The American Journal of Medical Sciences and Pharmaceutical Research
ISSN 2689-1026 | Open Access

TYPE Original Research
PAGE NO. 25-28
DOI 10.37547/tajmspr/Volume07Issue05-05

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The role of risk factors in the development of diabetes mellitus in pregnant women

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OPEN ACCESS

SUBMITED 15 March 2025
ACCEPTED 11 April 2025
PUBLISHED 13 May 2025
VOLUME Vol.07 Issue05 2025

CITATION

Azimova S.B., Tadjibaeva R.B., & Abdunazarova M.I. (2025). The role of risk factors in the development of diabetes mellitus in pregnant women. The American Journal of Medical Sciences and Pharmaceutical Research, 7(05), 25–28. https://doi.org/10.37547/tajmspr/Volume07Issue05-05

Abstract: Gestational diabetes mellitus (GDM) is a disease characterized by hyperglycemia, first detected during pregnancy, but not corresponding to the diagnostic criteria of manifest diabetes mellitus (DM). According to modern concepts, pregnancy is a "diabetogenic factor", since during gestation there is a change in hemostasis of the female body, including carbohydrate metabolism. Hyperglycemia during pregnancy is associated with the development of complications both on the part of the mother and the fetus. In addition, GDM is a risk factor for the development of obesity, type 2 diabetes and cardiovascular diseases in the mother and offspring in the future. According to the International Diabetes Federation, approximately 14% of pregnancies are associated with GDM, resulting in 18 million births per year. All of these children are at risk of developing obesity and type 2 diabetes. The increasing prevalence of this disease, the high probability of adverse pregnancy outcomes for the mother and fetus, and a number of long-term consequences of GDM dictate the need for its prevention by correcting risk factors, timely diagnosis, and effective treatment of the disease.

Keywords: Gestational diabetes mellitus, risk factor, hyperglycemia, insulin resistance, pregnancy, obesity, prediabetes.

Introduction: Gestational diabetes mellitus (GDM) is

one of the most common diseases during pregnancy and the most common type of diabetes mellitus (DM) in pregnant women. Gestational diabetes mellitus (GDM) is a common complication of pregnancy and can lead to adverse maternal and fetal outcomes, such as cesarean section, birth trauma, and the development of type 2 diabetes mellitus (DM) in the future. Gestational diabetes mellitus is characterized by hyperglycemia that is first detected during pregnancy but does not meet the diagnostic criteria for overt diabetes mellitus (DM).

Most cases of gestational diabetes mellitus develop in women with obesity, with a body mass index (BMI) greater than 30. For example, in Finland in 2018, the average BMI among pregnant women exceeded 25, meaning they were overweight. More than 16% of pregnant women were obese, with a BMI greater than 30. The American Diabetes Association estimates that gestational diabetes occurs in 10% of pregnant women in the United States [1]. According to the 2019 International Diabetes Federation Atlas, 15.8% (20.4 million) of women had hyperglycemia during pregnancy, and 83.6% of these cases were diagnosed with gestational diabetes mellitus [2]. The increase in the number of pregnant women with this pathology is directly related to the incidence of diabetes in the world, improved quality of GDM diagnostics, an increase in the proportion of women of reproductive age who are overweight or obese, as well as late planning of pregnancy and childbirth, and an increase in the frequency of concomitant pathology [3].

The first prospective studies of glucose metabolism during pregnancy were conducted in the 1950s and 1960s. In the late 1960s, the term gestational diabetes mellitus was first coined [4], diagnostic criteria for gestational diabetes were formulated, and screening during pregnancy was introduced. Until recently, there was no consensus in the world regarding the diagnostic criteria for gestational diabetes. In European countries, the diagnostic criteria of the WHO were most widely used, according to which a glucose tolerance test (GTT) was performed, similar to that performed outside of pregnancy. The most recent large-scale multinational study HAPO (Hyperglycemia and Adverse Pregnancy Outcomes Study), which involved more than 25,000 pregnant women, showed a convincing relationship between maternal hyperglycemia and adverse pregnancy outcomes for both the mother and the fetus and the child in the future. In 2008, in Pasadena (USA), the International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed new diagnostic criteria for carbohydrate metabolism disorders during pregnancy for discussion, based on the results of the HAPO study. During 2010-2011, a number of countries (USA, Japan, Germany, Israel, etc.) adopted these criteria. In 2012, after repeated discussions, the Russian Federation adopted the Consensus on the Diagnosis and Treatment of GDM, approved by the Ministry of Health of the Russian Federation in 2013 [5]. Differences in epidemiological indicators may be associated with the diversity of the population groups studied. Thus, in countries with a low risk of developing GDM in pregnant women, such as Sweden, Australia, the USA (with the exception of Native Americans and some other population groups), the prevalence of this pathology is less than 2%, about 9.5% and 4.8%, respectively. Higher rates are observed in the Middle East countries: the United Arab Emirates (20.6%), Qatar (16.3%), Bahrain (13.5%) and Saudi Arabia (12.5%). Some developed countries, such as Canada (17.8%) and France (12.1%), also have higher rates of prevalence of gestational carbohydrate metabolism disorders. According to domestic authors, the incidence of GDM in Russia varies widely - from 1 to 14%, averaging about 7%, and significantly depends on diagnostic methods, ethnic composition of the population, prevalence of type 2 diabetes in individual populations, and economic conditions. It should be noted that 91.6% of cases of hyperglycemia during pregnancy are noted in low- and middle-income countries, where maternal health care is often limited [6]. In the modern world, gestational diabetes mellitus (GDM) is a common disorder of carbohydrate metabolism in pregnant women, which indicates the undoubted relevance of this problem in women of reproductive age. During pregnancy, genetically determined changes occur in the woman's body, aimed primarily at creating optimal conditions for the functioning of the organs and systems of the pregnant woman, ensuring the normal development of the fetus. In the first trimester, a decrease in fasting glycemia is noted (on average by 0.5-1.0 mmol / l), which is also due to a decrease in the consumption of glucose and gluconeogenesis substrates to meet energy needs during the formation of the fetoplacental complex. An increase in cortisol levels due to stimulation of the adrenal cortex of a pregnant woman by adrenocorticotropic hormone of the pituitary gland under the influence of placental corticoliberin also contributes to a decrease in tissue sensitivity to insulin. The pathophysiology of gestational diabetes is based on a functional decrease in insulin sensitivity (IS) or an increase in insulin resistance (IR) in a pregnant woman [7]. As a result, the β-cells of the islet apparatus of the pancreas perceive the level of glycemia abnormally, which leads to insufficient insulin secretion for a given level of glycemia. In the third trimester of pregnancy, women with GDM experience an increase in insulin concentration and a decrease in the suppression of

glucose production by the liver during insulin administration. Hyperinsulinemia, developing in response to hyperglycemia, increases peripheral IR due to impaired autoregulation of insulin receptors, which leads to a decrease in the sensitivity of peripheral tissues to the effects of insulin and causes compensatory hyperinsulinemia aimed at overcoming the IR barrier. Thus, a “vicious circle” of the “ascending spiral” type develops, since each new high level of compensatory hyperinsulinemia leads to worsening insulin resistance.

GDM has risk factors similar to type 2 DM. Common factors include age, heredity for DM, previous GDM, birth of a fetus weighing more than 4000 g, carbohydrate metabolism disorders, history of glucosuria, obesity and overweight, female gender, arterial hypertension, hyperlipidemia. Special risk factors for GDM are complicated obstetric and gynecological history, multiple pregnancy, polyhydramnios during this pregnancy, use of high reproductive technologies, pathological weight gain [8]. It is also necessary to note a number of non-hormonal factors influencing the development of hyperglycemia, such as decreased physical activity of the pregnant woman, increased caloric intake, weight gain due to the fat component, decreased gastrointestinal motility [9]. The leading role in the pathogenesis of pregnancy complications associated with hyperglycemia belongs to microcirculatory disorders. Oxidative stress induced in the ischemic placenta is accompanied by activation of apoptosis, endothelial dysfunction with possible development of placental insufficiency, preeclampsia, fetal hypoxia [10]. Considering the causes of GDM development in women, it is important to note that this disease is polyetiological. Etiological factors of GDM development also include mutation of one or more genes and genetic heterogeneity causing genetic polymorphism. Specific monoclonal antibodies (AB) are detected in 1.6–38% of pregnant women with GDM – GAD to β-cells, insulin and HLA-DR3, HLA-DR4, which are usually characteristic of individuals with a genetic risk of developing type 1 diabetes mellitus. diabetes mellitus (DM 1). Tumor necrosis factor-α (TNF-α) also plays a known role in the development of IR. Certain risk factors influence the development of GDM, including: overweight or obesity (BMI over 30 kg/m2), significant weight gain after the age of 18, smoking, multiple pregnancies, family history of type 2 diabetes, impaired glucose tolerance before pregnancy, polyhydramnios or a history of a large fetus, the birth of a child weighing more than 4000 g or stillbirth - a history of pregnancy, the development of defects in children, rapid weight gain during this pregnancy, the woman's age over 30 years.[11]

CONCLUSION

GDM is an important medical and social problem that significantly increases the risk of obstetric and metabolic complications in women and their offspring. Conducting additional studies assessing the epidemiological characteristics of GDM, the structure of risk factors, as well as an in-depth study of the pathogenetic mechanisms of its development is advisable to expand our understanding of the real scale of the problem and improve the possibilities of managing this disease.

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