

Diabetes in Pregnancy

Done by: Haneen alsubki , Layla AlBreacan , Ghadah Almazrou , Monera Alayuni

Revised by: Allulu Alsulayhim , Dina Aldussary

References: 436 doctor's slides and notes , Kaplan

Color code: Notes | Important | Extra | Kaplan

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Objectives:

1. Define GDM and Pre-gestational DM
2. Identify how common is GDM in Saudi Arabia and worldwide.
3. Discuss how pregnancy predisposes to the development of GDM
4. Describe the maternal and fetal complications of D.M.
5. Describe the screening and diagnostic tests for GDM.
6. Identify the importance of multidisciplinary approach of management of these cases.

Terminology:

- 1st trimester → 14 weeks
- 2nd trimester → 14-26 weeks
- Full term → 37-42 weeks
- >42 weeks → post term
- Post date → after the expected date of birth
- <37 weeks → preterm
- <20 weeks → abortion
- >20 weeks → labor

Types of Diabetes

	Definition
Type 1 Diabetes	Early onset, insulin dependent. They have it before birth and discover it in childhood.
Type 2 Diabetes	<ul style="list-style-type: none"> ● Late onset, insulin non-dependent ● Middle aged or elderly. If discovered late they start with insulin but commonly start with diet modifications, then oral hypoglycemic agents then insulin.
Gestational Diabetes	<ul style="list-style-type: none"> ● The most common type with onset during pregnancy. Pathophysiology involves the diabetogenic effect of human placental lactogen (hPL), placental insulinase, cortisol, and progesterone. Thirty-five percent of women with GDM will develop overt diabetes within 5 to 10 years after delivery. ● Carbohydrate intolerance that occurs in pregnancy after the 24th week of gestation ● So pregnancy doesn't cause diabetes, patient is usually prediabetes prior to pregnancy and pregnancy shows it as GD. after pregnancy we don't consider her diabetic but has glucose intolerance. So she doesn't need intervention. ● 50% of GD patients will be type 2 diabetics later in their life, so in counseling we must inform patients about that.

Carbohydrate Metabolism in Pregnancy

- Pregnancy is potentially diabetogenic
- Diabetes may be aggravated by pregnancy the patient may be diabetic controlled on diet prior to pregnancy, but after pregnancy her glucose levels start shooting up and now she needs to be medicated. But as soon as she gives birth (the placenta is out) she won't be needing medications anymore. After 6 weeks of birth we check her levels again to check if her glucose levels are still high. Then will be labeled as type 2.
- Normal pregnancy is characterized by:
 1. Mild fasting hypoglycemia, ↑ insulin level (dizziness in 1st trimester) because insulin resistance causes a positive feedback for insulin secretion and thus it increases.
 2. Postprandial hyperglycemia
 3. Hyperinsulinemia
 4. Suppression of glucagon (role of glucagon in pregnancy is not fully understood)

Table I-10-4. White Classification of Diabetes in Pregnancy

Class A1	GDM with normal FBS not requiring insulin
Class A2	GDM with elevated FBS requiring insulin
Class B	Overt DM onset after age 20 years and duration <10 years
Class C	Overt DM onset age 10–19 years or duration 10–19 years
Class D	Overt DM onset before age 10 years or duration ≥20 years
Class E	Overt DM with calcified pelvic vessels
Class F	Overt DM with nephropathy
Class R	Overt DM with proliferative retinopathy

From KAPLAN p97

Diagnosis During Pregnancy

- Diabetes can be diagnosed for the 1st time during pregnancy. **If diagnosis is prior to 24 weeks of gestation, this is overt diabetes (or type 2 DM) and not gestational.** Because human placental lactogen is high at 24 weeks. So we test for it at 24-26 weeks and not earlier so I don't miss diagnose her. If it's high then GD diagnosis is confirmed.
- Patients presenting with the following symptoms are easy to diagnose:
 - I. Hyperglycemia
 - II. Glucosuria in non-pregnant it's abnormal, in pregnant ladies (up to a certain limit) it's normal because of increased renal clearance and GFR. But we should not ignore it. If her history is suggestive of diabetes I should investigate more.
 - III. Ketoacidosis
- Patients with mild carbohydrate metabolic disturbance need to be screened early based on the following risk factors:
 - I. Strong family history of diabetes
 - II. History of giving birth to large infants (**fetal macrosomia**)
 - III. Obesity
 - IV. Unexplained fetal loss
 - V. Glucosuria which does not always indicate impaired glucose tolerance, but rather \uparrow glomerular filtration rate. Nonetheless the detection of glucosuria in pregnancy mandates further investigations.
 - VI. Age **>30 years**
 - VII. **Previous history of GDM**
 - VIII. Polyhydramnios
 - IX. previous traumatic delivery

Screening for Gestational Diabetes

- Screening is performed on all pregnant women 24–28 weeks' gestation when the anti-insulin effect of hPL is maximal. On patients with risk factors it is performed on the first prenatal visit then repeated at 24–28 weeks if initially negative.

50 gm glucose challenge test (Old screening test)

- Done between 24-28 weeks and a Plasma value of >7.8 or 140 mg/dl (not fasting) not diagnostic. The screening test is a 1-h 50-g oral glucose challenge test (OGTT) with normal values being <140 mg/dL. This does not need to be in a fasting state.
- Old diagnostic test The 3hr **100 gm** Oral Glucose Tolerance test after 8hrs of fasting patients don't tolerate it, they throw up and don't complete it)
 - FBS 5.8
 - 1 hr 10.6
 - 2 hr 9.2
 - 3 hr 8.1
- Impaired glucose tolerance is diagnosed if **only one value** is abnormal.
- At least **2 values** have to be abnormal (GDM is diagnosed) regardless of which ones they are. (diagnostic test)

2-h 75g OGTT (standard of care and what's currently used)

- 2-h **75-g** OGTT be performed on all women at 24 to 28 weeks' gestation not previously found to have overt diabetes or gestational diabetes mellitus (GDM) during early testing in their current pregnancy.
- 8 - 14 hours and after at least 3 days of unrestricted diet (>150 grams carbohydrates per day) and unlimited physical activity
- **One** or more of the values from a 75-g OGTT must be equaled or exceeded for the diagnosis of GDM
- A fasting plasma glucose > 7.0 mmol/L (126 mg/dl) is diagnostic of overt diabetes
- Screening postpartum is done with 75 gm glucose at 6 weeks after delivery

2 hour 75-g Oral Glucose Tolerance Test, OGTT, GTT (plasma)

Units	Fasting	1 hour	2 hour
mg/dL	92	180	153
mmol/L	5.1	10	8.5

1st we take a fasting reading and then we give the 75g glucose and we take a reading after 2 hrs.

Effect of pregnancy on DM¹

- Insulin antagonism happens in pregnancy due to the action of HPL (produced by the placenta as well as estrogen, Progesterone → difficulty in controlling diabetes.
- Increase in infection rate

A. Maternal effects:

- I. Pre-eclampsia (after 20 weeks) obstetric emergency / eclampsia increases 4 folds, even in the absence of vascular disease Infections (lower immunity) comes with recurrent vaginal discharge and candidiasis. Pregnancy and hypertension are related, if a patient develops diabetes they're at risk of becoming hypertensive and vice versa.
- II. Injury to the birth canal secondary to macrosomia (if diabetes is uncontrolled the baby will be big and cause birth canal injuries)
- III. ↑ Incidence of C/S baby is big and can't pass the pelvis so C-section is indicated
- IV. Hydramnios (increase amniotic fluid) leading to cardiorespiratory symptoms. Membrane rupture and early labor and prematurity and might even die
- V. ↑ Maternal Mortality (diabetic ketoacidosis, anesthesia complications during C/S)

B. Fetal and Neonatal Effects:

- I. ↑ Risk of congenital anomalies especially cardiac and CNS Type 1 is the most related to congenital anomalies cuz it happens during organogenesis of the fetus, but GD happens at week 24 so after organogenesis. after type1 type 2 is also related to congenital anomalies.
- II. ↑ Risk of abortion
- III. ↑ Risk of perinatal death
- IV. ↑ Risk of preterm labor
- V. ↑ Neonatal morbidity, for example:
 - birth injury – shoulder dystocia (baby gets stuck after his head passes so we fracture his clavicle to help him get out, can cause brachial plexus injuries)
 - RDS (delayed lung maturity): Caused by delayed pulmonary surfactant production.
 - Metabolic such as hypoglycemia: Caused by persistent hyperinsulinemia from excessive prenatal transplacental glucose. baby is exposed to his mom's high blood

¹ When approaching any medical disease in pregnancy we think about it in 3 ways:

- What's the effect of the disease on the mother
- What's the effect of the disease on the baby
- What's the effect of the pregnancy on the disease
- and in some cases what's the effect of the medications on the pregnancy. (epilepsy, SLE.. etc)

glucose levels and produces lots of insulin so as soon as the baby's circulation is detached from his mother he's exposed to high insulin and it causes hypoglycemia) so pediatricians check babies of diabetic mothers right after birth to see if the need glucose)

- VI. Inheritance of diabetes or its predisposition babies are exposed to have type 2 and GD later in their life.
- Hypocalcemia caused by failure to increase parathyroid hormone synthesis after birth.
 - Polycythemia caused by elevated erythropoietin from relative intrauterine hypoxia.
 - Hyperbilirubinemia caused by liver immaturity and breakdown of excessive neonatal red blood cells (RBCs).

- It is to be noted that congenital anomalies and abortion are not risks with gestational diabetes.

Management of Diabetes in Pregnancy

The most significant factor in management of diabetic pregnancies is achieving maternal euglycemia.

If newly diagnosed:

- Put patient on diet x 3 days
- 30-35 kcal /kg of **ideal** body wt.
 - 40 – 50 % carbs
 - 12 – 20 % proteins
 - 30 – 35 % Fat
- **American Diabetes Association diet:** Educate patient regarding spreading calories evenly throughout the day, encourage complex carbohydrates. Eighty percent of patients with GDM can maintain glucose control with diet therapy.
- **Home blood glucose monitoring:** Patient checks her own blood glucose values at least four times a day with target values of FBS <90 mg/dL and 1 h after meal of <140 mg/dL.
- Do BSS (blood sugar series, for 24 hrs fasting reading then have her eat her regular meals and take a reading 2 hrs after each meal) if controlled → continue with monitoring
- if not → insulin (doses depending on when her readings are high, if it's at night then her dose should be at night)
- **Insulin therapy:** Start subcutaneous insulin with type 1 and type 2 DM and with GDM if home glucose values are consistently above the target range. Initial dose is based on pregnancy trimester.
 - **Total daily insulin units** = actual body weight in kilograms × 0.8 (first trimester), 1.0 (second trimester), or 1.2 (third trimester)

2/3 am 2/3 NPH, 1/3 Reg.

1/3 pm ½ NPH, ½ Reg.

Insulin is divided with two thirds of total daily dose in morning (split into 2/3 NPH and 1/3 regular) and one third of total daily dose in evening (split into 1/2 NPH and 1/2 regular). Insulin is a large molecule and does not cross the placenta. Insulin requirements will normally increase through the course of the pregnancy. 15% of patients with GDM will require insulin.

- Oral hypoglycemic agents. These were contraindicated in the past because of concern that they would cross the placenta and cause fetal or neonatal hypoglycemia.
- Glyburide appears to cross the placenta minimally, if at all, and is being used for patients with GDM who cannot be controlled by diet alone.

Table I-10-5. Gestational Diabetes

Questions	Criteria/Problems	Diag/Mgmt
1-hr 50g OGTT Screening test	<140 mg/dL	GDM ruled out
3-hr 100g OGTT Definitive diagnosis	≥2 values ↑	GDM diagnosed
Home glucose monitoring	Mean glucose values FBS >90; 1 hr pp >140	Start insulin or glyburide
Fetal demise risk factors	1: needs insulin or glyburide 2: HTN 3: previous demise	Starting 32 wk NST & AFI 2/wk
L&D problems	Arrest stage 1 or 2 Shoulder dystocia	CS if estimated fetal weight >4500 g
Post partum management	Prevent postpartum hemorrhage	FBS ≥126 mg/dL 2 hr 75 gm OGTT

From KAPLAN p98

Antepartum Overt Diabetes Management:

- **Hemoglobin A1c:** Obtain a level on the first visit to ascertain degree of glycemic control during the previous 60–120 days. Repeat levels each trimester.
- **Renal status:** Obtain an early pregnancy baseline 24-h urine collection for total protein and creatinine clearance.
- **Retinal status:** Obtain an early pregnancy ophthalmologic fundoscopic evaluation for proliferative retinopathy.
- **Home blood glucose monitoring:** Patient checks her own blood glucose values at least 4 times a day with target values of FBS 60–90 mg/dL and 1 h after a meal of <140 mg/dL.

Antepartum Fetal Assessment:

- **Anomaly screening:** Anomalies are mediated through hyperglycemia and are highest with poor glycemic control during embryogenesis. Anomalies are not increased in GDM because

hyperglycemia is not present in the first half of pregnancy. **Most common fetal anomalies with overt DM are NTD and congenital heart disease.** An uncommon anomaly, but one highly specific for overt DM, is caudal regression syndrome. Obtain a quadruple-marker screen at 16–18 weeks to assess for NTD as well as a targeted ultrasound at 18–20 weeks to look for structural anomalies. **If the glycosylated hemoglobin is elevated, order a fetal echocardiogram at 22–24 weeks to assess for congenital heart disease.**

- **Fetal growth:** Monthly sonograms will assess fetal macrosomia (most commonly seen) or IUGR (seen with longstanding DM and vascular disease).
- **Fetal surveillance:** Start weekly NSTs and amniotic fluid index (AFIs) at 32 weeks if taking insulin, **macrosomia**, previous stillbirth, or hypertension. Start NSTs and AFIs at 26 weeks if small vessel disease is present or there is poor glycemic control. Biophysical profiles can be performed at the time of monthly sonograms.

Timing and Mode of Delivery

- **Timing of delivery:** Fetal maturity is often delayed in fetuses of diabetic mothers, yet prolonging the pregnancy may increase the risk of stillbirth; delivery planning is a result of balancing these factors. The target delivery gestational age is 40 weeks, but may be necessary earlier in the presence of fetal jeopardy and poor maternal glycemic control. An amniotic fluid lecithin to sphingomyelin (L/S) ratio of 2.5 in the presence of **phosphatidyl glycerol** ensures fetal lung maturity.
- **Mode of delivery:** **The cesarean section rate in diabetic pregnancies approaches 50% because of fetal macrosomia, arrest of labor, and concern regarding shoulder dystocia.**
- IOL at completed 38 weeks for diabetics on oral hypoglycemic/ insulin (if she shows signs of uncontrolled diabetes such as large baby, polyhydramnios I intervene early on to avoid sudden death)
- IOL at term for diabetics on diet. Provided sugar is well controlled.
- C/S for **ONLY** for obstetric indications (very huge baby unable to pass vaginally)
- Glycemic control. Maintain maternal blood glucose levels between 80 and 100 mg/dL using 5% dextrose in water and an insulin drip.

Postpartum Management:

- **Postpartum hemorrhage:** Watch for uterine atony related to an overdistended uterus.
- **Hypoglycemia:** Turn off any insulin infusion because insulin resistance decreases with rapidly falling levels of hPL after delivery of the placenta. Maintain blood glucose levels with a sliding scale.

Management before conception

- Pre conceptual counseling:
 - I. Reduction of weight
 - II. Exercise
- Blood sugar control patient should control her blood sugar before pregnancy because of high chances of congenital anomalies.
- HbA1c
- Early dating and FU of the pregnancy

Preconception Anomaly Prevention:

- **Anomaly risk:** Women with overt diabetes are at increased risk of fetal anomalies. This risk can be minimized by lifestyle modification.
- **Euglycemia:** Maintaining glucose values at normal levels reduces anomaly risk close to that of non diabetes; start 3 months prior to discontinuing contraception.
- **Folate supplementation:** Folic acid, 4 mg a day, should be started 3 months prior to conception to prevent both fetal neural tube defects, as well as congenital heart defects.

MCQs

Q1: A 35-year-old lady G4 P2 +1, presented at 30 weeks' gestation to the clinic with abnormal OGTT result that ultimately required insulin therapy. Which one of the following places her fetus at an increased risk?

A- Congenital heart disease

B- Intrauterine growth restriction

C- Down syndrome

D- Macrosomia

Answer: D

Q2: A lady with diabetes on insulin. What fetal anomalies that she might have when she get pregnant?

A- Renal agenesis. B- Cataract. C- Caudal regression. D- Pyloric stenosis.

Answer: C

Q3: 27-year-old Pregnant lady, she is diabetic on insulin, which one of the following complication might she has?

A- Intrauterine growth restriction (IUGR).

B- Polycystic ovarian disease (PCO)

C- Respiratory distress syndrome.

Answer: A

Q4: A known diabetic is G3 P2 + 0 , both were normal deliveries. She has been in insulin throughout this pregnancy, which has been otherwise uneventful. She is now 40 weeks of gestation. Which one of the following is the best management?

A- Cesarean section.

B- Blood sugar series.

C- Induction of labor.

D- Wait for spontaneous labor.

Answer: C