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Gestational Diabetes Mellitus (GDM): Effects on pregnancy, delivery and long-term health outcomes in mothers and offspring

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Abstract

Introduction: Gestational Diabetes Mellitus (GDM) is conventionally defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. GDM has been consistently associated with a spectrum of adverse obstetric and neonatal outcomes [2]. The purpose of this study was to evaluate the effects of Gestational Diabetes Mellitus (GDM) on maternal and neonatal outcomes during pregnancy and delivery, and its long-term effects on both mothers and their offspring's health.

Materials and methods: A review of chosen literature in the PubMed database was conducted, using the following key words: „diabetes", „gestational diabetes mellitus'', „glucose intolerance'', „macrosomia'', „perinatal complications''

Summary: Gestational Diabetes Mellitus (GDM) is among the most common metabolic disorders of pregnancy and is linked to multiple adverse maternal and neonatal outcomes. Risk factors of developing gestational diabetes were taken into consideration, as well as a pathophysiological mechanism of gestational diabetes was examined in order to elaborate on the short-range and long-range consequences for both mothers and their offspring [3]. Furthermore, diagnosis of GDM, medical treatment and prevention of its effects were also discussed in this study.

Conclusion: Recognition of GDM impact on the course of pregnancy, delivery, and their outcomes and identifying it as an important predictor of long-term cardiometabolic risk of both mothers and their offspring, what is crucial for optimizing care and planning strategies of medical interventions [4].

Keywords: gestational diabetes, glucose intolerance, macrosomia, cardiometabolic risk, obesity, insulin resistance, perinatal complications, maternal hyperglycemia, fetal hyperinsulinemia, neonatal hypoglycemia, neonatal hyperbilirubinemia

Introduction

Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy and affects a growing number of women worldwide. With the increasing prevalence of obesity, sedentary lifestyles and changes in dietary habits, the incidence of GDM is increasing significantly, making it a concerning public health issue. GDM is defined as a glucose

tolerance disorder that first appears or is diagnosed during pregnancy, regardless of the need for insulin or persistent hyperglycemia after delivery [1].

The pathophysiology of GDM is complex and primarily involves a gradual increase in insulin resistance induced by placental hormones, along with an inadequate compensatory response of pancreatic β cells [5].

This results in hyperglycemia, which adversely affects both the mother and the fetus. Early diagnosis and proper glycemic control are crucial to reducing the risk of obstetric complications, such as fetal macrosomia, preterm birth, shoulder dystocia, and the need for cesarean section. GDM may also contribute to small-for-gestational-age (SGA) outcomes [6].

The impact of gestational diabetes does not end with delivery; numerous studies indicate that children born to mothers with gestational diabetes are at increased risk of developing obesity, insulin resistance, autism spectrum disorders [7] and type 2 diabetes later in life.

Women who have had gestational diabetes have an elevated risk of ultimately developing cardiovascular disease in the future [8].

Growing evidence suggests that individuals with GDM, compared to those without GDM, have an increased risk of subsequent type 2 diabetes (T2D) [9].

Therefore, this problem requires a comprehensive approach encompassing early diagnosis, effective treatment, health education, and long-term follow-up for both the mother and the child.

The aim of this paper is to present the current state of knowledge about Gestational Diabetes Mellitus (GDM), with particular emphasis on its diagnosis, pathophysiology, and impact on the course of pregnancy, labor, the health of both mother and the newborn, and its subsequent development.

Classification of diabetes and hyperglycemia in pregnancy

Disturbances of glucose metabolism identified during pregnancy can be broadly categorized into two main groups: pre-gestational diabetes mellitus (PGDM) and hyperglycemia first encountered during pregnancy.

Pre-gestational diabetes mellitus refers to all forms of diabetes that are present prior to conception. This includes type 1 diabetes mellitus, type 2 diabetes mellitus, and other specific types of diabetes, such as those secondary to cystic fibrosis, monogenic mutations (e.g., MODY) or induced by pharmacologic agents, including corticosteroids [10]. Women who conceive with

pre-pregnancy diabetes constitute a high-risk population requiring strict metabolic control before and throughout gestation to reduce the risk of congenital malformations and perinatal complications [11].

Hyperglycemia in pregnancy, on the other hand, refers to elevated blood glucose levels first diagnosed during pregnancy. This category includes two distinct entities: Diabetes In Pregnancy (DIP), also referred to as overt diabetes identified during gestation, denotes hyperglycemia that fulfills the diagnostic criteria for diabetes outside of pregnancy and is therefore expected to persist after delivery [12] and Gestational Diabetes Mellitus (GDM) represents glucose intolerance of variable severity with onset or first recognition during pregnancy. Two subtypes of GDM can be distinguished: early GDM; diagnosed in the first or early second trimester, may reflect previously unrecognized preexisting glucose intolerance and standard GDM; diagnosed typically in the second or third trimester, resulting primarily from pregnancy-induced insulin resistance and hormonal changes [13].

This classification emphasizes the heterogeneous nature of hyperglycemic conditions occurring during pregnancy and underlines the clinical relevance of distinguishing pre-existing diabetes from gestational diabetes in order to ensure optimal treatment strategies, accurate prognostic assessment, and appropriate postnatal monitoring and management.

Risk factors and pathophysiological pathways associated with Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus (GDM) develops as a result of complex interactions between preconceptional, gestational and environmental factors influencing maternal and fetal metabolism. Prior to conception, there are several determinants that may increase the risk of gestational diabetes such as maternal obesity, genetic predisposition, ethnicity, inadequate nutrition, and low physical activity. Those are major risk factors predisposing to impaired glucose tolerance during pregnancy [2]. Some of them can be targeted and modified in order to improve overall health, prevent the onset of gestational diabetes mellitus or mitigate its adverse maternal and fetal outcomes. This topic has been elaborated on in greater detail in a subsequent chapter.

During pregnancy, the risk factors contribute to increased maternal insulin resistance, accompanied by elevated plasma concentration of glucose, triglycerides and free fatty acids, as well as by excessive gestational weight gain. Pathophysiological mechanisms mediating these alterations include epigenetic modifications, placental hormone secretion, such as progesterone,

human chorionic gonadotropin (hCG), estrogens, mainly estriol, estradiol and estrone and low-grade cellular inflammation [14]. Gestational diabetes mellitus (GDM) and maternal hyperglycemia exert multifactorial effects on fetal development through complex metabolic and hormonal interactions between the mother, placenta and fetus. Increased maternal insulin resistance during pregnancy leads to elevated concentrations of circulating glucose and free fatty acids, those substances readily cross the placenta, resulting in the enhanced placental transfer of glucose and lipids to the fetus [5]. Consequently, the fetus experiences hyperinsulinemia and elevated levels of insulin-like growth factor 1 (IGF-1), which stimulate fetal substrate uptake and anabolic growth. This phenomenon may lead to the occurrence of hypoglycemia and hyperbilirubinemia in the newborn after delivery [15].In pregnancies complicated by gestational diabetes mellitus, elevated maternal blood glucose concentrations enhance transplacental glucose transfer to the fetus. Hence, the pancreas of the fetus adapts to the environmental conditions and performs hypertrophy of the β-cells, which produce abnormally great amounts of insulin, leading to fetal hyperinsulinemia. This endocrine imbalance stimulates disproportionate fetal growth and increased lipid storage, contributing to macrosomia [16].

Following delivery, the maternal glucose supply is abruptly interrupted, while neonatal insulin secretion remains temporarily elevated. This sustained hyperinsulinemia in the absence of exogenous glucose leads to neonatal hypoglycemia.

Moreover, infants with macrosomia frequently experience polycythemia, which is defined as an increment of the red blood cell mass. This additional growth is a compensatory response to relative hypoxia, resulting from the hyperglycemia of the mother. After delivery, breakdown of these erythrocytes results in excessive bilirubin production, contributing to neonatal hyperbilirubinemia [17].

Short-term and long-term consequences of Gestational Diabetes Mellitus (GDM)

Gestational Diabetes Mellitus (GDM) is associated with a wide spectrum of adverse outcomes that can manifest both in the perinatal period and later in life. Epidemiological data indicate that GDM affects approximately 2–6% of pregnancies in Europe, with prevalence rates increasing globally due to rising maternal age and obesity [18]. Short-term maternal complications include an elevated risk of pregnancy-induced hypertension, preeclampsia, and operative delivery [19]. In the fetus, hyperglycemia and subsequent hyperinsulinemia promote excessive

growth, predisposing to macrosomia, neonatal hypoglycemia, and shoulder dystocia at birth [20]. In the long term, women who experienced GDM have a substantially increased risk of developing type 2 diabetes mellitus (T2DM) and metabolic syndrome. Cohort studies report that the risk of T2DM is more than seven-fold higher compared to women without prior GDM, and up to 50% of affected women may develop T2DM within 10 years postpartum [21,22]. Other long-term maternal sequelae include higher rates of cardiovascular disease and persistent glucose intolerance [23]. Offspring exposed to intrauterine hyperglycemia also face long-term metabolic consequences. Numerous studies have demonstrated an increased incidence of childhood and adulthood obesity, insulin resistance, and glucose intolerance in this population [24]. Moreover, some evidence suggests a slightly higher risk of congenital anomalies; particularly cardiac defects among infants of mothers with GDM [25]. Collectively, these findings emphasize the importance of early diagnosis, glycemic control, and postpartum monitoring to mitigate both immediate and future health risks associated with GDM. In the short term, GDM increases the risk of several maternal and neonatal complications. Affected pregnancies are associated with a higher incidence of preeclampsia, increased obstetric interventions [26]. Sequence of metabolic events promotes adverse perinatal outcomes such as congenital malformations, preterm birth, macrosomia, defined as excessive fetal growth, which increases the risk of shoulder dystocia and brachial plexus injury during delivery, related to birth trauma [27]. Additionally, the chronic intrauterine hyperglycemic environment predisposes to fetal hypoxia, which can result in stillbirth, polycythemia, and subsequent hyperbilirubinemia due to accelerated red blood cell turnover [28]. In parallel, the metabolic adaptations impair fetal lung maturity by decreasing surfactant synthesis and function, thereby increasing the risk of respiratory distress syndrome, especially in the setting of iatrogenic preterm delivery [29]. Moreover, neonatal hypoglycemia frequently occurs postpartum as a consequence of persistent fetal hyperinsulinemia following abrupt discontinuation of maternal glucose supply.

Finally, chronic fetal exposure to hyperglycemia and hyperinsulinemia may contribute to fetal cardiomyopathy, further increasing perinatal morbidity and mortality [30].

Collectively, these mechanisms illustrate how maternal metabolic dysregulation in GDM drives a cascade of pathophysiological changes that compromise both immediate and long-term neonatal health outcomes. Both mothers and offspring are at increased risk of developing metabolic disorders [3]. Until early adolescence, offspring of mothers with gestational diabetes have a higher BMI and appear to be at a particularly higher risk of being overweight in adolescence compared with children from non-GDM pregnancies, putting them also at a higher lifetime risk of being overweight and developing obesity. These results emphasize the importance of

adequate recognition and timely treatment of maternal gestational diabetes to prevent fetal macrosomia in obstetrics [31].

Women with a history of GDM have a markedly higher probability of persistent dysglycemia, type 2 diabetes mellitus, and cardiovascular disease. Similarly, children born to mothers with GDM exhibit an elevated risk of obesity, glucose intolerance, and metabolic syndrome later in life [5]. Fetal macrosomia and large for gestational age (LGA), which predisposes to a higher risk of childhood obesity and type 2 diabetes mellitus later in life.

HbA1c level around 24 to 28 weeks may predict the development of fetal macrosomia or a LGA baby in women with GDM, which could be useful for better prevention of fetal macrosomia and LGA [32].

These findings emphasize the necessity of comprehensive metabolic monitoring before, during, and after pregnancy to mitigate both short- and long-term adverse outcomes associated with GDM.

Diagnosis and clinical management of Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [33].

In women diagnosed with diabetes early in pregnancy, overt non-gestational diabetes is diagnosed (fasting glucose ≥ 126 mg/dL, spontaneous glucose ≥ 200 mg/dL, or HbA1c ≥ 6.5% before 20 weeks of pregnancy). GDM is diagnosed based on an oral glucose tolerance test (oGTT) or an elevated fasting glucose level (≥ 92 mg/dL). Screening for undiagnosed type 2 diabetes during the first prenatal visit is recommended in women at increased risk. An acute glucose tolerance test (OTGTT) (120 min; 75 g glucose) may be indicated as early as the first trimester in high-risk women. It is mandatory to perform measurement between 24 and 28 weeks of pregnancy in all women with a history of non-pathological glucose metabolism [1**].**

Management of GDM aims to maintain euglycemia throughout pregnancy, prevent fetal overgrowth, and minimize maternal complications. Treatment strategies include lifestyle modification, self-monitoring of blood glucose, and pharmacologic therapy when necessary. The recommended first-line approach is lifestyle modification, followed by pharmacotherapy if necessary. The definition of lifestyle modification includes dietary modification, emphasizing complex carbohydrates, high fiber, and low glycemic index foods is the cornerstone of therapy. Physical activity, such as moderate-intensity walking or prenatal yoga, improves insulin sensitivity and

glycemic control. Patients are typically advised to monitor fasting and postprandial glucose levels daily. When lifestyle modification is insufficient, appropriate pharmacotherapy is initiated. Insulin remains the gold standard due to its safety and efficacy. Oral hypoglycemic agents, such as metformin or glyburide, may be considered in selected cases, though their long-term safety data are still under evaluation [34,35,36]. Fetal Monitoring and Delivery Planning with usage of ultrasound assessments for fetal growth and amniotic fluid volume are recommended [37]. Timing of delivery depends on glycemic control and obstetric conditions, with elective induction considered at 39–40 weeks in well-controlled cases.

Approaches to the prevention and clinical management of Gestational Diabetes Mellitus (GDM)

To reduce maternal, fetal and neonatal morbidity and mortality, continuous monitoring of both the mother and fetus is essential. Regular obstetric assessments, including ultrasonographic examinations are strongly recommended [37]. Neonatal care for infants born to mothers with gestational diabetes;particularly those at high risk of hypoglycemia should involve immediate postnatal blood glucose monitoring and timely medical intervention when required. Follow-up of child development and the promotion of healthy lifestyle habits are crucial elements of care that should encompass the entire family. After delivery, all women diagnosed with gestational diabetes should undergo reassessment of glucose tolerance through a fasting plasma glucose test with a 75 g oral glucose load (according to WHO criteria) within 4-12 weeks postpartum. Glycemic parameters-including fasting glucose, random glucose, and HbA1c-should also be evaluated. In women with normal glucose tolerance, an oral glucose tolerance test (oGTT) is advised every 2–3 years. All patients should be informed about their increased risk of developing type 2 diabetes and cardiovascular disease during the postpartum follow-up visit [38]. Preventive strategies-particularly lifestyle modifications such as maintaining a healthy body weight and engaging in regular physical activity should be discussed in detail. Specific treatment, which includes dietary recommendations and insulin therapy in cases of mild gestational diabetes- reduces the risk of maternal and perinatal complications [34]. Aspart, glargine and detemir insulin have confirmed safety and effectiveness. However, Lispro was related to higher birth weight [35]. In women with gestational diabetes, metformin (used as monotherapy or in combination with insulin) is not associated with an increased risk of perinatal complications compared with insulin [36].

Summary and conclusions

Gestational diabetes mellitus (GDM) is associated with a range of adverse maternal and neonatal outcomes, it represents one of the most prevalent metabolic disorders complicating pregnancy, with global prevalence increasing due to demographic shifts, sedentary lifestyle patterns, and the growing burden of obesity. It is characterized by impaired glucose tolerance first recognized during pregnancy, resulting from the interplay between placental hormone–induced insulin resistance and insufficient pancreatic β-cell compensation. These metabolic disturbances lead to maternal hyperglycemia, which negatively affects both the mother and fetus. The short-term maternal consequences of GDM include an increased risk of gestational hypertension, preeclampsia, preterm birth, cesarean delivery, due to complications such as fetal overgrowth and labor dystocia. For the fetus and newborn, hyperglycemia and hyperinsulinemia contribute to macrosomia, perinatal morbidity, including birth trauma, shoulder dystocia, neonatal hypoglycemia, polycythemia, hyperbilirubinemia, and, in some cases, respiratory distress syndrome or cardiomyopathy. These complications collectively increase perinatal morbidity and mortality. Long-term outcomes are equally significant. Women with a history of GDM face a markedly higher risk of developing type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease within the first decade postpartum. Offspring exposed to intrauterine hyperglycemia are predisposed to obesity, insulin resistance, and impaired glucose tolerance later in life, highlighting the intergenerational impact of maternal metabolic dysregulation. GDM diagnosis relies on standardized oral glucose tolerance testing (OGTT) protocols applied during mid-pregnancy, typically performed between 24 and 28 weeks of gestation, with earlier screening recommended for high-risk women. Management strategies focus on maintaining euglycemia through lifestyle modification, nutritional therapy, and, when necessary, pharmacological intervention—most commonly insulin, with metformin as an alternative in selected cases. Close maternal and fetal monitoring, including regular ultrasonographic assessments, is essential for optimal outcomes. Effective prevention and management require a multidisciplinary approach encompassing early screening, patient education, and individualized treatment. Postpartum follow-up is crucial to identify women at risk of persistent glucose intolerance and to implement preventive strategies for future metabolic disorders. Early identification, rigorous glycaemic control during pregnancy, and structured postpartum monitoring are essential com-

ponents of comprehensive management. These measures not only mitigate perinatal complications but also play a crucial role in preventing the transition to chronic metabolic disorders in the years following delivery.

In conclusion, GDM remains a major obstetric and public health concern with profound short- and long-term consequences. Continuous metabolic monitoring throughout the preconception, gestational, and postpartum periods, along with health promotion and lifestyle interventions, are key to mitigating adverse maternal and neonatal outcomes and breaking the cycle of transgenerational metabolic disease.

Disclosure

The authors declare no conflict of interest in relation to this study.

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