

Diabetes in Pregnancy

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Fetal medicine

Introduction

- Diabetes and obesity is sharply increases due to dietary practices and reduced physical activity.
- specific risks of diabetes in pregnancy include :
 - spontaneous abortion
 - fetal anomalies
 - preeclampsia
 - fetal demise
 - macrosomia
 - neonatal hypoglycemia
 - hyperbilirubinemia,and neonatal respiratory distress syndrome.

Preconception Counseling

- Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible

*****ideally A1C = 6.5% (48 mmol/mol), to reduce the complications**

Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until a woman's treatment regimen and A1C are optimized for pregnancy

Spontaneous miscarriage
Congenital anomalies
Pre-eclampsia
**Progression of retinopathy in
pregnancy**

Switch to insulin if on oral agents

Folic Acid 5 mg/d (3 months pre-conception to 12 weeks post-conception)

Discontinue potential embryopathy medicine like

Ace-inhibitors/ARBs

Achieving a healthy weight is essential (obesity associated with adverse pregnancy outcomes)

Assess for and manage any complications :

Retinopathy: Need ophthalmological evaluation

Nephropathy: Assess creatinine + urine microalbumin / creatinine ratio (ACR)

(Women with microalbuminuria or overt nephropathy are at ↑ risk for hypertension and preeclampsia)

Classification of Diabetes Mellitus

Pregestational Diabetes Mellitus (type 1 and 2).

Gestational diabetes mellitus

Type 1 Diabetes

- **Type 1 diabetes have an increased risk of hypoglycemia in the first trimester**
- **The situation rapidly reverses by approximately 16 weeks as insulin resistance increases exponentially during the second and early third trimesters to 2–3 times the pre-prandial requirement**
- **Pregnancy is a ketogenic state and women are at risk for diabetic ketoacidosis (DKA) at lower blood glucose levels than in the nonpregnant state**
- **Women with type 1 diabetes should be prescribed ketone strips and receive education on diabetic ketoacidosis prevention and detection**
- **Retinopathy is a special concern in pregnancy. Rapid implementation of euglycemia in the setting of retinopathy is associated with worsening of retinopathy**

Type 2 Diabetes

- **Type 2 diabetes is often associated with obesity**
- **Glycemic control is often easier to achieve in women with type 2 diabetes than in those with type 1 diabetes but can require much higher doses of insulin**
- **Diabetes in pregnancy is associated with an increased risk of preeclampsia**

Gestational diabetes mellitus (GDM)

- **Defined as diabetes diagnosed during pregnancy that hyperglycemia first detected during pregnancy**
- **Formally recognized by O'Sullivan and Mahan in 1964**

GDM complications

- **Maternal hyperglycemia independently increased the risk of :**
- **preterm delivery**
- **caesarean delivery**
- **infants born large for gestational age**
- **admission to a neonatal intensive care unit**
- **neonatal hypoglycemia**
- **Hyperbilirubinemia**
- **Hypoglycemia**
- **Infection (vaginal candidiasis, UTI)**
- **Ketoacidosis**
- **Deterioration in retinopathy**
- **Increased proteinuria + edema**
- **Miscarriage**
- **Polyhydramnios**
- **Preeclampsia**
- **Thrombo-embolic and cardiovascular diseases**

Pathogenesis

- **Pregnancy is characterized by insulin resistance and hyperinsulinemia, which ensures an adequate supply of glucose for the fetus.**
- **The resistance due to placental secretion of diabetogenic hormones including growth hormone, corticotropin releasing hormone, placental lactogen, and progesterone, as well as increased maternal adipose deposition.**
- **These and other endocrinologic and metabolic changes ensure that the fetus has a good supply of fuel and nutrients at all times.**
- **Gestational diabetes occurs in women whose pancreatic function is not sufficient to secrete adequate amounts of additional insulin to overcome the insulin resistance created by changes in diabetogenic hormones during pregnancy.**

Metabolic changes during pregnancy:

- **there is a significant 30% increase in basal hepatic glucose production by the third trimester of pregnancy.**
- **50% to 60% decrease in insulin sensitivity in late gestation.**
- **Normal pregnancy is characterized by:**
 - **Mild fasting hypoglycemia**
 - **Postprandial hyperglycemia**
 - **Hyperinsulinemia**

women with GDM had Elevated Fasting plasma glucose, and elevated post-prandial glucose levels.

There is an increase in basal endogenous glucose production, similar to that observed in subjects with normal glucose tolerance.

the ability of insulin to suppress endogenous glucose production is decreased in women with GDM compared with a matched control group (approximately 80% versus 95%).

**Impairment of insulin secretion by the beta cells of the pancreas
Increased insulin resistance**

Screening for gestational diabetes

- Patients at high risk of developing GDM :
- A family history of diabetes, especially in first degree relatives
- BMI >30 kg/m²
- Age >25 years
- Previous delivery of a macrosomic baby (4 kg)
- Personal history of impaired glucose tolerance
- Previous unexplained perinatal loss or birth of a malformed infant
- Glycosuria at the first prenatal visit
- Polycystic ovary syndrome
- Current use of glucocorticoids
- Essential hypertension or pregnancy-related hypertension

Screening for gestational diabetes

ACOG recommended for diagnosis of GDM:

Universal screening for low risk pregnant at 24 to 28 weeks, via a two-step regimen, which consisting of:

- A 50-g, 1-hour glucose challenge test (GCT)
- For GCT results exceeding the selected threshold, a 100-g, 3-hour OGTT is performed.

Early pregnancy screening of women at high risk for pre gestational diabetes and GDM, or in areas in which the prevalence of insulin resistance is 5% or higher. (a 1-step approach can be used by proceeding directly to the 100-g, 3-hour OGTT)

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study recruited a large multinational cohort and clarified the risks of adverse outcomes associated with hyperglycemia

Glucose challenge test (GCT)

A 50-g, 1-hour GCT, which may be administered in the fasting or non fasting state.

(Sensitivity is improved if the test is performed in the fasting state)

A threshold value of $\geq 135 - 140$ mg/dL can be used.

For GCT results exceeding the selected threshold, a 100-g, 3-hour OGTT is performed.

If initial screening is negative, repeat testing is performed at 24 to 28 weeks.

3 hours Oral Glucose Tolerance Test(OGTT)

Assessment for GDM	Plasma Glucose Level after a 100-g Glucose Load mg/dL (mmol/L)
Fasting	95 (5.3)
1 hr	180 (10.0)
2 hr	155 (8.6)
3 hr	140 (7.8)

Test prerequisites:

1-hr, 50-g glucose challenge result ≥ 135 or 140 mg/dL

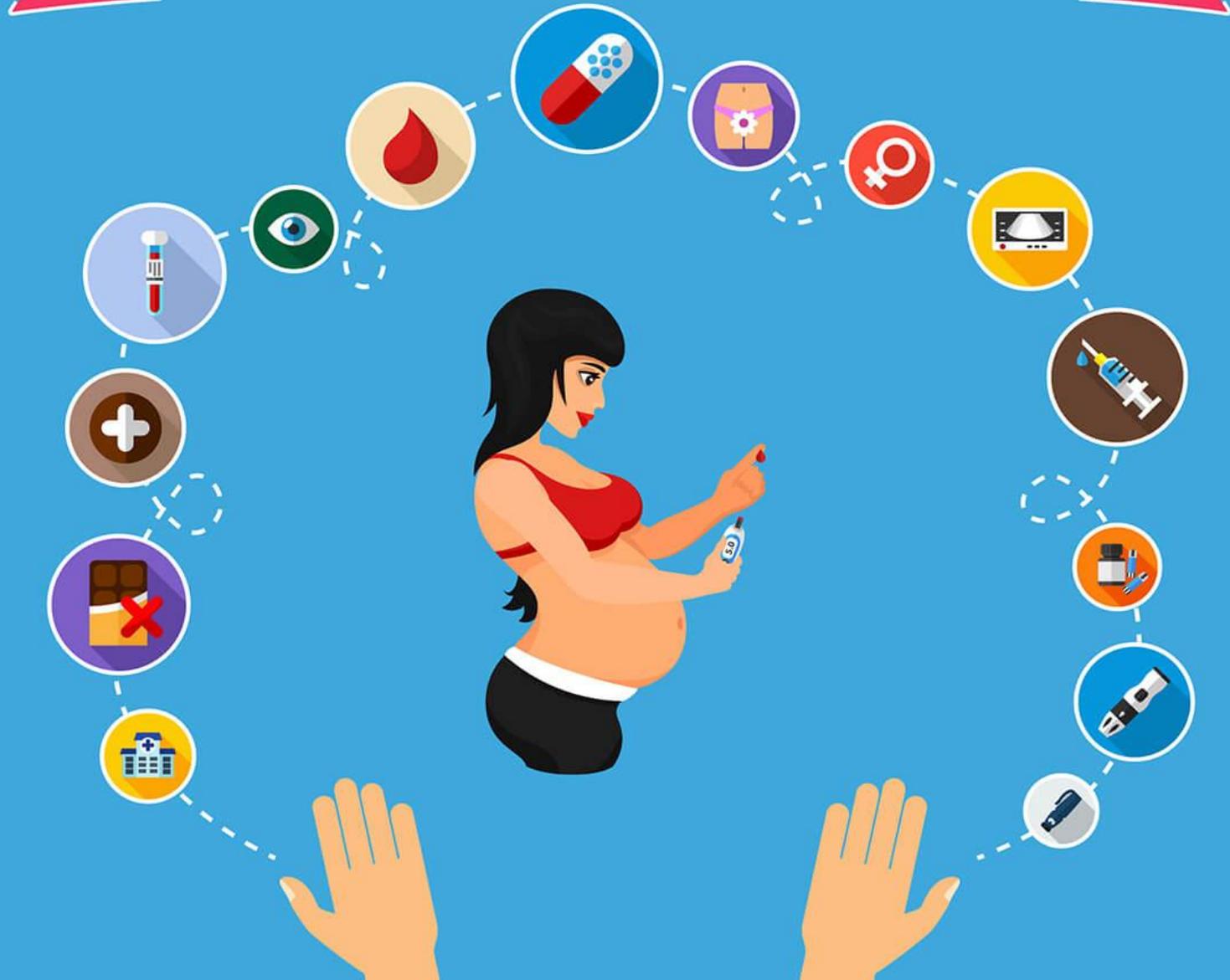
Overnight fast of 8-12 hr

Carbohydrate loading for 3 days, including ≥ 150 g of carbohydrate

Seated, not smoking during the test

Two or more values must be met or exceeded for a diagnosis of GDM

GESTATIONAL DIABETES



Management of pregnancies complicated by DM

- Periconceptional counselling
- Achieve normoglycemia
- Prevent ketosis
- Provide adequate weight gain
- Contribute to fetal well-being
- Prevention of obstetric complications.
- Timing the delivery.
- Select mode of delivery.
- Intensive neonatal care.

Glycemic Management During Pregnancy

Glycemic Targets during pregnancy:

Target glucose values

Fasting PG ≤ 95 mg/dL (5.3 mmol/L)

1h postprandial PG ≤ 140 mg/dL (7.8 mmol/L)

2h postprandial PG ≤ 120 mg/dL (6.7 mmol/L)

Glycemic Management During Pregnancy

- Measurements of glycohemoglobin have proved to be a useful index of glycemic control over 4 to 6 weeks.
- providing a numeric index of the patient's overall compliance and an indication of her average plasma glucose level over the past 30 to 60 days.
- Hb A1C, should be less than 6.0%.

Principles of Medical Nutritional Therapy

- avoid single, large meals containing foods with a high percentage of simple carbohydrates.
- Three major meals and three snacks are preferred.
- A bedtime snack may be needed to prevent accelerated (starvation) ketosis overnight.
- Carbohydrates should account for no more than 50% of the diet, with protein and fats equally accounting for the remainder.

Principles of Medical Nutritional Therapy

Recommended total weight gain and caloric intake for singleton Pregnancies according to pre-pregnancy BMI

Pre-Pregnancy BMI	Recommended range of total weight gain (Kg)	Recommended caloric requirement
BMI <18.5	12.5 – 18.0	up to 40 kcal/kg/day
BMI 18.5 - 24.9	11.5 – 16.0	30 kcal/kg/day
BMI 25.0 - 29.9	7.0 – 11.5	22 - 25 kcal/kg/day
BMI ≥30	5.0 – 9.0	12 – 14 kcal/kg/day

Insulin therapy

- **recommended when medical nutrition therapy fails to maintain self-monitored glucose at the acceptable levels.**
- **Any insulin regimen for pregnant women requires combinations and timing of insulin injections different from those that would be effective in the non pregnant state.**
- **The regimens must be modified continually as the patient progresses from the first to the third trimester and as insulin resistance rises.**
- **The regimen should always be matched to the patient's unique physiology, work, rest, and food intake schedule.**

Insulin therapy

- In the 1st trimester from 6-10 weeks, progressively reduce the insulin dose by a total of 10% to 25% to avoid hypoglycemia.
- Insulin requirements normally peak at 36 weeks gestation and drop significantly thereafter.
- A combination of short- and intermediate-acting insulins can be employed to maintain glucose levels in an acceptable range.
- Approximately two thirds of the daily insulin dose is given in the morning and one third in the afternoon and at bedtime.
- A typical total insulin dose is 0.6 U/kg in the 1st trimester, but this must be increased weekly or every other week with pregnancy duration from the 2nd trimester onward.

Insulin therapy

The total first dose of insulin is calculated according to the patient's weight as follow:

- In the 1st trimester weight x 0.6
- In the 2nd trimester..... weight x 0.7
- In the 3rd trimester..... weight x 0.8

Use of Oral Hypoglycemic Agents

- **Glyburide :**
 - maternal use of glyburide was not associated with an excess risk of neonatal hypoglycemia or congenital anomalies.
 - minimal transport across the human placenta.
 - glyburide should be taken at least 30 minutes before a meal.
- **Metformin :**
 - equivalent to insulin in effectiveness.
 - Recommended dosing begins with 500 mg twice daily.
 - crosses the placenta.

Use of Oral Hypoglycemic Agents

- **α -Glucosidase Inhibitors:**
 - inhibit pancreatic amylase and α -glucosidase enzymes in the small intestine.
 - delaying cleavage of complex sugars to monosaccharides and reducing the increase of blood glucose levels after a meal.
 - Acarbose is given before meals, initially in an oral dose of 25 mg three times daily up to a maximum of 100 mg three times daily.

Fetal complication with diabetes

- 1. Miscarriage .**
- 2. Increased congenital malformation (cardiac and NTD)**
- 3. Preterm delivery.**
- 4. Intra uterine death.**
- 5. Macrosomia.**
- 6. Shoulder dystocia**

Fetal complication with diabetes

Maternal hyperglycemia

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Fetal hyperglycemia

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Fetal pancreatic beta-cell hyperplasia

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Fetal hyperinsulinemia

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**Macrosomia, organomegaly,
polycythemia, hypoglycemia, RDS**

Fetal Surveillance in Pregnancies complicated by diabetes

- **The goals are to accomplish the following:**
 - ✓ **Verify fetal viability in the first trimester**
 - ✓ **Validate fetal structural integrity in the second trimester**
 - ✓ **Monitor fetal growth during most of the third trimester**
 - ✓ **Ensure fetal well-being in the late third trimester**

Fetal Surveillance in Pregnancies complicated by diabetes

Weeks of Gestation	Test
Preconception	Maternal glycemic control
8-10	Sonographic crown-rump measurement , fetal viability
18-20	High-resolution sonography to detect congenital anomalies
20-22	Fetal cardiac echography
28	Baseline sonographic growth assessment of the fetus; daily fetal movement counting
32	Repeat sonography for fetal growth
34	weekly biophysical profile
36	Estimation of fetal weight, head and abdominal circumference percentiles by sonography
37-38	delivery for patients with poor glucose monitoring compliance, persistently poor glycemic control, or suspicious findings on fetal biophysical testing
39-40	Delivery for patients in good glycemic control

Timing and Route of Delivery

- **Because of the apparent delay in fetal lung maturity in diabetic pregnancies, delivery before 39 weeks should be performed only for compelling maternal or fetal reasons.**
- **For women who remain euglycemic with diet, discuss induction of labor at 40 weeks, and recommend elective induction when she reaches 41 weeks of gestation.**
- **When glucose levels are medically managed with insulin or oral agents, undergo induction of labor at 39 weeks.**
- **If a concomitant medical condition (eg, hypertension) is present or glycemic control is suboptimal, induction of labor at 37-38 weeks of gestation after confirmation of fetal lung maturity.**

Intrapartum Glycemic Management

- 1. Withhold AM insulin injection.**
- 2. Begin and continue glucose infusion (5% dextrose in water) at 100 mL/hr throughout labor.**
- 3. Begin infusion of regular insulin at 0.5 U/hr.**
- 4. Begin oxytocin as needed.**
- 5. Monitor maternal glucose levels hourly.**
- 6. Adjust insulin infusion according to blood glucose readings**

Intrapartum Glycemic Management

- **When cesarean delivery is planned:**
 - 1.** The procedure should be performed early in the day to avoid prolonged periods of fasting.
 - 2.** No morning insulin or oral hypoglycemic agents should be taken.
 - 3.** Begin and continue glucose, with short-acting insulin given on a sliding scale as needed every 1 to 4 hours to maintain the maternal plasma glucose level in the range of 80 to 160 mg/dL.

Postpartum Management

- **Women with pregestational diabetes should be carefully monitored postpartum as they have a high risk of hypoglycemia, and should be returned to their pre pregnancy doses of insulin.**
- **All women should be encouraged to breast-feed, since this may reduce offspring obesity, especially in the setting of maternal obesity.**
- **Oral hypoglycemic agents may be used during breast-feeding.**
- **Women should be screened with OGTT between 6 weeks-6 months postpartum to detect prediabetes and diabetes.**
- **Discuss increased long-term risk of diabetes – Importance of returning to pre-pregnancy weight.**

The end