DR Omar Abu-Azzam

Diabetes in Pregnancy

Introduction

- An epidemic of diabetes and obesity is sweeping the globe.

(dietary practices and reduced physical activity).

- In 2011, 366 million people worldwide had diabetes; by 2030, that number is projected to almost double to 552 million.
- Studies suggest that the prevalence of diabetes among women of childbearing age is increasing.
- fetal and neonatal mortality remain threefold or fourfold higher for mothers with type 1 or type 2 diabetes than for the normoglycemic population, but it is preventable or at least reducible by meticulous prenatal and intrapartum care.

Classification of Diabetes Mellitus

- The classification of diabetes are issued and updated periodically by the American Diabetes Association (ADA),and includes four clinical types:

1. **Type 1 diabetes mellitus (T1DM),** which results from pancreatic beta cell destruction usually leading to absolute insulin deficiency.
2. **Type 2 diabetes mellitus (T2DM),** which results from a progressive insulin secretory defect on the background of insulin resistance.
3. **Diabetes from other causes**, such as genetic defects in beta cell function, genetic defects in insulin action, diseases of the exocrine pancreas (cystic fibrosis, chronic pancreatitis), and drug- or chemical-induced conditions.
4. **Gestational diabetes mellitus (GDM),** which is defined as diabetes diagnosed during pregnancy that is not clearly overt diabetes.

Criteria for the Diagnosis of Diabetes

- An HBA1C level ≥6.5%.
- A fasting plasma glucose (FPG) measurement ≥126 mg/dL (7.0 mmol/L). (Fasting is defined as no caloric intake for at least 8 hr)
- A 2-hr plasma glucose measurement ≥200 mg/dL (11.1 mmol/L) during an OGTT.
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose level ≥200 mg/dL (11.1 mmol/L).

Classification of DM in pregnancy

Pregestational diabetes	Gestational diabetes
The disease exists prior to pregnancy •Type 1 diabetes •Type 2 diabetes	The disease diagnosed or develops for the first time during the pregnancy

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

Metabolic changes in gestational diabetes:

- women with GDM had **Elevated FPG, 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.

Incidence

- Diabetes is the most common clinical condition encountered during pregnancy **(0.5 – 5%).**
- It is estimated that **3% to 25%** of a population of pregnant women will be diagnosed with GDM.
- Clinical recognition of GDM is important because therapy can reduce pregnancy complications and potentially reduce long-term sequelae in the offspring.

Screening for gestational diabetes

Patients at high risk of developing GDM :

- A family history of diabetes, especially in first degree relatives
- BMI >30 kg/m ^{2}
- 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 pregnants 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)

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 **≥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 8-14 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

Maternal complication with diabetes

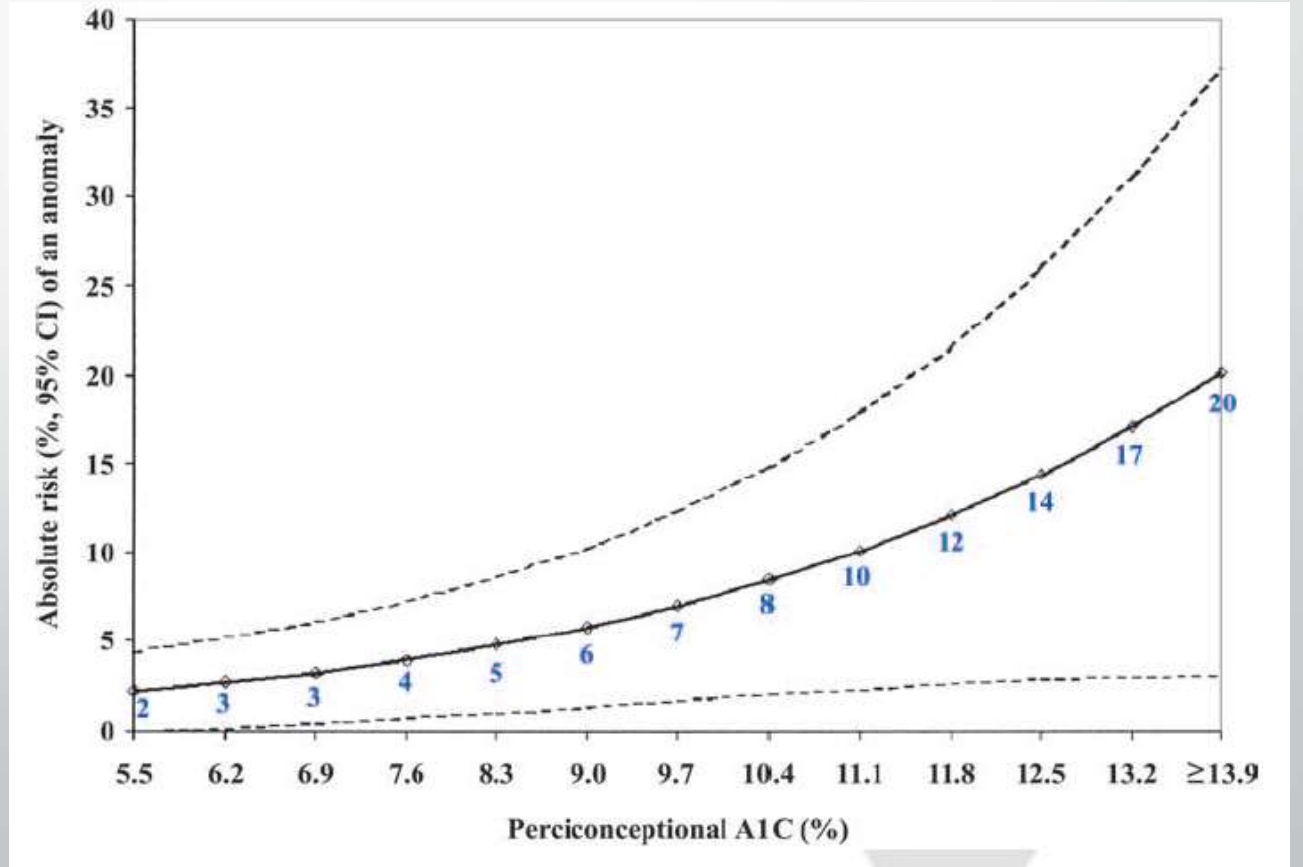
1. Hypoglycemia
2. Infection (vaginal candidiasis, UTI)
3. Ketoacidosis
4. Deterioration in retinopathy
5. Increased proteinuria + edema
6. Miscarriage
7. Polyhydramnios
8. Preeclampsia
9. Increased caesarean rate
10. Thrombo-embolic and cardiovascular diseases

Management of pregnancies complicated by DM

- **Objectives :**
  - ✓ Preconceptional 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.

Preconception Counseling for Pregestational Diabetes

1. Attain a preconception A1C of ≤7.0%, to decrease the risk of:
   - Spontaneous miscarriage
   - Congenital anomalies
   - Pre-eclampsia
   - Progression of retinopathy in pregnancy



Preconception Counseling for Pregestational Diabetes

2. Switch to insulin if on oral agents.
3. Folic Acid 5 mg/d (3 months pre-conception to 12 weeks post-conception).
4. Discontinue potential embryopathic meds:
   - ✓ Ace-inhibitors/ARBs (prior to or upon detection of pregnancy)
   - ✓ Statin therapy

Preconception Counseling for Pregestational Diabetes

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

6. 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)

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 A_{1C}, 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 hyperinsulinaemia

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Macrosomia,organomegaly,

polycythaemia, 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.
- ACOG has recommended that primary cesarean delivery be discussed with diabetic patient with an EFW greater than 4500 g.
- The decision to attempt vaginal delivery or perform a cesarean delivery depends on the patient's obstetric history, the best EFW, and the fetal adipose profile (i.e., abdomen larger than head).

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 **prepregnancy 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.

Neonatal complications with diabetes

1. Birth asphyxia and birth trauma.
2. RDS.
3. Hypoglycemia.
4. Hypomagnesaemia.
5. Polycythemia.
6. Hyperbilirubinaemia.
7. Hypocalcemia.
8. Cardiomyopathy.