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Comparative Review on Carbohydrate Metabolism in Gestational Diabetes Mellitus and Normal Gestational Female.

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ABSTRACT

Gestational diabetes mellitus (GDM) incidence is rising in developing countries. It is associated with varied fetal and maternal morbidities. Normal pregnancy is also associated with insulin resistance in later half of pregnancy, which along with other pathogenic mechanism like decreased β cell response is associated with GDM. Glucose tolerance test is used to diagnose GDM but there is controversy in cut-off values in different group. As HAPO (Hyperglycemia associated Pregnancy outcome) trial results are showing fetal and maternal morbidities associated with maternal hyperglycemia, there is a need of early diagnosis of GDM and proper management using appropriate diagnostic cut-off.

Keywords: Gestational Diabetes Mellitus, Pregnancy, Glucose tolerance test, Hyperglycemia.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy.[1] It affects about 3.8% to 17.8% of Indian pregnant women annually and it is the most common metabolic disorder complicating pregnancy.[2-4] However, the pathogenesis of GDM is still largely unknown. Given the fact that women with a history of GDM are at an increased risk of developing type 2 diabetes (T2D) later in their lives[5,6] and women with a family history of diabetes may be predisposed to an increased risk of GDM[7], GDM may share the same risk factors and genetic susceptibilities with T2D. An important role in the pathogenesis of GDM is studied to be insulin resistance increasing during pregnancy, followed by inadequate insulin secretion, in a similar fashion as observed in type 2 diabetes. After delivery, glucose levels usually return to normal, but GDM diagnosis increases the risk of developing Type 2 Diabetes Mellitus in the future. It is observed that 30–70% of women who have a history of GDM will develop Type 2 Diabetes Mellitus or a pre-diabetic state within 5–10 years.[5,6]

Toward the second half of gestation, the mother develops a resistance to insulin. This is brought about by combined effects of hormones antagonistic to insulin action, such as GH, PRL, HPL, glucagon, and cortisol.

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As a result, maternal glucose use declines and gluconeogenesis increases, maximizing the availability of glucose to the fetus.[7]

Late pregnancy is associated with reduced insulin-stimulated glucose disposal, increased hepatic glucose release and elevated gluconeogenesis[8,9], which in predisposed women can lead to gestational diabetes. One of the animal study also demonstrated that Progesterone inhibits cell respiration and at the same time suppresses a compensatory increase in glucose transport, causing cellular carbohydrate deficiency in isolated rat skeletal muscle. This effect is mediated by a direct, rapid and non-genomic mechanism and could contribute to pregnancy-associated changes in glucose homeostasis.[10]

Difference in Carbohydrate metabolism: Due to increasing demand of fetal development and growth glucose metabolism in mother is directed towards decreased glucose utilization by mother and to direct it for fetus for its nutrition and growth. So to understand the difference in normal gestation and GDM, we will highlight the differences under these subheadings:

1. Difference in insulin sensitivity
2. Difference in insulin secretion and β cell function
3. Glucose tolerance test

1) Difference in insulin sensitivity: Pregnancy is normally associated with decreased insulin sensitivity from 2nd trimester onward. In GDM there is additional insulin resistance and also develops earlier that that of normal pregnancy. This insulin resistance is likely to be caused by placental hormones and/or proteins, such as placental growth hormone, cortisol, human placental lactogen or TNF-a, given that for the majority of women with GDM the glucose intolerance resolves post-partum.[11,12] In GDM

insulin sensitivity is decreased to one third of normal and in some cases there is also continuation of decrease in sensitivity in postpartum period.[9]

2) Difference in insulin secretion and β cell function: In normal gestation, although insulin resistance builds up with advancement of gestation due to interplay of various placental hormones, it is well compensated by robust plasticity of β cell by secreting more insulin.[13] GDM results from inadequate insulin secretion for the degree of insulin resistance. In both normal gestation and GDM insulin secretion increases with the advancement of gestation but relative increase in insulin secretion in GDM is lower than that of normal pregnancy.[14] Glucose stimulated insulin secretion is increased more in normal pregnant woman than that of GDM.[14] Various polymorphism studies also found association between genes regulating insulin secretion from β cell and GDM.[15] As previously stated that risk of Type II DM is more common in females who had GDM in their life. One recent study on Hispanic women found declining β cell compensation in postpartum period and weight gain was associated with it.[16]

3) Glucose tolerance test: Gestational diabetes mellitus is associated with various maternal and fetal outcome. HAPO study results are showing adverse fetal outcome with maternal hyperglycemia. Various criteria to diagnose GDM have been developed. WHO and IADPSG criteria's using 75 g, 2h OGTT test are in use but still GDM is associated with adverse maternal and fetal outcome.[17]

IADPSG: International association of diabetes and pregnancy study group criteria to diagnose GDM-

Perform a 75-gram OGTT, with plasma glucose measurement fasting and at 1 and 2 hours, at 24 to 28 weeks of gestation in women not previously diagnosed with overt diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 hours. The diagnosis of GDM is made when any one of the following plasma glucose values are exceeded:

Fasting ≥5.1 mmol/L (≥92 mg/dL)
1 hour ≥10.0 mmol/L (≥180 mg/dL)
2 hours ≥8.5 mmol/L (≥153 mg/dL).

CONCLUSION

Normal pregnancy is also associated with insulin resistance as that of gestational diabetes mellitus but β cells of pancreas have great plasticity to release insulin and overcome the resistance. Mild to moderate hyperglycemia in normal gestation is beneficial because this helps growing fetus to carry out its metabolic demand. But if this level also exceeds in fetus it stimulates fetal pancreas to release insulin which leads to fetal macrosomia. Fetus born to mother having GDM along with macrosomia will have other complications like hypoglycemia, hypo-calcemia, hyper-bilirubinemia and respiratory distress. Results of HAPO study are also showing similar complications in spite of well diagnosed GDM patient who had been properly treated for this condition. So still there is a debate for proper diagnostic criteria and cut-off value which will take care of these fetal and maternal morbidity.

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