

Brief overview of gestational diabetes mellitus

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ABSTRACT

As obesity increases worldwide, so do the incidence of gestational diabetes mellitus (GDM) and the related perinatal complications. Pancreatic β -cell secretion is altered by hormonal changes during pregnancy. It appears, however, that patients who develop gestational diabetes have pre-existing insulin resistance. However, there are other risk factors to be considered, such as obesity, age, ethnicity, and polycystic ovary syndrome. Screening for gestational diabetes is very important to avoid maternal and fetal complications. For most pregnant women, glycemic control is achieved through dietary and lifestyle changes, although a small percentage requires pharmacological treatment.

Keywords: gestational diabetes mellitus, hyperglycemia, complications, insulin resistance, macrosomia, pregnancy, risk factors

INTRODUCTION

Gestational diabetes mellitus is a medical condition characterized by rapid glucose intolerance and insulin resistance first discovered during pregnancy [1]. Several medical conditions may occur during or related to pregnancy, for example, the installation of glucose intolerance, which is followed by hyperglycemia and the onset of gestational diabetes. The pathophysiology of this condition is still poorly understood, but research is incriminating hormonal abnormalities, insulin resistance and malfunctions of pancreatic β -cell [2,3]. The increased obesity rate among the general population and reproductive-aged women is often associated with a high incidence of diabetes during pregnancy, as well as adverse pregnancy complications and outcomes. In addition, gestational diabetes is also related to advanced maternal age, preexisting obesity, ethnicity, and

diabetes history within family members [4,5]. The Center of Disease Control estimates that the incidence of GDM in the U.S. is approximately 10% [5].

MATERIALS AND METHODS

A PubMed, NCBI and Medical Journals systematic electronic research was performed using keywords like "gestational diabetes mellitus", "type 2 diabetes", "pancreatic β -cell dysfunction", "body mass index", "macrosomia", "maternal glucose control", and "screening". The search included randomized controlled trials, review articles, systematic reviews, and meta-analyses and resulted in 205 articles, from which only 28 papers were further reviewed and included in the final review. The aim of this paper is to briefly highlight the importance of gestational diabetes mellitus screening in

pregnancy and to summarize its associated complications during gestation and postpartum for both mother and fetus/child.

ETIOLOGY AND PATHOPHYSIOLOGY

During pregnancy, the maternal body undergoes important metabolic changes. Initially, the changes are mainly anabolic with a progressive increase in maternal adipose tissue, while in the latter part of pregnancy, catabolic changes predominate with accentuated lipolysis and an increase in blood glucose, insulin levels, postprandial fatty acid levels and a decrease in maternal fat depots. These changes are largely induced by hormones and other mediators secreted by the placenta, which facilitate peripheral insulin resistance [6,7]. The placental hormones responsible for these changes are human placental lactogen, progesterone and estrogen [8]. According to studies, women who develop gestational diabetes have a higher insulin resistance before pregnancy compared to those who do not develop this pathology [9]. Impaired pancreatic beta-cell secretion is an important factor in the pathophysiology of GDM. After delivery, insulin sensitivity returns to pre-pregnancy values. GDM can be considered an early stage of type 2 diabetes mellitus onset during pregnancy [10].

RISK FACTORS

Maternal age has a crucial role in the onset of GDM. Patients older than 25-30 years will be more likely to develop GDM compared to younger patients. Studies report a directly proportional relationship between increased maternal age and the occurrence of GDM [2,11,12].

Race and ethnicity are also risk factors, with the prevalence of GDM being higher among Hispanic, North African, and Asian women than among non-Hispanic white women [13].

Pre-existing obesity and overweight may frequently precede GDM. The pathophysiology is based on an elevated production and deposit of lipids in the adipose tissues, but also in the liver and other organs. In obese patients, there is high insulin resistance in the hepatic tissue that exacerbates during pregnancy and increases the risk of GDM occurrence [14].

Endocrine disorders may also be associated to reproductive-age women pathologies, Among them, polycystic Ovary Syndrome (PCOS) and GDM are considered to be among the most common endocrine conditions that can determine both pregnancy and non-pregnancy complications. PCOS is characterized by hyperandrogenism, chronic oligomenorrhoea and, like GDM, obesity and insulin resistance. Studies show that PCOS itself is not a risk factor for GDM, but in associa-

tion with other comorbidities, such as obesity or maternal age, the risk increases [2,15].

A family history of hyperglycemia and diabetes is considered to be an independent risk factor for the onset of gestational diabetes. Genetically, there is an important link between type 2 diabetes and GDM. Epigenetic alterations may be associated with glucose intolerance and early obesity during childhood [16,17]. There are also other risk factors to be mentioned, such as glycosuria, previous pregnancies with GDM, hypertension and pre-eclampsia, glucocorticoid consumption, excessive weight gain in pregnancy or adolescence, and low vitamin D levels.

SCREENING AND DIAGNOSIS

Research regarding the diagnosis and the screening of GDM has an extended history of more than 10 years. After the first publication of the HAPO Cooperative Research study in 2008, in 2010 recommendations were assessed and published by the International Association of Diabetes and Pregnancy Study Group (IADPSG) [19,20]. Until 2008, gestational diabetes was diagnosed on the same criteria as in non-pregnant women. In some countries, screening is based on the risk class in which the gynecologist classifies the pregnant woman. Low risk for gestational diabetes was considered for women with a normal weight, under the age of 25, with no additional obstetrical risk or family history of type 2 diabetes [19].

There is no international consensus regarding the screening of gestational diabetes, although the oral glucose tolerance test (OGTT) is the most frequent method in use. There are two methods currently used to detect gestational diabetes mellitus, as shown in Table 1. At first, the one-step approach is based on a single glucose test with 75 g of glucose. The second, also known as the two-step approach, is performed sequentially. Initially, there is a first test done using 50 g oral glucose. If the result shows serum glucose above 130-240 mg/dL, is it mandatory to be performed a second test after a few days, with 100 g glucose, in order to confirm the diagnosis [21]. Both screening methods have advantages and disadvantages. The first method is superior to the second, regarding both cost-effectiveness and the time for diagnosis, and determines a precocious diagnosis and prevention of pregnancy complications [22,23].

MANAGEMENT

Appropriate management of pregnant women diagnosed with GDM requires a multidisciplinary medical approach. The patient must learn to monitor her blood glucose levels, change her lifestyle, adjust her weight,

TABLE 1. Criteria for gestational diabetes mellitus diagnosis

Plasma glucose	WHO (75 gm; One Step)	IADPSG (75 gm; One Step)	CDA (75 gm; Two-Step)	Carpetner-Coustan (100 gm; Two-Step)	NDDG (100 gm; Two-Steps)
Fasting(mg/dL)	92-125	92-125	95	95	105
One-hour(mg/dL)	180	180	191	180	190
Two-hour(mg/dL)	153-199	153	160	155	165
Three-hour(mg/dL)	-	-	-	140	145

Abbreviations: WHO-World Health Organization; IADPSG- International Association of Diabetes and Pregnancy Study Groups; CDA- Canadian Diabetes Association; NDDG- National Diabetes Data Group.

and make nutritional changes. Most patients are able to control gestational diabetes with diet, and pharmacological treatment is needed in about 15-30% of cases [5,24].

Blood glucose monitoring is recommended daily, pre-prandial (if the pregnant woman has pre-existing diabetes), fasting and postprandial glycemia. The American Diabetes Association (ADA) recommended values are fasting blood glucose <95 mg/dL, one-hour postprandial <140 mg/dL, or two-hour postprandial <120 mg/dL.

Regarding nutrition, the patient should be educated by a diabetes specialist to have three meals and two snacks a day. Initially, it is recommended to note blood glucose values with meals to observe foods that contribute to postprandial hyperglycemia. The patient should adopt a balanced diet with healthy fats, complex carbohydrates, and 20% protein [25].

In cases when diet and lifestyle modification are not enough to control blood glucose values in gestational diabetes, pharmacological treatment is necessary. There is no protocol specifying when the optimal time is to start pharmacological therapy, but if after 10-14 days of diet hyperglycemia persists, drug treatment is initiated. Insulin is the drug of choice in pregnancy because it is a large molecule that does not cross the placenta. Oral therapy studied in GDM includes glyburide and metformin, shown to cross the placenta and reach the fetus [26].

COMPLICATIONS

Several complications may be determined by gestational diabetes mellitus during pregnancy. It is well

Conflict of interest: none declared

Financial support: none declared

known the association between pre-eclampsia and pre-term birth and other possible complications include macrosomia, large-for-gestational-age babies, increased rate of cesarean section, and shoulder dystocia [20]. For newborns, there is an increased risk of hypoglycemia, respiratory distress syndrome, and hypocalcemia. Also, they are at risk for early-onset obesity, type 2 diabetes and cardiovascular conditions [27].

POSTPARTUM FOLLOW-UP

Follow-up recommendations for patients who have had GDM are to perform 75g 2-hour OGTT at 6-12 weeks postpartum. Because of the associated risk for diabetes onset, women with GDM should be evaluated for type 2 diabetes, with screening tests performed every 1 to 3 years, in relation also to additional diabetes risk factors. Patients should also be informed that they are predisposed to cardiovascular disease, type 2 diabetes and a high risk of GDM in future pregnancies [5,26].

CONCLUSIONS

Early detection of gestational diabetes mellitus is very important because although this pathology is transient, the sequelae it leaves are long-term, so GDM screening should be a public health issue. As mentioned above, there are consequences for both the mother and the fetus. Once diagnosed, the patient must be educated to change her lifestyle and diet to maintain optimal blood glucose and the long-term risks must be explained.

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