Dr Sheikholeslam

Internist

Gestational Diabetes Mellitus

Teleolgy

- CAMPETITION BETWEEN FETUS AND MOTHER FOR FINITE RESOURSES

ENDOCRINOLOGY OF PREGNANCY

- The placenta produces larger quantities of more hormones than any other human organ
- Human placental lactogen
- Estrogen / progestron
- The majority of its products are released into the maternal circulation to induce changes on the fetuses behalf .

Glucose metabolism in pregnancy

- Fetal growth is dependent upon maternal glucose
- Carbohydrates from maternal diet
- Stored glycogen converted to glucose
- High levels of glucose transported by diffusion to the fetus
- Fetal production of insulin

Glucose metabolism in pregnancy

- First half of pregnancy (Anabolic)
- Pancreatic beta cell hyperplasia causes hyperinsulinemia
- Increased uptake and storage of glucose
- Second half of pregnancy (Catabolic)
- Placental hormones block glucose receptors and cause insulin resistance
- Increased lipolysis
- Increased gluconeogenesis
- Decreased glycogenesis
- Increased glucose and amino acids for the fetus

ETIOLOGY

- Pregnancy → pre-diabetic state
- Pregnancy → marked insulin resistance → increased insulin requirement → GDM
- Complicates 4% of all pregnancies
- **60% to 80 % of women with GDM are obese & experience insulin resistance & GDM**

PHYSIOLOGICAL CHANGES

During pregnancy, there is a state called **DIABETOGENIC STATE, peak @ 28-32w**

Due to ↑ hormone produced by placenta : HPL, CORTISOL (insulin antagonist) → relative insulin resistance

Glucose crosses the placenta by facilitated diffusion & fetal blood glucose level closely follow the maternal level

Pregnancy Pathophysiology

- Glucose is a teratogen at high levels
- Crosses placenta readily while insulin cannot
- Insulin resistance occurs because hormonal changes associated with pregnancy partially block the effects of insulin
- Insulin resistance causes glucose to be shunted from mother to the fetus to facilitate fetal growth and development

- subsequent increase in insulin resistance causes maternal glucose levels to increase 80% of non-pregnant women

Increased insulin resistance

↓

Decreased insulin secretion

↓

Increased maternal glucose

↓

GDM

- GDM disappears after pregnancy
- Useful physiologic process out of balance

Pregnancy is characterized by insulin resistance and hyperinsulinemia.

The resistance stems from placental secretion of diabetogenic hormones including GH, CRH, hpl, and progesterone, as well as increased maternal adipose deposition, decreased exercise, and increased caloric intake.

Gestational diabetes occurs when pancreatic function is not sufficient to overcome the insulin resistance created by changes in diabetogenic hormones during pregnancy.

Overt diabetes

A diagnosis of overt diabetes can be made in women who meet any of the following criteria at their initial prenatal visit:

FBS≥126 mg/dL
or
A1C ≥6.5 percent using a standardized assay,
or
Random BS≥200 mg/dL that is subsequently confirmed by elevated FBS or A1C.

The rationale for this change is that an increasing proportion of young women have overt but as yet unrecognized type 2 diabetes due to the increasing prevalence of obesity and lack of routine glucose screening/testing in this age group.

Gestational diabetes in lean pregnant women, need for insulin treatment of gestational diabetes, diabetic ketoacidosis during pregnancy, and postpartum hyperglycemia also suggest preexisting unrecognized type 1 diabetes.

Identifying overt diabetes early in pregnancy may be important because these women are at increased risk of having a child with a congenital anomaly and may be at increased risk of complications from diabetes .

Gestational diabetes

A diagnosis of GDM can be made in women who meet either of the following criteria :

FBS≥92 mg/dL , but <126 mg/dL at any gestational age (FBS≥126 mg/dL is consistent with overt diabetes)

At 24 to 28 weeks of gestation: 75 gram GTT with at least one abnormal result: FBS≥92 mg/dL ,
but <126 mg/dL or one hour ≥180 mg/dL or two hour ≥153 mg/dL .

Adverse outcomes

Several adverse outcomes have been associated with diabetes during pregnancy .

Importantly, the risk of these outcomes increases continuously as maternal FBS levels increase from the ≤75 mg/dL range, and as the one hour and two hour oral GTT values increase;

there is no clear threshold that defines patients at increased risk.

Adverse outcomes include:

Preeclampsia
Hydramnios
Fetal macrosomia
Fetal organomegaly
Birth trauma
Operative delivery
Perinatal mortality
Neonatal respiratory problems and metabolic complications (hypoglycemia, hyper bilirubinemia, hypocalcemia, erythremia

If maternal hyperglycemia is present during organogenesis because of overt (also termed pregestational) diabetes, there is an increased risk of miscarriage and congenital anomalies)

There are also potential long-term consequences to the infant, such as;

development of obesity and diabetes during childhood

impaired fine and gross motor functions,

and higher rates of inattention and/or hyperactivity .

RISK FACTORS FOR DIABETES DURING PREGNANCY

A FH of diabetes, especially in first degree relatives
Prepregnancy weight ≥110 percent of ideal body weight or BMI over 30 kg/m2 or significant weight gain in early adulthood and between pregnancies

Age greater than 25 years

Previous delivery of a baby greater than 9 pound[4.1 kg]

Personal history of abnormal glucose tolerance

RISK FACTORS FOR DIABETES DURING PREGNANCY

Member of an ethnic group with higher than the background rate of type 2 diabetes
Previous unexplained perinatal loss or birth of a malformed child
Maternal birth weight greater than 9 pounds [4.1 kg] or less than 6 pounds [2.7 kg]
Glycosuria at the first prenatal visit
Polycystic ovary syndrome
Current use of glucocorticoids
Essential hypertension or pregnancy-related hypertension

Excessive weight gain in early to mid pregnancy has been associated with impaired glucose tolerance at gestational diabetes screening , and increased prevalence of gestational diabetes.

SCREENING VERSUS DIAGNOSTIC TESTING

The purpose of screening is to identify asymptomatic individuals with a high probability of having or developing a specific disease.

SCREENING VERSUS DIAGNOSTIC TESTING

One step approach - The one step approach has been proposed by the IADPSG and endorsed by the ADA , but not by ACOG .

It was made practical by simplifying diagnostic testing for diabetes in pregnancy to the performance of a 75 gram two hour oral GTT and requiring only a single elevated value for diagnosis, rather than the previous three hour GTT requiring two elevated values for diagnosis.

Whom to screen

Universal screening appears to be the optimum approach because 90 percent of pregnant women have risk factors for glucose impairment during pregnancy

When to screen

Universal screening has traditionally been performed at 24 to 28 weeks of gestation .
Screening should be performed as early as the first prenatal visit if there is a high degree of suspicion that the pregnant woman has undiagnosed type 2 diabetes .
In particular, women with a history of GDM have a 33 to 50 percent risk of recurrence, and some of these recurrences may represent unrecognized type 2 diabetes .

diagnosis of gestational diabetes

A diagnosis of GDM is made at the initial prenatal visit if the FBS is ≥92 mg/dL,but <126 mg/dL

diagnosis of gestational diabetes

When overt diabetes or gestational diabetes has not been diagnosed with initial testing at the first prenatal visit, a 75 gram two hour oral GTT should be administered at 24 to 28 weeks of gestation to all patients

PATIENTS UNABLE TO TOLERATE ORAL HYPEROSMOLAR GLUCOSE

The highly concentrated hyperosmolar glucose solution can cause gastric irritation, delayed emptying, and gastrointestinal osmotic imbalance, leading to nausea and vomiting. Other types of oral screening (and glucose tolerance) tests have been proposed and are better tolerated, but appear to be less sensitive and have not been validated in large studies. These approaches typically use candy, a predefined meal, or commercial soft drinks instead of a standard glucose monomer or polymer solution

Serial glucose monitoring

Periodic random FBS and two-hour postprandial blood glucose testing is a monitoring option for women at high risk for gestational diabetes who are unable to take an oral glucose load.

There is a large overlap in the distribution of A1C values between women with normal, borderline abnormal, and mildly abnormal blood glucose levels.

Therefore, A1C is **not** a suitable test to detect mildly impaired glucose tolerance.

An A1C ≥6.5 percent suggests type 2 diabetes, and is one of the criteria for diagnosis of overt diabetes in pregnancy proposed by the IADPSG and endorsed by the ADA .

However, an A1C below this level should not be taken as evidence against the diagnosis of diabetes.

In fact, data are accruing that an A1C level greater than two standard deviations above the normal mean during pregnancy, when A1C levels are generally slightly lower than in the non pregnant state (in most laboratories this level is approximately 5.3 percent), may identify those women at risk for delivering a large for gestational age infant

Gestational Diabetes Mellitus

2.25 Test for undiagnosed prediabetes and diabetes at the first prenatal visit in those with risk factors using standard diagnostic criteria. B

2.26 Test for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant women not previously found to have diabetes. A

2.27 Test women with gestational diabetes mellitus for prediabetes or diabetes at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. B

Gestational Diabetes Mellitus (continued)

2.28 Women with a history of gestational diabetes mellitus should have lifelong screening for the development of diabetes or prediabetes at least every 3 year. B

2.29 Women with a history of gestational diabetes mellitus found to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent diabetes. A

GDM diagnosis (Table 2.7) can be accomplished with either of two strategies:

1. The “one-step” 75-g OGTT derived from the IADPSG criteria, or
2. The older “two-step” approach with a 50-g (nonfasting) screen followed by a 100-g OGTT for those who screen positive, based on the work of Carpenter and Coustan’s interpretation of the older criteria.

Table 2.7—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

If the plasma glucose level measured 1 h after the load is ≥130, 135, or 140 mg/dL (7.2, 7.5, or 7.8 mmol/L, respectively), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made when at least two* of the following four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria [193]):

- Fasting: 95 mg/dL (5.3 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 155 mg/dL (8.6 mmol/L)
- 3 h: 140 mg/dL (7.8 mmol/L)

GDM, gestational diabetes mellitus; GLT, glucose load test; OGTT, oral glucose tolerance test.
*American College of Obstetricians and Gynecologists notes that one elevated value can be used for diagnosis (189).

Classification and Diagnosis of Diabetes:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S15-S33

RATIONALE FOR TREATMENT

Identifying women with GDM is important because appropriate therapy can decrease maternal and fetal morbidity, particularly macrosomia .