure S33:** Association between gestational diabetes mellitus and brain cancer as a maternal outcome. **Figure S34:** Association between gestational diabetes mellitus and blood cancer as a maternal outcome. **Figure S35:** Association between gestational diabetes mellitus and leukemia cancer as a maternal outcome. **Figure S36:** Association between gestational diabetes mellitus and endometrium cancer as a maternal outcome. **Figure S37:** Association between gestational diabetes mellitus and skin cancer as a maternal outcome. **Figure S38:** Association between gestational diabetes mellitus and urological organs cancer as a maternal outcome. **Figure S39:** Association between gestational diabetes mellitus and infections during pregnancy as a maternal outcome. **Figure S40:** Association between gestational diabetes mellitus and chronic hepatitis B infection during pregnancy as a maternal outcome. **Figure S41:** Association between gestational diabetes mellitus and maternal rectovaginal colonization by group B Streptococcus as a maternal outcome. **Figure S42:** Association between gestational diabetes mellitus and delayed onset of lactogenesis as a maternal outcome. **Figure S43:** Association between gestational diabetes mellitus and atopic dermatitis or eczema as a neonatal outcome. **Figure S44:** Association between gestational diabetes mellitus and asthma as a neonatal outcome. **Figure S45:** Association between gestational diabetes mellitus and NAFLD as a neonatal outcome. **Figure S46:** Association between gestational diabetes mellitus and gestational diabetes mellitus as a neonatal outcome. **Figure S47:** Association between gestational diabetes mellitus and systolic blood pressure (mmHg) as a neonatal outcome. **Figure S48:** Association between gestational diabetes mellitus and BMI *z*-score as a neonatal outcome. BMI, body mass index. **Figure S49:** Association between gestational diabetes mellitus and fasting glucose level as a neonatal outcome. **Figure S50:** Association between gestational diabetes mellitus and autism spectrum disorder as a neonatal outcome. **Figure S51:** Association between gestational diabetes mellitus and attention deficit hyperactivity disorder as a neonatal outcome. **Figure S52:** Association between gestational diabetes mellitus and congenital health disease as a neonatal outcome. **Figure S53:** Association between gestational diabetes mellitus and atrial septal defect as a neonatal outcome. **Figure S54:** Association between gestational diabetes mellitus and ventricular septal defect as a neonatal outcome. **Figure S55:** Association between gestational diabetes mellitus and tetralogy of Fallot as a neonatal outcome. **Figure S56:** Association between gestational diabetes mellitus and general developmental defects of enamel as a neonatal outcome. **Figure S57:** Association between gestational diabetes mellitus and hypoplasia as a neonatal outcome. **Figure S58:** Association between gestational diabetes mellitus and molar incisor hypomineralization as a neonatal outcome. **Figure S59:** Association between gestational diabetes mellitus and hypomineralized primary second molars as a neonatal outcome. **Figure S60:** Association between gestational diabetes mellitus and developmental defects of enamel in the deciduous dentition as a neonatal outcome. **Figure S61:** Association between gestational diabetes mellitus and major congenital malformations as a neonatal outcome. **Figure S62:** Association between gestational diabetes mellitus and shoulder dystocia as a maternal adverse outcome at delivery. **Figure S63:** Association between gestational diabetes mellitus and emergent cesarean delivery as a maternal adverse outcome at delivery. **Figure S64:** Association between gestational diabetes mellitus and polyhydramnios as a maternal adverse outcome at delivery. **Figure S65:** Association between gestational diabetes mellitus and hypertensive disorders of pregnancy as a maternal adverse outcome at delivery. **Figure S66:** Association between gestational diabetes mellitus and induction of labor as a maternal adverse outcome at delivery. **Figure S67:** Association between gestational diabetes mellitus and cesarean delivery as a maternal adverse outcome at delivery. **Figure S68:** Association between gestational diabetes mellitus and gestational hypertension as a maternal adverse outcome at delivery. **Figure S69:** Association between gestational diabetes mellitus and preeclampsia as a maternal adverse outcome at delivery. **Figure S70:** Association between gestational diabetes mellitus and instrumental delivery as a maternal adverse outcome at delivery. **Figure S71:** Association between gestational diabetes mellitus and postpartum bleeding as a maternal adverse outcome at delivery. **Figure S72:** Association between gestational diabetes mellitus and neonatal respiratory distress syndrome as a neonatal adverse outcome at delivery. **Figure S73:** Association between gestational diabetes mellitus and neonatal hypoglycemia as a neonatal adverse outcome at delivery. **Figure S74:** Association between gestational diabetes mellitus and neonatal hyperbilirubinemia as a neonatal adverse outcome at delivery. **Figure S75:** Association between gestational diabetes mellitus and small for gestational age as a neonatal adverse outcome at delivery. **Figure S76:** Association between gestational diabetes mellitus and large for gestational age as a neonatal adverse outcome at delivery. **Figure S77:** Association between gestational diabetes mellitus and preterm birth as a neonatal adverse outcome at delivery. **Figure S78:** Association between gestational diabetes mellitus and low Apgar score as a neonatal adverse outcome at delivery. **Figure S79:** Association between gestational diabetes mellitus and admission to neonatal intensive care unit as a neonatal adverse outcome at delivery. **Figure S80:** Association between gestational diabetes mellitus and neonatal death as a neonatal adverse outcome at delivery. **Figure S81:** Association between gestational diabetes mellitus and perinatal mortality as a neonatal adverse outcome at delivery. **Figure S82:** Association between gestational diabetes mellitus and macrosomia as a neonatal adverse outcome at delivery. **Figure S83:** Association between gestational diabetes mellitus and low body weight as a neonatal adverse outcome at delivery. **Figure S84:** Association between gestational diabetes mellitus and neonatal jaundice as a neonatal adverse outcome at delivery. **Figure S85:** Association between gestational diabetes mellitus and stillbirth as a neonatal adverse outcome at delivery.

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