

The Treatment of Gestational Diabetes Mellitus

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Abstract

Pre-pregnancy glucose metabolism is normal, only during pregnancy diabetes known as gestational diabetes mellitus. Currently, the diagnostic criteria for gestational diabetes mellitus are IADPSG criteria (International Association of Diabetes and Pregnancy Study Group), and 75 g oral glucose tolerance test is recommended at 24 - 28 weeks of gestation. Gestational diabetes is associated with many pregnancy complications, such as macrosomia, preterm delivery and increased cesarean section rates, and neonatal complications such as hypoglycemia, hypoxia, and respiratory distress syndrome. Early identification of high-risk groups can be carried out for early prevention and intervention which are conducive to improving mothers and infants perinatal outcome. For the treatment of gestational diabetes, lifestyle interventions, such as improved diet combined with exercise to control blood sugar, are recommended first. For patients with poor blood glucose control, insulin is recommended for blood glucose control, and oral drug use is still controversial.

Keywords

Gestational Diabetes Mellitus, Pregnancy, Diagnosis, Treatment, Impact

1. Introduction

Diabetes, which occurs during pregnancy after normal glucose metabolism before pregnancy, is called gestational diabetes (GDM). The pathogenesis of GDM is very complex β Cell decompensation that leads to insulin resistance, hyperglycemia and increased blood glucose supply of the fetus. There is evidence that the expansion of fat, low-grade chronic inflammation, gluconeogenesis, oxidative stress and placental factors are related to the pathology of GDM. However, the pathogenesis of GDM still needs further study in order to find effective treatment and intervention measures [1].

The abnormal glucose metabolism of GDM patients mostly returned to normal after delivery, but some patients still had abnormal glucose metabolism after

delivery. The incidence of postpartum abnormal glucose metabolism in women with a history of GDM had been reported to vary between 2.6% and 38 % within 6 - 12 weeks of delivery [2]. Multifactor logistic regression analysis showed that: age ≥ 35 years, pre pregnancy BMI ≥ 25 kg/m², family history of diabetes, and daily exercise time < 1 h after delivery were the risk factors for abnormal glucose metabolism of GDM patients after delivery [3] [4].

2. Diagnosis

The diagnostic criteria of GDM originated from the study of O'Sullivan and others in 1964, and the later diagnostic criteria are constantly changing. The criteria of GDM are shown in **Table 1**. Currently, the diagnostic criteria of the International Association of diabetes and Pregnancy Study Group (2010) and IADPSG2010 are mostly used. IADPSG diagnostic criteria expand the population with diabetes in pregnancy, increase the prevalence of GDM [5], and strengthen the inspection and treatment of diabetes in pregnancy, which can reduce the occurrence of multiple maternal and infant complications [6].

It is now recommended that medical institutions conduct 75 g oral glucose tolerance test (OGTT) for all pregnant women who are not diagnosed with pre pregnancy diabetes or GDM at the first visit 24 - 28 weeks and 28 weeks after pregnancy [7]. The blood glucose values on an empty stomach and 1 hour and 2 hours after taking sugar should be lower than 5.1 mmol/L, 10.0 mmol/L and 8.5 mmol/L. GDM is diagnosed when any point of blood glucose reaches or exceeds the above criteria. Pregnant women with high risk factors of GDM or lack of medical resources are recommended to check fasting plasma glucose (FPG) at 24 - 28 weeks of pregnancy. FPG ≥ 5.1 mmol/L, can be directly diagnosed as GDM, and 75 g OGTT is not necessary. High risk factors of GDM [1] [8] [9] [10] include: 1) Factors of pregnant women: age ≥ 35 years old, overweight or obesity before pregnancy, and history of abnormal glucose tolerance; 2) Family history: family history of diabetes; 3) Pregnancy and delivery history: delivery history of giant fetus, history of polyhydramnios, GDM history. Early identification of high-risk groups can carry out early prevention and intervention, which is conducive to improving the perinatal outcome of mothers and infants [9].

Table 1. Diagnostic criteria for gestational diabetes mellitus.

Blood glucose (mmol/L)	100 g OGTT			7 5g OGTT
	O'Sullivan-Mahan Whole Blood [11]	NDDG Plasma-Autoanalyzer [11]	Carpenter-Coustan Plasma-Glucose Oxidase [12]	IADPSG Plasma Enzymatic [13]
Fasting blood glucose	5	5.8	5.3	5.1
1 hour after taking sugar	9.5	10.6	10	10.0
2 hours after taking sugar	8.5	9.2	8.6	8.5
3 hours after taking sugar	7	8.1	7.8	/

a. NDDG, National Diabetes Data Group.

3. Influence of Diabetes in Pregnancy

The effect of GDM on mothers and infants and its extent depend on the level of blood glucose control. Poor blood glucose control has a great impact on the mother and infant, and the mother and infant have high short-term and long-term complications. Some studies have pointed out that the higher the blood glucose during pregnancy, the greater the risk of obesity in the offspring at the age of 5 - 7 [14]. GDM will increase the risk of perinatal complications such as macrosomia, premature delivery and cesarean section rate [15]. A systematic review and meta-analysis included more than 7.5 million pregnant women in 156 studies from 1990 to 2021. In the non-insulin group, the probability of cesarean section rate, premature delivery, low 1-minute Apgar score, macrosomia and greater than gestational age infants of GDM patients increased. In the insulin group, infants older than gestational age, neonatal respiratory distress syndrome, neonatal jaundice, and newborns were also more likely to be transferred to the intensive care unit [16].

Another systematic review and meta-analysis studied more than 5 million pregnant women from 1950 to 2018. The study pointed out that the risk of cardiovascular events in GDM pregnant women was twice that of normal pregnant women [17]. GDM is associated with many pregnancy and perinatal complications, such as hypertension, preeclampsia, premature delivery, macrosomia, shoulder dystocia, and birth injury. At the same time, the prenatal and perinatal mortality and cesarean section rate are also higher. Neonatal complications such as hypoglycemia, hypoxia, respiratory distress syndrome, etc. GDM patients have a higher risk of metabolic diseases, and 70% of GDM patients will develop diabetes 22 - 28 years after delivery. The offspring of GDM have a higher risk of cardiovascular disease, metabolic disease, obesity and type 2 diabetes in adulthood. More and more evidence links GDM with abnormal brain development, with consequences such as general cognition and concentration problems [18].

Among GDM patients, the older they are, the higher the risk that pregnant women with a family history of diabetes will develop diabetes after childbirth. Compared with the normal population, this type of population needs prenatal counseling and closer follow-up after childbirth [18]. Some studies have suggested that GDM patients have a higher probability of long-term complications due to abnormal glucose metabolism, but the probability of overweight or obesity in offspring in childhood (10 - 14 years old) seems to be no significant difference from the normal group [19]. Some studies also believe that intrauterine hyperglycemia environment is related to children's obesity, including overweight or obesity, body fat rate, skin fold thickness and waist circumference [20].

Some studies have pointed out that among pregnant women with gestational diabetes, fasting blood glucose in OGTT, pre pregnancy body mass index, and pregnancy weight growth are independent risk factors for macrosomia; when the fasting blood glucose in OGTT was >5.185 mmol/L, the BMI before pregnancy was >23.02 kg/m², and the body mass growth during pregnancy was >13.75 kg,

the risk of macrosomia in GDM pregnant women was significantly increased; Macrosomia increases the risk of postpartum hemorrhage in GDM pregnant women [21]. Some studies have pointed out that the elderly and OGTT fasting blood glucose increase is independent risk factors for spontaneous preterm delivery in pregnant women with diabetes [22].

The early neonatal blood sugar of pregnant women with diabetes gradually increased after delivery, poor maternal blood sugar control during pregnancy, hypertension, neonatal body weight < 2.50 kg, hypothermia and asphyxia were risk factors for neonatal hypoglycemia [23]. Some studies have pointed out that GDM and the offspring of pregnant women with hyperglycemia during pregnancy are more likely to have metabolic diseases, and a few studies have compared the offspring of pregnant women with normal blood glucose and the offspring of untreated GDM patients. Before the age of 10, there is no metabolic difference between the two [24]. Mothers in a hyperglycemic environment may be at risk of type 2 diabetes, hypertension and other cardiovascular diseases. Their offspring are also at increased risk of obesity, impaired glucose metabolism and cardiovascular disease. The severe high glucose environment may even affect the cognitive function of their offspring. For patients with hyperglycemia during pregnancy, improving the awareness of the lifelong effects of hyperglycemia rather than limiting to the effects of pregnancy will improve the possibility of early prevention and treatment of long-term complications of mother and infant [25].

4. Treatment

Intrauterine high glucose environment is closely related to blood glucose and insulin resistance of offspring. The higher the mother's blood glucose, the greater the frequency of impaired fasting blood glucose, impaired glucose tolerance and glycosylated hemoglobin in the offspring, and the lower the insulin sensitivity and disposal index [26]. Blood glucose control has a positive impact on reducing the adverse pregnancy outcomes of pregnant women with diabetes in pregnancy, and has important value in protecting the safety of newborns and pregnant women [27].

The blood glucose of GDM patients during pregnancy should be controlled to be ≤ 5.3 mmol/L and 6.7 mmol/L before and 2 hours after meal; the blood glucose at night is not less than 3.3 mmol/L; Glycated hemoglobin in pregnancy should be less than 5.5%. Some studies have pointed out that glycosylated hemoglobin in early pregnancy is a risk factor for gestational diabetes. The level of prenatal glycosylated hemoglobin has an important impact on the pregnancy outcome of pregnant women with gestational diabetes, which is closely related to perinatal complications, and should be actively intervened clinically [28].

Diet is of great significance to the control of blood glucose, glycosylated hemoglobin and insulin requirements in the treatment history [29]. Clinical dietitians should give all GDM patients dietary suggestions. Diet can prevent preg-

nancy complications by affecting blood sugar, especially the type, quantity and distribution of carbohydrates [30]. A diet with low glycemic index is conducive to improving fasting blood glucose, blood glucose and blood lipids 2 hours after meal, and reducing the amount of insulin treatment [31]. In addition to diet control, aerobic exercise and anti-resistance exercise are effective for blood glucose, glycosylated hemoglobin and insulin control. For GDM patients, adequate intensity and long duration of exercise are beneficial. GDM patients need at least 20 - 50 minutes of moderate intensity exercise at least twice a week [29]. Most GDM patients can control their blood sugar in a satisfactory range after reasonable diet control and proper exercise treatment. A prospective cohort study pointed out that there was no significant difference in the length, weight and body mass index between the offspring of GDM patients with good blood glucose control and those of normal pregnant women without medication at birth, and the weight growth of the former was relatively slow in infancy (0 - 12 months) [32]. Intervention in lifestyle is conducive to achieving the target weight of GDM patients within one year after delivery, and is also conducive to reducing the risk of postpartum depression. At the same time, it is also beneficial to reduce the incidence of over-gestational age infants. After lifestyle intervention, the birth weight and the incidence of macrosomia in the offspring of GDM patients are lower than those in the non-intervention group [33]. Standardized treatment combined with nutritional intervention can significantly reduce the blood sugar level of pregnant women with diabetes, improve their nutritional status, increase the vaginal delivery rate, and achieve good pregnancy outcomes [34]. For patients with diabetes during pregnancy, diet control and exercise therapy can enhance the overall clinical efficacy, stabilize the blood sugar level, prevent and reduce the incidence of adverse pregnancy outcomes, and improve the prognosis of patients [35].

After diet and exercise management, if the blood glucose during pregnancy cannot meet the standard, insulin is first recommended to control blood glucose. Although the data available at present show that there is no significant difference between the offspring of GDM patients treated with metformin and insulin, [23] [35] the use of oral drugs, including metformin and glibenclamide, is still controversial, because there is still a lack of research data on the effect of oral drugs on the long-term outcome of offspring, [12] especially the study on cardiovascular metabolic risk of GDM offspring after the use of oral hypoglycemic drugs [36]. Although some studies have pointed out that insulin combined with metformin is better than insulin alone in controlling blood sugar in GDM [37], according to the dietary requirements of diabetes, individualized diet adjustment combined with appropriate exercise therapy, insulin and other drug treatments are currently routinely used in clinical treatment [38]. A retrospective analysis of 66 GDM patients compared the blood glucose level, treatment compliance, adverse pregnancy outcome and the incidence of maternal and infant complications of two groups of GDM patients who were treated with insulin to control blood glucose before and after 32 weeks of pregnancy. It is recommended that

insulin treatment be performed in the early pregnancy [39].

During novel coronavirus infection (COVID-19), the maternal metabolic status of the pregnant women who had undergone COVID-19 control in late pregnancy was worse than that of the pregnant women who had not undergone COVID-19 control, and the weight gain of the pregnant women in the former was lower than that in the latter. Among GDM pregnant women, the glycosylated hemoglobin that experienced COVID-19 control in late pregnancy is higher and the high-density lipoprotein is lower. Among the pregnant women with normal blood glucose, the fasting blood glucose of those who experienced COVID-19 control in late pregnancy was higher and the high-density lipoprotein was lower, and the risk of pregnancy related hypertension disease was higher. From the early pregnancy to the late pregnancy, the fasting blood glucose of pregnant women who had experienced COVID-19 control decreased less, and the high-density lipoprotein also increased less. However, there was no significant difference between the perinatal outcome and the weight of the offspring at 1 year old [40].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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