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The Impact of Gestational Diabetes Mellitus on the Physical Development of Offspring During Infancy and Early Childhood

Yujie Tang[1], Yang Mi[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Department of Obstetrics and Gynecology, Northwest Women and Children's Hospital, Xi'an 710061, Shaanxi, China
**Correspondence Author*

Abstract: ***Gestational Diabetes Mellitus (GDM) is a glucose intolerance disorder that arises or is first diagnosed during pregnancy in women without a prior history of diabetes. With the global rise in obesity and type 2 diabetes, the prevalence of GDM continues to increase, posing serious threats to maternal and child health. Evidence shows that intrauterine exposure to maternal hyperglycemia can predispose offspring to obesity, glucose intolerance, and metabolic diseases later in life. This review summarizes the impact of GDM on offspring birth outcomes, growth trajectories during infancy and early childhood, explores the underlying biological mechanisms, and discusses research limitations and future perspectives.***

Keywords: Gestational Diabetes Mellitus, Physical Development, Infancy and Early Childhood, Type 2 diabetes**.**

1. Introduction

Gestational Diabetes Mellitus (GDM) refers to abnormal glucose tolerance that develops or is first detected during pregnancy in women without previous diabetes [1,2]. It is one of the most common and serious pregnancy complications. With the continuous global rise in obesity and type 2 diabetes, the prevalence of GDM has increased sharply, making it a critical public health concern [3,4].

In China, the prevalence of GDM has risen significantly, especially following the implementation of the "two-child policy," and may continue to increase in the future. Globally, GDM affects approximately 16.5% of pregnancies [1], with around 18 million newborns annually exposed to maternal hyperglycemia [4].

GDM adversely affects both mothers and offspring. For mothers, it increases the risk of preeclampsia, cesarean section, cardiovascular disease, and type 2 diabetes. For offspring, exposure to intrauterine hyperglycemia increases the risk of obesity, impaired glucose tolerance, type 2 diabetes, metabolic syndrome, and cardiovascular disease throughout life [1-6].

These intergenerational effects align with the Developmental Origins of Health and Disease (DOHaD) theory, which proposes that early-life environmental exposures—especially nutritional factors—can "program" physiological and metabolic responses, shaping adult health outcomes [7,8].

Since early childhood (0–3 years) represents a critical window for rapid growth and developmental plasticity, it is also a key period for the origins of obesity and metabolic disorders. This review summarizes the effects of GDM on birth outcomes, early growth trajectories, and biological mechanisms, while highlighting research limitations and directions for future study.

2. Effects of GDM on Offspring Birth Outcomes

2.1 Birth Weight (Low Birth Weight vs. Macrosomia)

Macrosomia (birth weight ≥ 4000 g) is a hallmark of GDM-related outcomes. Silva et al. (2024) [9] reported that 30% of macrosomic infants were born to mothers with GDM. The mechanism involves maternal hyperglycemia leading to excessive transplacental glucose transfer, stimulating fetal pancreatic β-cell proliferation and hyperinsulinemia, which in turn promotes fat deposition and somatic overgrowth [1].

Studies have consistently shown a strong correlation between GDM and macrosomia [10,11]. However, some cases of GDM are associated with low birth weight (LBW) due to placental insufficiency or preterm birth resulting from poor glycemic control [8,9]. Thus, GDM may have heterogeneous effects on fetal growth depending on maternal BMI, glucose control, gestational weight gain, and comorbidities. Early diagnosis and management of GDM can significantly reduce macrosomia rates and adverse neonatal outcomes [12,13].

2.2 Birth Length and Head Circumference

GDM may also influence other physical indices such as birth length and head circumference. Zhang (2019) [14] found that neonates born to GDM mothers had higher birth weights and lengths compared with controls ($P<0.05$), consistent with the trend of macrosomia. However, Wang et al. (2019) [15] observed no significant difference in head circumference or length, suggesting that GDM mainly promotes fat accumulation rather than skeletal or cranial growth.

These inconsistencies across studies likely arise from variations in diagnostic criteria, glycemic control, and population characteristics, underscoring the need for comprehensive evaluation using multiple anthropometric indicators.

2.3 Neonatal Physical and Metabolic Abnormalities

Beyond weight and size abnormalities, infants of GDM mothers often present with neonatal hypoglycemia, respiratory distress syndrome, polycythemia, and hyperbilirubinemia [9,11]. These complications result from persistent fetal hyperinsulinemia following the sudden removal of maternal glucose supply at birth.

Macrosomic infants are at particular risk of shoulder dystocia, birth trauma, and low Apgar scores [9]. Severe neonatal complications can disrupt early nutrition (e.g., breastfeeding) and influence subsequent growth trajectories.

3. Effects of GDM on Physical Growth During Infancy and Early Childhood (0–3 Years)

3.1 Growth Trajectories After Birth

Multiple studies have reported that GDM offspring exhibit accelerated postnatal growth. Zhang (2019) [14] and Wang et al. (2019) [15] found that infants born to GDM mothers had significantly higher body weight and BMI during the first 12 months of life compared with controls. Similarly, Qiao et al. (2023) [16] demonstrated that at age 3, the prevalence of overweight and obesity was significantly higher in GDM offspring, with maternal GDM being an independent risk factor.

This early “catch-up” or “overgrowth” pattern has been linked to increased risks of obesity and metabolic syndrome later in life [3,8].

3.2 Growth Heterogeneity and Contributing Factors

Although overgrowth is common, not all GDM offspring follow this pattern. Some exhibit growth restriction, particularly in cases with poor maternal glycemic control or comorbid complications [10]. Heterogeneity in growth trajectories may be attributed to maternal glucose control, obesity, treatment type, and feeding practices. Understanding this variability is essential for identifying high-risk subgroups and implementing individualized interventions.

3.3 Influence of Gender and Feeding Practices

Infant feeding practices and sex differences also modulate the effects of GDM exposure. Studies have shown that breastfeeding may attenuate rapid weight gain and improve metabolic programming [17]. Conversely, formula feeding may exacerbate postnatal overgrowth. Moreover, environmental exposures may interact with sex-specific factors to influence physical development trajectories [18].

4. Possible Biological Mechanisms

4.1 Fetal Overnutrition and Insulin Dysregulation

The central pathophysiology of GDM involves maternal hyperglycemia, which increases transplacental glucose transfer, leading to fetal hyperinsulinemia [1,3,11]. Insulin acts as a growth factor, stimulating adipogenesis and somatic growth. Chronic intrauterine exposure to excess glucose and lipids results in fetal overnutrition and permanent changes in insulin sensitivity, predisposing offspring to early obesity and insulin resistance [5,18].

4.2 Inflammation, Oxidative Stress, and Placental Dysfunction

GDM is characterized by chronic low-grade inflammation and oxidative stress within maternal and placental tissues [19-21]. Elevated reactive oxygen species (ROS) and inflammatory mediators such as IL-1β and TLR pathways impair placental function, altering nutrient transport and hormone secretion [21,22]. This dysfunction disrupts fetal nutrient balance and contributes to abnormal growth and metabolic regulation.

4.3 DOHaD Theory and Epigenetic Regulation

According to the DOHaD theory, intrauterine environmental stressors can permanently alter fetal physiology through epigenetic modifications, including DNA methylation, histone modification, and non-coding RNA regulation [23-25]. Studies have demonstrated altered methylation patterns in metabolic genes in the placentas, cord blood, and peripheral blood of GDM offspring [6,24]. These changes may mediate long-term metabolic risks associated with intrauterine hyperglycemia.

4.4 Metabolic Programming and Gut Microbiota

GDM-induced metabolic programming affects multiple fetal organs such as the pancreas, liver, muscle, and adipose tissue [18,25]. Excessive insulin stimulation may initially promote β-cell hyperplasia but later impair function, contributing to insulin resistance [5]. Emerging evidence also suggests that GDM alters the establishment of the infant gut microbiome, influencing metabolic health and growth patterns postnatally [26].

5. Current Limitations and Challenges

5.1 Heterogeneity in Study Design

Existing studies vary greatly in design—retrospective, cross-sectional, and prospective cohort studies—with inconsistent sample sizes and follow-up durations. Small-scale or short-term studies lack statistical power to detect subtle effects [13,14,16]. Large, well-designed longitudinal cohorts (e.g., the Hokkaido Birth Cohort) are needed to clarify developmental trajectories [18].

5.2 Inadequate Control of Confounding Factors

Maternal obesity, gestational weight gain, socioeconomic status, and feeding practices are significant confounders that are often not adequately controlled [10,15,16,17,27]. Maternal pre-pregnancy obesity, for example, is both a risk factor for GDM and for offspring obesity. Future studies should collect detailed maternal and postnatal data to isolate the independent effects of GDM exposure.

5.3 Inconsistent Measurement Standards

Differences in national or regional growth standards (e.g.,

WHO vs. local reference charts) complicate comparisons across studies. Standardization of anthropometric indices and outcome definitions (e.g., overweight, obesity) is essential for reliable meta-analyses and global comparisons.

6. Future Directions

6.1 Strengthen Longitudinal Cohort Studies

Future research should employ large-scale, long-term prospective cohorts starting from early pregnancy or preconception, systematically collecting maternal, perinatal, and offspring data. Continuous follow-up into adolescence and adulthood will help elucidate the long-term health implications of early growth trajectories [8,18].

6.2 Evaluate Interventional Approaches

Few randomized controlled trials (RCTs) have assessed whether strict glycemic control or lifestyle interventions during pregnancy can modify offspring growth and metabolic outcomes. More intervention studies are needed to provide evidence for optimizing GDM management and reducing offspring health risks [12,13,27].

6.3 Integrate Multi-Omics Approaches

Integrating metabolomics, epigenomics, and microbiome analyses can reveal molecular networks underlying GDM-induced developmental programming [6,18,23,24,26]. These approaches may identify biomarkers for early risk assessment and potential therapeutic targets.

6.4 Establish Regional Birth Cohorts and Follow-up Systems

Given regional differences in GDM prevalence and healthcare infrastructure, establishing standardized, region-specific birth cohorts with long-term follow-up is essential [18]. Such systems should incorporate periodic growth assessments, lifestyle data, and biological sampling to facilitate research and early intervention for high-risk children [10].

7. Conclusion

GDM profoundly affects both short-term and long-term offspring outcomes. It increases the incidence of macrosomia, neonatal hypoglycemia, and accelerated BMI growth during early childhood. These outcomes reflect intrauterine metabolic programming driven by hyperglycemia, hyperinsulinemia, inflammation, and oxidative stress [7].

Despite significant progress, research remains limited by design heterogeneity, uncontrolled confounders, and inconsistent growth standards. Future studies should focus on rigorous longitudinal designs, intervention trials, and multi-omics approaches to elucidate mechanisms and guide prevention strategies.

Recognizing GDM as a key determinant of offspring metabolic health emphasizes the importance of standardized GDM management, early screening, and personalized lifestyle guidance for at-risk children to mitigate adverse long-term consequences [4,10].

References

[1] Plows J F, Stanley J L, Baker P N, et al. The Pathophysiology of Gestational Diabetes Mellitus [J]. International Journal of Molecular Sciences, 2018, 19(11): 3342.

[2] Alejandro E U, Mamerto T P, Chung G, et al. Gestational Diabetes Mellitus: A Harbinger of the Vicious Cycle of Diabetes [J]. International Journal of Molecular Sciences, 2020, 21(14): 5003.

[3] Sweeting A, Wong J, Murphy H R, et al. A Clinical Update on Gestational Diabetes Mellitus [J]. Endocrine Reviews, 2022, 43(5): 763-793.

[4] Alum E U, Ugwu O P C, Obeagu E I. Beyond Pregnancy: Understanding the Long-Term Implications of Gestational Diabetes Mellitus [J]. INOSR Scientific Research, 2024, 11(1): 63-71.

[5] Lowe W L, Scholtens D M, Kuang A, et al. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): Maternal Gestational Diabetes Mellitus and Childhood Glucose Metabolism [J]. Diabetes Care, 2019, 42(3): 372-380.

[6] Al Bekai E, Beaini C E, Kalout K, et al. The Hidden Impact of Gestational Diabetes: Unveiling Offspring Complications and Long-Term Effects [J]. Life, 2025, 15(3): 440.

[7] Kwon E J, Kim Y J. What is Fetal Programming? A Lifetime Health Is Under the Control of In Utero Health [J]. Obstetrics & Gynecology Science, 2017, 60(6): 506.

[8] Fall C H D, Kumaran K. Metabolic Programming in Early Life in Humans [J]. Philosophical Transactions of the Royal Society B: Biological Sciences, 2019, 374(1770): 20180123.

[9] Sousa K S, Leite H V, Corrêa M D, et al. Prevalence of Macrosomic Newborns and Maternal and Neonatal Complications in a High-Risk Maternity [J]. Revista Brasileira de Ginecologia e Obstetrícia, 2024, 46.

[10] Jiang X, Guo B, Wei Y, et al. Effect of Gestational Diabetes Mellitus on Offspring Physical Development [J]. Chinese Journal of Child Health, 2016(07): 709-711+778.

[11] Mitanchez D. Neonatal Complications Pediatricians Should Be Aware of in Case of Maternal Gestational Diabetes [J]. World Journal of Diabetes, 2015, 6(5): 734.

[12] Simmons D, Immanuel J, Hague W M, et al. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy [J]. New England Journal of Medicine, 2023, 388(23): 2132-2144.

[13] Zhang Q, Su L. Effect of Dietary and Exercise Intervention during Pregnancy on the Incidence of Gestational Diabetes Mellitus and Pregnancy Outcomes [J]. Hebei Medical Journal, 2017(03): 475-477.

[14] Zhang Y. Effect of Gestational Diabetes Mellitus on Infant Physical Development and Glucose Metabolism [J]. Journal of Clinical Traditional Chinese Medicine, 2019(08): 1494-1496.

[15] Wang Y, Liu G, Ou P, et al. Physical and Cognitive Development of Offspring of Mothers with Gestational Diabetes Mellitus in Fuzhou and Influencing Factors [J]. Chinese Journal of Maternal and Child Health, 2019(02): 5-9.

[16] Qiao Y, Wang Y, Cui Z, et al. Effect of Gestational Diabetes Mellitus on Physical Development and Insulin Resistance in Offspring at 3 Years of Age [J]. Anhui Medical Journal, 2023(04): 394-398.
[17] Huo Z, Du K, Li L, et al. Effects of Different Feeding Methods on Physical Development of Infants at 6–18 Months [J]. Journal of Medical Research, 2009(10): 61-63.
[18] Kishi R, Kobayashi S, Ikeno T, et al. Ten Years of Progress in the Hokkaido Birth Cohort Study on Environment and Children's Health: Cohort Profile—Updated 2013 [J]. Environmental Health and Preventive Medicine, 2013, 18(6): 429-450.
[19] Phoswa W N, Khaliq O P. The Role of Oxidative Stress in Hypertensive Disorders of Pregnancy and Gestational Diabetes Mellitus [J]. Oxidative Medicine and Cellular Longevity, 2021, 2021(1).
[20] Saucedo R, Ortega-Camarillo C, Ferreira-Hermosillo A, et al. Role of Oxidative Stress and Inflammation in Gestational Diabetes Mellitus [J]. Antioxidants, 2023, 12(10): 1812.
[21] Zgutka K, Tkacz M, Tomasiak P, et al. Gestational Diabetes Mellitus-Induced Inflammation in the Placenta via IL-1β and Toll-like Receptor Pathways [J]. International Journal of Molecular Sciences, 2024, 25(21): 11409.
[22] Calvo M J, Parra H, Santeliz R, et al. The Placental Role in Gestational Diabetes Mellitus: A Molecular Perspective [J]. touch REVIEWS in Endocrinology, 2024, 20(1).
[23] Wu Y L, Lin Z J, Li C C, et al. Epigenetic Regulation in Metabolic Diseases: Mechanisms and Advances in Clinical Study [J]. Signal Transduction and Targeted Therapy, 2023, 8(1).
[24] Wu D, Ge L. Advances in DNA Methylation Research in Patients with Gestational Diabetes Mellitus [J]. Journal of Shanghai Jiao Tong University (Medical Edition), 2021(08): 1120-1124.
[25] Zhu Z, Cao F, Li X. Epigenetic Programming and Fetal Metabolic Programming [J]. Frontiers in Endocrinology, 2019, 10.
[26] Wang S, Cui Z, Yang H. Interactions between Host and Gut Microbiota in Gestational Diabetes Mellitus and Their Impacts on Offspring [J]. BMC Microbiology, 2024, 24(1).
[27] Logman H, Mohamed G M M, Altaf F, et al. Maternal Obesity as a Risk Factor for Pregnancy-Related Metabolic Disorders and Neonatal Adversities: A Meta-Analysis of Randomized Controlled Trials [J]. Indus Journal of Bioscience Research, 2025, 3(2): 157-162.