Understanding the Link Between Gestational Diabetes and Intrauterine Growth Restriction: A Comprehensive Narrative Review

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ABSTRACT

Gestational diabetes is a condition that affects a substantial number of expectant mothers, with profound implications for maternal and fetal health. Among its complications, intrauterine growth restriction (IUGR) has garnered significant scientific attention. IUGR, characterized by impaired fetal growth, presents both immediate and long-term health risks. The relationship between gestational diabetes and IUGR has been a subject of extensive investigation, with studies exploring its nature and strength. IUGR, arising from gestational diabetes, is a matter of growing concern due to its potential impacts on both mothers and infants. This narrative review aims to consolidate existing knowledge on this topic, discerning the connection between gestational diabetes and IUGR.
We provide a detailed comparison of IUGR and macrosomia (excessive fetal growth) in patients with gestational diabetes, highlighting the variations in prevalence, risk factors, management, and maternal and neonatal implications. While IUGR is less common (around 5%-10%), macrosomia occurs more frequently (20%-40% or higher) in gestational diabetes cases. The balance between preventing these conditions is a key challenge, requiring vigilant monitoring of blood glucose levels during pregnancy.

Keywords: Intrauterine Growth Restriction; IUGR; Gestational Diabetes.

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Introduction

Gestational diabetes is a condition that affects a significant number of expectant mothers and carries a multitude of potential implications for both maternal and fetal health. Among the complications associated with gestational diabetes, intrauterine growth restriction (IUGR) has emerged as a subject of intense scientific scrutiny. IUGR is a condition in which the developing fetus fails to achieve the expected growth milestones during pregnancy, a circumstance that can have profound consequences for both immediate and long-term health. The link between gestational diabetes and IUGR has been the focus of extensive investigation, with various studies aiming to elucidate the nature and strength of this association (1-5).

The term "intrauterine growth restriction" paints a vivid picture of a fetus not thriving as anticipated. It suggests a complex interplay of factors that hinder the fetus from achieving the growth milestones that are typically expected during pregnancy. A developing baby's growth is a finely orchestrated dance of biological processes, and any disruption to this symphony can result in IUGR, a condition that warrants meticulous investigation (6-8).

IUGR, as an outcome of gestational diabetes, has captured the attention of researchers and healthcare professionals alike due to its potential to affect both the mother and the child. A comprehensive understanding of this relationship is pivotal for designing effective strategies to mitigate the risks and complications associated with gestational diabetes (9-11).

Numerous research endeavors have been undertaken to unravel the association between gestational diabetes and IUGR. This review aims to present a summary of the existing body of knowledge on this topic. By examining and analyzing the findings of multiple studies, this review seeks to discern the nature and strength of the relationship between gestational diabetes and IUGR, unraveling the intricate threads that connect them.

Macrosomia or IUGR in patients with gestational diabetes:

The rates of macrosomia and intrauterine growth restriction (IUGR) in pregnancies complicated by gestational diabetes mellitus (GDM) can vary based on several factors, including the population studied, the diagnostic criteria for GDM, and the level of glycemic control. It's important to note that these rates are not static and may change over time as diagnostic and management guidelines evolve. Additionally, the prevalence can vary by region and population (12). IUGR may be more common in GDM cases where glycemic control is extremely tight and maternal glucose levels are too low. It's important to note that there is a trade-off between preventing macrosomia and avoiding IUGR when managing GDM. Clinicians aim to strike a balance through careful monitoring and management of blood glucose levels during pregnancy (13).

Pregnant individuals with GDM should receive close medical supervision, including dietary counseling, blood glucose monitoring, and, in some cases, insulin therapy. Achieving and maintaining target blood glucose levels can help reduce the risk of both macrosomia and IUGR (14). It's also worth mentioning that early and consistent prenatal care, as well as adherence to healthcare provider recommendations, can have a significant impact on reducing adverse outcomes associated with GDM. Pregnant individuals should work closely with their healthcare team to manage their condition and minimize the risks of complications like macrosomia and IUGR. Table 1 compares IUGR and macrosomia during pregnancy (15).

Table 1. Comparison of IUGR and macrosomia in GDM patients.

Aspect	IUGR (Intrauterine Growth Restriction)	Macrosomia
Definition	A condition where the fetus fails to achieve the expected growth rate during pregnancy.	The birth of a larger-than-average baby.
Prevalence in GDM	Typically lower, approximately 5% to 10%.	More common, ranging from 20% to 40% or more.
Risk Factors	- Tight glycemic control with excessively low blood glucose levels.	- Poorly controlled GDM with consistently elevated blood glucose levels.
Management Challenges	May require careful monitoring to ensure that maternal glucose levels do not drop too low, affecting fetal growth.	Involves controlling and maintaining maternal blood glucose levels within target ranges to prevent excessive fetal growth.
Maternal Implications	Typically lower risk of complications related to giving birth to a larger baby (e.g., birth injuries).	Increased risk of labor and delivery complications, such as shoulder dystocia.
Neonatal Implications	-Increased risk of neonatal morbidity and mortality.	- Increased risk of birth injuries.

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	- May require additional medical care after birth.	- Potential need for interventions during delivery.
Gestational Care Focus	Balancing maternal glucose levels to promote fetal growth while avoiding excessive weight gain.	Emphasizing strict glycemic control to prevent excessive fetal growth.
Monitoring and Testing	May require additional fetal monitoring and ultrasounds to assess growth.	Monitoring maternal glucose levels and fetal growth throughout pregnancy.
Long-Term Health Impact	Associated with a lower risk of neonatal complications, but potential for long-term health consequences for the small baby.	Increased risk of neonatal complications but less potential for long-term health consequences.

IUGR a risk factor of gestational diabetes:

An essential study by Thekkedathu in 2015 made a significant discovery. This study found a clear and statistically significant association between gestational diabetes mellitus and IUGR. In essence, it suggests that women diagnosed with gestational diabetes face an elevated risk of developing IUGR compared to those who do not experience this condition (16).

Nisar, in a subsequent study in 2021, reaffirmed these findings by asserting that maternal diabetes, inclusive of gestational diabetes, is intricately linked to the occurrence of IUGR. These findings not only underscore the importance of diagnosing and managing gestational diabetes effectively but also shed light on the potential prevention strategies for IUGR (17).

Furthermore, the relationship between gestational diabetes and IUGR appears to be more intricate than initially meets the eye. A pivotal study conducted by Simmons and colleagues in 2001, although based on experiments with rats, provided groundbreaking insights. This research indicated that IUGR might not be a one-way street. Instead, it hinted at a bidirectional relationship involving gestational diabetes, IUGR, and the subsequent development of diabetes. The study also illuminated the mechanisms involved, showing that IUGR might lead to impaired glucose tolerance, ultimately progressing to overt diabetes due to the incapacity of beta cells in the pancreas to compensate for secretory defects and insulin resistance. These findings underscore the critical importance of early detection and management of gestational diabetes to forestall the long-term health implications for both the mother and the infant (17).

However, it's essential to recognize that gestational diabetes is not the sole risk factor for IUGR. The study by Thekkedathu identified a range of maternal risk factors significantly associated with IUGR, including chronic hypertension, pre-eclampsia, low socioeconomic status, anemia, and hypothyroidism. This suggests that a holistic approach to prenatal care is paramount, as the reduction of IUGR incidence necessitates the identification and management of these risk factors (16, 18).

Moreover, the consequences of IUGR extend beyond the perinatal period. A study by Novitskaya et al. in 2011 shed light on the long-term effects of late gestational placental insufficiency, a common cause of asymmetric IUGR. Their research demonstrated that this condition is associated with an increased incidence of diabetes, cardiovascular disease, and renal disease in adults, painting a sobering picture of the lasting impact of IUGR (19).

Pathophysiology of gestational diabetes and IUGR

pathophysiology of how gestational diabetes leads to intrauterine growth restriction (IUGR) is complex and multifactorial. While it's not fully understood, several mechanisms have been proposed based on research and clinical observations (20). Elevated blood glucose levels in gestational diabetes lead to increased glucose transport across the placenta to the fetus. While glucose is essential for fetal growth, excessive levels can overwhelm the fetal pancreas and lead to hyperinsulinemia. This excess insulin promotes fetal growth by stimulating anabolism, but it also causes maternal nutrients, including glucose, to be diverted to the fetus (21).

Moreover, increased insulin levels in the fetus can cause increased fat deposition and a corresponding increase in the size of fat cells. This fat accumulation can lead to "visceral adiposity," which refers to the excess storage of fat in the abdominal area, including around internal organs. Visceral adiposity can compromise placental function, leading to reduced oxygen and nutrient delivery to the fetus (22).

It should be noted that the placenta plays a critical role in fetal development by facilitating the exchange of nutrients and oxygen between the mother and the fetus. In gestational diabetes, the placenta may become compromised due to factors such as oxidative stress and inflammation caused by chronic hyperglycemia. This placental dysfunction can result in reduced nutrient and oxygen delivery to the fetus, impeding its growth (23).

Also, chronic hyperglycemia in the mother can lead to vascular and microvascular changes that affect placental blood flow. These changes include endothelial dysfunction, increased vascular resistance, and impaired vasodilation. Consequently, the placental blood supply may be compromised, reducing the delivery of vital nutrients and oxygen to the developing fetus (24).

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In response to maternal hyperglycemia, the fetus often increases its production of insulin. This enhanced fetal insulin secretion aims to regulate glucose metabolism, but it also promotes growth. The constant demand for insulin, along with the metabolic stress imposed by hyperglycemia, can strain the fetal pancreas and other vital organs, potentially leading to IUGR (25).

Furthermore, Gestational diabetes leads to hormonal and metabolic imbalances, including increased levels of insulin, insulin-like growth factor (IGF), and other growth-promoting hormones. These imbalances can overstimulate fetal growth, which, when combined with other factors, can eventually lead to IUGR (12). Interestingly, chronic inflammation, often seen in individuals with diabetes, can lead to systemic and placental inflammation. This inflammatory milieu can have a detrimental impact on fetal growth by disrupting placental function and impairing nutrient and oxygen transport to the fetus (14).

The pathophysiology of how gestational diabetes leads to IUGR is undoubtedly multifaceted. It involves a delicate interplay of factors, including maternal hyperglycemia, fetal hyperinsulinemia, placental dysfunction, vascular changes, and the resultant metabolic and hormonal imbalances. The overall outcome is a fetus that experiences both excessive growth (macrosomia) and restricted growth (IUGR), depending on the stage and severity of the gestational diabetes, the adequacy of glycemic control, and various individual factors. Managing gestational diabetes through proper medical care, including glucose monitoring and insulin therapy when necessary, is critical to minimizing the risk of IUGR and promoting optimal fetal growth (15)

Conclusion

In summary, the cumulative body of evidence strongly suggests that a substantial association exists between gestational diabetes and IUGR. Women afflicted by gestational diabetes face a heightened risk of IUGR, and this condition, in turn, appears to be a potential precursor to the development of type 2 diabetes later in life. These findings emphasize the paramount importance of vigilant monitoring and effective management of gestational diabetes to mitigate the risk of IUGR and its associated complications. As we traverse the landscape of these studies and their implications, we aim to provide healthcare professionals, researchers, and policymakers with a comprehensive understanding of the intricate relationship between gestational diabetes and IUGR, with far-reaching consequences for maternal and child health, thereby facilitating more informed decisions and enhancing the quality of clinical care.

Ethical Issue

There was no ethical issue in this review.

Conflict of Interests

There was no conflict of interest in this study.

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Reference:

١. Davenport MH, Meah VL, Ruchat SM, Davies GA, Skow RJ, Barrowman N, et al. Impact of prenatal exercise on neonatal and childhood outcomes: a systematic review and meta-analysis. Br J Sports Med. 2018;52(21):1386-96.

٢. Mao Y, Zhang C, Wang Y, Meng Y, Chen L, Dennis CL, et al. Association Between Paternal Age and Birth Weight in Preterm and Full-Term Birth: A Retrospective Study. Front Endocrinol (Lausanne). 2021;12:706369.

٣. Maulik D. Fetal growth restriction and macrosomia: an apparently intriguing combination. J Matern Fetal Neonatal Med. 2003;13(3):145-6.

٤. Monk D, Moore GE. Intrauterine growth restriction--genetic causes and consequences. Semin Fetal Neonatal Med. 2004;9(5):371-8.

٥. Romero R, Kingdom J, Deter R, Lee W, Vintzileos A. Fetal Growth: Evaluation and Management. Am J Obstet Gynecol. 2018;218(2s):S608.

٦. Dumolt JH, Powell TL, Jansson T. Placental Function and the Development of Fetal Overgrowth and Fetal Growth Restriction. Obstet Gynecol Clin North Am. 2021;48(2):247-66.

٧. Hong M, Liang F, Zheng Z, Chen H, Guo Y, Li K, et al. Weight gain rate in the second and third trimesters and fetal growth in women with gestational diabetes mellitus: a retrospective cohort study. BMC Pregnancy Childbirth. 2022;22(1):424.

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٨. Kajdy A, Modzelewski J, Herman K, Muzyka-Placzynska K, Rabijewski M. Growth charts and prediction of abnormal growth - what is known, what is not known and what is misunderstood. Ginekol Pol. 2019;90(12):717-21.

٩. Meek CL, Corcoy R, Asztalos E, Kusinski LC, López E, Feig DS, et al. Which growth standards should be used to identify large- and small-for-gestational age infants of mothers with type 1 diabetes? A pre-specified analysis of the CONCEPTT trial. BMC Pregnancy Childbirth. 2021;21(1):96.

١٠. Sabri A, Lai D, D'Silva A, Seeho S, Kaur J, Ng C, et al. Differential placental gene expression in term pregnancies affected by fetal growth restriction and macrosomia. Fetal Diagn Ther. 2014;36(2):173-80.

١١. Sibiak R, Jankowski M, Gutaj P, Mozdziak P, Kempisty B, Wender-Ożegowska E. Placental Lactogen as a Marker of Maternal Obesity, Diabetes, and Fetal Growth Abnormalities: Current Knowledge and Clinical Perspectives. J Clin Med. 2020;9.(4).

١٢. Lewandowska M. Maternal Obesity and Risk of Low Birth Weight, Fetal Growth Restriction, and Macrosomia: Multiple Analyses. Nutrients. 2021;13.(4).

١٣. Obesity in Pregnancy: ACOG Practice Bulletin, Number 230. Obstet Gynecol. 2021;137(6):e128-e44.

١٤. Mistry SK, Das Gupta R, Alam S, Kaur K, Shamim AA, Puthussery S. Gestational diabetes mellitus (GDM) and adverse pregnancy outcome in South Asia: A systematic review. Endocrinol Diabetes Metab. 2021;4(4):e00285.

١٥. Venkatesh KK, Lynch CD, Powe CE, Costantine MM, Thung SF, Gabbe SG, et al. Risk of Adverse Pregnancy Outcomes Among Pregnant Individuals With Gestational Diabetes by Race and Ethnicity in the United States, 2014-2020. Jama. ٢٠٢٢;٣٢٧(١٤):١٣٥٦-٦٧.

١٦. Thekkedathu VC. Maternal and Placental Risk Factors Associated With Intrauterine Growth Restriction and the Perinatal Outcomes. Journal of South Asian Federation of Obstetrics and Gynaecology. 2015.

١٧. Nisar S. Doppler evaluation of IUGR babies at a tertiary hospital. Hypertension.5:5.

١٨. Gao X, Lin S, Jiang P-Y, Ye MY, Chen W, Hu CX, et al. Gestational Cholestasis Induced Intrauterine Growth Restriction Through Triggering IRE1α-mediated Apoptosis of Placental Trophoblast Cells. The Faseb Journal. 2022.

١٩. Novitskaya T, Baserga M, Caestecker MPd. Organ-Specific Defects in Insulin-Like Growth Factor and Insulin Receptor Signaling in Late Gestational Asymmetric Intrauterine Growth Restriction in Cited1 Mutant Mice. Endocrinology. 2011.

٢٠. Bedell S, Hutson J, de Vrijer B, Eastabrook G. Effects of Maternal Obesity and Gestational Diabetes Mellitus on the Placenta: Current Knowledge and Targets for Therapeutic Interventions. Curr Vasc Pharmacol. 2021;19(2):176-92.

٢١. Brown HL, Smith GN. Pregnancy Complications, Cardiovascular Risk Factors, and Future Heart Disease. Obstet Gynecol Clin North Am. 2020;47(3):487-95.

٢٢. Damhuis SE, Ganzevoort W, Gordijn SJ. Abnormal Fetal Growth: Small for Gestational Age, Fetal Growth Restriction, Large for Gestational Age: Definitions and Epidemiology. Obstet Gynecol Clin North Am. 2021;48(2):267-79.

٢٣. Fasoulakis Z, Koutras A, Antsaklis P, Theodora M, Valsamaki A, Daskalakis G, et al. Intrauterine Growth Restriction Due to Gestational Diabetes: From Pathophysiology to Diagnosis and Management. Medicina (Kaunas). 2023;59.(6).

٢٤. Gantenbein KV, Kanaka-Gantenbein C. Highlighting the trajectory from intrauterine growth restriction to future obesity. Front Endocrinol (Lausanne). 2022;13:1041718.

٢٥. Joo EH, Kim YR, Kim N, Jung JE, Han SH, Cho HY. Effect of Endogenic and Exogenic Oxidative Stress Triggers on Adverse Pregnancy Outcomes: Preeclampsia, Fetal Growth Restriction, Gestational Diabetes Mellitus and Preterm Birth. Int J Mol Sci. 2021;22.(18).

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