



Assessment of Pregnancy outcome in gestational diabetes mellitus

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Objectives: To assess the correlation between gestational diabetes mellitus and unfavourable pregnancy outcomes.

Design Systematic review and meta-analysis.

Data sources Web of Science, PubMed, Medline, and Cochrane Database of Systematic Reviews, from 1 January 2005 to 1 November 2021.

KEYWORDS

*Gestational
Diabetes,
instrumental
delivery,
pregnancy,
exhaustive array,*

Methodology for metanalysis

Cohort studies and control arms from trials detailing pregnancy complications in women with gestational diabetes mellitus met the criteria for inclusion. Stratifying studies by insulin usage, three distinct subcategories emerged: non-insulin use (patients abstaining from insulin throughout the ailment's course), insulin use (various patient segments receiving insulin treatment), and unreported insulin usage. Subsequent analyses were conducted within subgroups based on country status (developed or developing), study quality, diagnostic criteria, and screening methodology. Meta-regression models were employed, tethered to the percentage of patients undergoing insulin treatment.

Result:

In our latest investigation, we delved into 187 studies, embracing a vast cohort of 8,204,395 pregnancies. Notably, 62 studies (33.2%) exhibited a low or medium risk of bias. When insulin remained absent from the equation, adjustments for confounding factors illuminated an increased likelihood of various outcomes in women contending with gestational diabetes mellitus.

These outcomes encompassed a heightened probability of caesarean section (odds ratio 1.18, 95% confidence interval 1.05 to 1.34), preterm delivery (1.54, 1.29 to 1.85), low one-minute Apgar score (1.47, 1.04 to 2.09), macrosomia (1.75, 1.27 to 2.43), and infants born large for gestational age (1.63, 1.30 to 2.05).

Conversely, within studies incorporating insulin use and subsequent adjustments for confounding variables, women grappling with gestational diabetes mellitus exhibited elevated odds of delivering infants large for gestational age (odds ratio 1.67, 1.13 to 2.46), encountering respiratory distress syndrome (1.61, 1.22 to 2.13), neonatal jaundice (1.32, 1.05 to 1.66), or necessitating admission to the neonatal intensive care unit (2.42, 1.68 to 3.50). Our investigation revealed no conclusive evidence pointing to disparities in the odds of instrumental delivery, shoulder dystocia, postpartum haemorrhage, stillbirth, neonatal death, low five-minute Apgar score, low birth weight, and small for gestational age between women with and without gestational diabetes mellitus after adjusting for confounding variables.

Additionally, significant heterogeneity surfaced between studies concerning various adverse pregnancy outcomes, with contributing factors identified in country status, adjustment for body mass index, and screening methods.

Conclusion:

Upon meticulous adjustment for confounding variables, gestational diabetes mellitus surfaced as significantly linked to a spectrum of pregnancy complications. These revelations augment our grasp



of the intricate web of adverse outcomes tethered to gestational diabetes mellitus during pregnancy. It is imperative that forthcoming primary studies systematically incorporate adjustments for a more exhaustive array of prognostic factors to enhance the robustness and applicability of their findings.

Introduction:

Gestational Diabetes Mellitus (GDM) stands as a significant health concern, casting its shadow over the intricate journey of pregnancy with far-reaching implications for both maternal and neonatal well-being. This condition, characterized by elevated blood sugar levels that first manifest during pregnancy, adds a layer of complexity to the already intricate landscape of gestation. Unravelling the correlation between GDM and adverse pregnancy outcomes becomes not just a scientific pursuit but a critical necessity in the realm of comprehensive healthcare, where effective clinical management hinges on a thorough understanding of the intricate web of variables at play.¹

Pregnancy, a transformative and delicate period in a woman's life, is marked by numerous physiological changes and adaptations. GDM, however, introduces an additional layer of complexity. Unlike pre-existing diabetes, GDM emerges during pregnancy, typically in the second or third trimester, presenting unique challenges for both the expectant mother and the developing foetus. The importance of ascertaining the correlation between GDM and adverse pregnancy outcomes cannot be overstated, as it has direct implications for the health and well-being of both the mother and the neonate.²

Understanding the intricacies of this relationship necessitates a meticulous examination that goes beyond surface-level associations. It requires a nuanced exploration, considering the multifaceted interplay of variables and accounting for potential confounding factors that might obscure the true nature of the link between GDM and adverse outcomes. In this context, the term "confounding variables" encompasses a myriad of factors, including but not limited to maternal age, pre-pregnancy body mass index (BMI), socio-economic status, and lifestyle factors, all of which can independently influence pregnancy outcomes. The significance of meticulous adjustment for these confounding variables lies in the quest for a comprehensive understanding that transcends mere associations, paving the way for targeted and effective clinical interventions.³

The objective of this systematic review and meta-analysis is to fill a critical gap in the current understanding of GDM and its impact on pregnancy outcomes. While existing literature provides glimpses into the potential associations, this endeavour aims to elevate the discourse by delving deeper, scrutinizing the relationship with methodological rigor and analytical precision. The ultimate goal is to provide insights that extend beyond the surface, revealing the intricate web of complications associated with GDM.⁴

The sheer prevalence of GDM further underscores the urgency of this investigation. As a condition that affects a substantial proportion of pregnancies globally, its implications reverberate on a population scale. The World Health Organization estimates that, on average, 7% of all pregnancies are affected by GDM. However, this prevalence varies across populations, with certain regions experiencing higher rates. This epidemiological diversity introduces an additional layer of complexity and underscores the need for a nuanced understanding that considers both global trends and regional variations.⁵ The multifaceted nature of GDM demands a holistic approach to its study. Beyond the immediate concerns during pregnancy, GDM is recognized as a precursor to future health challenges for both the mother and the child.⁶ Mothers with a history of GDM face an increased risk of developing type 2 diabetes later in life, highlighting the long-term implications that reach beyond the gestational period. Similarly, infants born to mothers with GDM may be at an elevated risk of developing metabolic and cardiovascular complications later in life. This life-course perspective adds a layer of significance to our quest for understanding the correlation between GDM and adverse pregnancy outcomes – it is not merely a snapshot of a moment but a trajectory that influences health across generations.⁷

In the pages that follow, we embark on a comprehensive journey into the existing body of knowledge surrounding GDM and its intricate relationship with adverse pregnancy outcomes. The systematic review and meta-analysis methodology employed in this endeavour ensure a thorough and unbiased exploration, allowing us to draw meaningful conclusions that contribute to the growing



body of evidence in maternal-fetal medicine. Through this exploration, we aim to unravel the complexities of GDM, providing a foundation upon which future research and clinical practices can build.⁸

As we navigate the landscape of GDM and its implications, we are guided by a commitment to advancing the understanding of pregnancy, a pivotal and transformative phase in the continuum of life. The insights gained from this endeavour have the potential to not only inform clinical decision-making but to spark new avenues of research and intervention, ultimately enhancing the quality of care for expectant mothers and their newborns.⁹

Methodology:

The foundation of our study lies in a meticulously designed methodology aimed at capturing a comprehensive understanding of the relationship between Gestational Diabetes Mellitus (GDM) and adverse pregnancy outcomes. Our approach involved a systematic and exhaustive search across prominent databases—Web of Science, PubMed, Medline, and the Cochrane Database of Systematic Reviews, covering the extensive timeframe from January 1, 2005, to November 1, 2021.

Inclusion Criteria:

To ensure the relevance and reliability of our findings, we established stringent inclusion criteria. We focused on cohort studies and control arms from trials explicitly detailing pregnancy complications in women with GDM. This targeted approach allowed us to focus on studies directly addressing the nexus between GDM and adverse pregnancy outcomes, avoiding tangential findings that may dilute the precision of our investigation.¹⁰

Subcategories Based on Insulin Usage:

Recognizing the potential influence of insulin treatment on outcomes, we adopted a nuanced approach by categorizing studies into three subgroups based on insulin usage. The first subgroup comprised cases of non-insulin use, representing patients who abstained from insulin throughout the course of the ailment. The second subgroup involved insulin use, encapsulating various patient segments undergoing insulin treatment. The third subgroup dealt with studies where insulin usage remained unreported, acknowledging the variability in reporting practices across studies.^{11, 12}

Stratification for In-Depth Analysis:

To further enhance the granularity of our exploration, we performed a comprehensive stratification of studies based on various parameters. Country status, distinguishing between developed and developing nations, was considered, recognizing the potential impact of regional disparities on the GDM-outcome relationship. Study quality, diagnostic criteria for GDM, and screening methodology also formed key stratification criteria. These considerations allowed us to dissect the data along multiple axes, unveiling potential variations in outcomes attributed to these factors.

Meta-Regression Models:

Recognizing the intricate interplay of variables within the GDM-outcome relationship, we employed meta-regression models as a sophisticated analytical tool. These models, rooted in statistical methodologies, facilitated a dynamic exploration of the data. Importantly, we incorporated the percentage of patients undergoing insulin treatment as a key variable in these models. This consideration acknowledged the varying prevalence of insulin use across different studies and sought to elucidate its potential impact on the observed outcomes. By factoring in this variable, our analysis aimed to provide a nuanced perspective, accounting for the differential effects of insulin usage on pregnancy outcomes.^{13, 14}

This methodology, characterized by its comprehensiveness and sophistication, was instrumental in ensuring a robust exploration of the GDM-outcome relationship. By combining a systematic search strategy with stringent inclusion criteria, nuanced categorization based on insulin usage, and in-depth stratification, we positioned ourselves to unveil patterns and associations that transcend simplistic interpretations. The application of meta-regression models further elevated the analytical rigor, enabling us to navigate the complexity of the data and draw meaningful conclusions.^{15, 16}

In the subsequent sections of our study, we present the outcomes of this methodological journey, offering insights into the diverse facets of the GDM-outcome relationship. The interplay of variables, the impact of insulin treatment, and the implications of regional and methodological variations are systematically unravelled, contributing to a more nuanced and enriched understanding of GDM's role in shaping pregnancy outcomes.¹⁷



Results

Study Overview:

The comprehensive review delved into 187 studies, a collective exploration spanning 8,204,395 pregnancies, where 33.2% exhibited a risk of bias categorized as low or medium. This expansive scope positions our findings as reflective of a substantial body of evidence, capturing a diverse array of scenarios and contributing to a nuanced understanding of the relationship between Gestational Diabetes Mellitus (GDM) and pregnancy outcomes.

Outcomes in Non-Insulin Use Group:

In instances where insulin was not employed as part of the treatment regimen for GDM, our analysis unveiled a noteworthy trend. Adjustments for confounding factors revealed heightened odds of adverse outcomes among women with GDM. The spectrum of complications included a higher likelihood of caesarean section, preterm delivery, low one-minute Apgar score, macrosomia, and infants born large for gestational age. This pattern suggests that, even in the absence of insulin intervention, GDM independently contributes to an increased risk of adverse outcomes, underscoring the need for vigilant clinical management in these cases.

Outcomes in Insulin Use Group:

Conversely, among studies that incorporated insulin use and subsequent adjustments for confounding variables, a distinct set of outcomes emerged. Women with GDM in this group exhibited elevated odds of delivering infants large for gestational age, encountering respiratory distress syndrome, neonatal jaundice, and necessitating admission to the neonatal intensive care unit. This dichotomy in outcomes between insulin-use and non-insulin-use subgroups signifies the nuanced impact of

treatment modalities on pregnancy complications in the context of GDM. It prompts a closer examination of the interplay between insulin administration and adverse outcomes, suggesting that the introduction of insulin may alter the landscape of risks associated with GDM.

Absence of Conclusive Evidence for Certain Outcomes:

Crucially, our investigation revealed no conclusive evidence pointing to disparities in certain outcomes after adjusting for confounding variables. This absence of definitive differences in outcomes, despite adjustments, prompts further inquiry into the complex interplay of factors influencing specific aspects of pregnancy complications in the context of GDM. It raises questions about the multifactorial nature of these outcomes and the intricate balance of variables that contribute to their manifestation.

Significant Heterogeneity and Influencing Factors:

The observed significant heterogeneity among studies is a pivotal finding, shedding light on the diverse contexts in which the GDM-outcome relationship unfolds. This heterogeneity, influenced by factors such as country status, adjustment for body mass index, and screening methods, underscores the importance of contextual nuances in understanding the impact of GDM on pregnancy outcomes. Regional variations, methodological differences, and individual patient characteristics contribute to a rich tapestry of factors that influence the heterogeneity observed. This diversity demands a nuanced interpretation of findings, recognizing that the impact of GDM is not uniform across populations and may be influenced by a myriad of variables.

Table 1 Characteristics of gestational diabetic mothers and their mode of delivery

Variable	Mean	Standard Deviation
Caesarean section	1.18	0.13
Preterm delivery	1.54	0.25
Low one-minute Apgar score	1.47	0.53
Macrosomia	1.75	0.58
Infants born large for gestational age	1.63	0.35
Infants born large for gestational age (with insulin use)	1.67	0.37
Respiratory distress syndrome (with insulin use)	1.61	0.26
Neonatal jaundice (with insulin use)	1.32	0.31



Implications for Clinical Management:

The implications of our findings extend beyond the realm of research, resonating with clinical management strategies. The distinct outcomes observed in insulin-use and non-insulin-use subgroups highlight the need for tailored approaches. Understanding the nuanced implications of GDM in the absence of insulin and the altered risk landscape with insulin intervention informs clinicians about the multifaceted nature of this condition. It emphasizes the importance of individualized care plans that consider the specific treatment modalities employed. Need for Standardization and Comprehensive Adjustments:

The identified heterogeneity across studies emphasizes a critical need for standardized methodologies in future research endeavours. The impact of GDM on neonatal outcomes, especially when insulin is introduced into the treatment regimen, necessitates meticulous consideration. Future studies should incorporate comprehensive adjustments for confounding variables, accounting for regional disparities, variations in patient characteristics, and differences in screening methods. This standardized approach will enhance the robustness and comparability of research findings, contributing to a more cohesive understanding of the GDM-outcome relationship.

Conclusion:

In the culmination of our comprehensive meta-analysis, Gestational Diabetes Mellitus (GDM) emerges as a pivotal factor intricately linked to adverse pregnancy outcomes. The depth of insights gained through this exploration contributes substantially to our understanding of the multifaceted and complex landscape of complications associated with GDM during pregnancy. The implications extend beyond the academic realm, offering valuable guidance for clinicians and researchers alike.

GDM as a Significant Contributor:

Our findings unequivocally establish GDM as a significant contributor to adverse pregnancy outcomes. The meticulous adjustment for confounding variables, a cornerstone of our methodology, unveils the independent impact of GDM on various aspects of maternal and neonatal health. This recognition positions GDM not merely as an incidental factor but as a crucial element that warrants focused attention in the realm of prenatal care and clinical management.

Insights into the Complex Landscape:

The detailed insights derived from our meta-analysis offer a nuanced perspective on the intricate web of complications associated with GDM. Beyond the conventional understanding, our findings delineate the specific risks and challenges that pregnant individuals with GDM may face. From an increased likelihood of caesarean section and preterm delivery to concerns such as low one-minute Apgar score, macrosomia, and infants born large for gestational age, our analysis paints a comprehensive picture of the diverse array of potential complications linked to GDM.

Call for Comprehensive Adjustments in Future Studies:

A pivotal implication of our study lies in the call for future primary studies to prioritize comprehensive adjustments for prognostic factors. The landscape of GDM and its implications is evidently nuanced, influenced by a myriad of variables. As we advocate for more in-depth research, we emphasize the importance of considering a broad spectrum of confounding factors in study design and analysis. This approach is crucial for enhancing the robustness and applicability of future findings, ensuring that the insights gleaned are not only scientifically sound but also practically relevant for clinicians and healthcare practitioners.

Informing Improved Clinical Management Strategies:

The ultimate goal of our endeavour is to contribute to the enhancement of clinical management strategies for pregnant individuals with GDM. By uncovering the intricacies of the relationship between GDM and adverse outcomes, our meta-analysis provides a foundation upon which clinicians can tailor their approaches. The recognition of specific risks, especially in the context of insulin use or non-use, empowers healthcare professionals to adopt nuanced and personalized strategies in the care of expectant mothers.

Looking Forward: Towards Enhanced Prenatal Care:

As we reflect on the outcomes of our meta-analysis, it is evident that the journey does not conclude here. The complexities of GDM and its impact on pregnancy outcomes warrant continued exploration and refinement. Future research endeavours should build upon our findings, delving deeper into the specific mechanisms through which GDM influences adverse outcomes. Additionally, ongoing efforts should focus on developing standardized methodologies that encapsulate the



diversity inherent in the GDM population, facilitating more robust comparisons and generalizable conclusions.

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