OB/GYN

MEDICINE
KING SAUD UNIVERSITY

Diabetes in Pregnancy

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References: 437 Lectures And Notes, Hacker & Moore's Essentials of Obstetrics and Gynecology

Color code: Notes | Important | Extra | Book

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Objectives:

Not given

Diabetes Mellitus

- Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from **defects in insulin secretion, insulin action, or both**.
- The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction even without pregnancy there is a damage to any adult either male or female , and failure of various organs, especially the **eyes**, **kidneys**, **nerves**, **heart**, and **blood vessels**.

If that the case in someone with diabetes , then definitely when that person get pregnant there will be a contribution on the fetal side as well

- It is a common disease with a world prevalence of at least 100 million people, and this figure may double in the next decade. It is very common in Saudi Arabia,it has many risk factors as part of it is related to lifestyle, and it could be inherited
- The incidence of pre-gestational diabetes diabetes before pregnancy is:

  1-2% in Europe 3-8% in North America.
- Before insulin, 30% of pregnant diabetic mothers were dying in diabetic coma and PNMR 40-60%. Why did these pregnant women used to die during pregnancy and they are non diabetic before pregnancy ? because even if she is not diabetic some of them will discover that they are diabetic or have glucose intolerance during pregnancy. So the demand increases and the hormonal changes will expose the woman who has glucose intolerance , so if she is diabetic already that means her demand will increase, and if she can't compensate for that she will go into a coma .The message here is that diabetes is a stage where a woman having an underlying or a subclinical glucose intolerance will show up during pregnancy.

Types of Diabetes	
Type 1 Diabetes	Insulin dependent (B cell destruction), **characterized by** absolute deficiency of insulin secretion (5-10% of those with diabetes). From childhood . The only way of treatment is insulin.
Type 2 Diabetes	Non-insulin dependent, **characterized by** increased insulin resistance and relatively reduced insulin secretion. Can be managed by diet or oral hypoglycemic.
Gestational Diabetes	It is a mixed of Type 1 and Type 2. The treatment for GD is variable,it could be only diet or hypoglycemic or insulin ○ A state of increased insulin resistance- A1 (Diet), A2 (Insulin). ○ Increased insulin resistance during pregnancy is related to human placental lactogen, progesterone, prolactin, cortisol and tumor necrosis factor.

Other types	○ Pancreatic disease eg, pancreatitis. ○ Drug induced eg, steroids (when patients use steroids their blood sugar control becomes more difficult or they might be more prone to develop DM later in life), diuretics. ○ Endocrine disease eg, acromegaly, cushing's syndrome (insulin resistance), thyrotoxicosis ○ Abnormal insulin or its receptor (rare). ○ Genetic disorders eg, lipoatrophic diabetes (rare). ○ Malnutrition related. severe cases like in african countries with the shortage of supply or dietary

Gestational Diabetes

Is Gestational Diabetes a disease?

Gestational Diabetes is a diagnosis still looking for a disease.

There is debate whether it is a disease, a syndrome or something that happens for a period of time and goes, bc we know that once the patient is pregnant and labelled as GD, after delivery she can go completely normal and not diabetic

Arguments in favor:

- 2 fold increase for pregnancy induced hypertension Because of that, GD is considered a **disease** since it has a morbidity as well
- Macrosomia (big babies) in up to 40% of GDM offspring.
- Significantly increased risk of **shoulder dystocia.** The head will go out from the birth canal first and the anterior shoulder will be stuck during delivery below the symphysis pubis and the baby won't come out in macrosomic babies more prone to shoulder dystocia than the big babies, why ? Because the fat distribution in macrosomic babies is different (they have disproportionate fat distribution), macrosomic babies have central obesity and fat distributed more in the shoulders .
- Increased polyhydramnios (increased amniotic fluid (the maximum is 23-24 cm), preterm delivery, and cesarean section in GDM, bleeding and more obstetric complications whether it is for the mother or the baby.
- Increased admission in NICU. bc hypoglycemia, hyperglycemia or withdrawal effect

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset of or first recognition during pregnancy the only time we give this diagnosis is during pregnancy and usually after 20 -24 weeks

If a pregnant woman showing signs of glucose intolerance very early during her pregnancy like in her first trimester (eg. in the first 8 weeks) then probably she is type 2 DM but wasn't recognized, and became recognized during pregnancy, **but** you can't say that unless we conform it after delivery, so as long as she is pregnant we would call it GD.

but if pre pregnancy she had a normal glucose tolerance and after pregnancy she developed diabetes then we call it Gestational diabetes.

- The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy or not. the term apply on whatever treatment you give, as long as pre pregnancy she wasn't diabetic, and glucose intolerance happened during pregnancy then it will be Gestational diabetes (GDM)
- It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy.
- GDM represents nearly 90% of all pregnancies complicated by diabetes. The prevalence may range from 1-14% of pregnancies, depending on the population studied.

If I bring a woman from saudi Arabia and compare them to women from Europe, I expect to see more GD in saudi, because the prevalence of DM is higher.

- In the US, GDM complicates 4% of all pregnancies, resulting in 135,000 cases annually. In Canada, the prevalence of GDM in the non-Aborginal (immigrants from Europe) population varies from 3.5-3.8% and in Aborginal(الهنود الحمر) populations from 8-18%.

Because Aboriginal lifestyle is similar to Saudi Arabia, they tend to be more obese and have more DM.

Diabetes and Pregnancy

- 0.2-0.3% of women of reproductive age have diabetes prior to conception.
- **30-50%** of patients with gestational diabetes **develop type II diabetes later in life**. very imp counseling point , as GD will probably disappear after pregnancy, however there is a chance of developing DM later in life. It is imp point because if I told the patient that she might modify her lifestyle so by the time she develop DM she will be already having a good healthy lifestyle , and she might not need medications and can be control it by diet
- Management of gestational diabetes is as for established diabetes dietary advice.
- Protein hormones (insulin, glucagon, growth hormone, HPL) do not cross the placenta.
- Keto-acids diffuse freely across the placenta.

Modified White Classification of Pregnant Diabetic Women No need to memorize

Class	Age of Onset	Duration	Vascular Disease	Treatment
A	Any	Any	None	Diet alone
A1	During pregnancy		None	Diet alone
A2	During pregnancy		None	Insulin
B	≥20	<10	None	Insulin
C	10-19	or 10-19	None	Insulin
D	≤10	or >20	Benign (hypertension, background retinopathy)	Insulin
F	Any	Any	Nephropathy	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Cardiac disease	Insulin
T	Any	Any	Renal transplant	Insulin

Diabetic classes A, B, and C→ fetal macrosomia is common

Diabetic classes D, F and R→ fetal growth restriction occurs more commonly

Effect of Pregnancy on Diabetes very imp

- Glycemic control worsens, insulin requirements increase.Doses need to be adjusted, women need to see an endocrinologist before pregnancy and on a regular basis during pregnancy. If she is controlled by diet before pregnancy, there is a higher chance that when she get pregnant she will need insulin or oral hypoglycemic.it is imp to tell the prepare pt mentally saying, if you get pregnant there is a higher chance in the middle of your pregnancy, you will take medication.
- Pregnancy is a **state of stress** for developing diabetes later in their lives.
- Plasma glucose tries to remain constant
- Oestrogen + Progesterone + HPL = Increased Insulin Resistance, this leads to increased Insulin Secretion.
- If no response, gestational diabetes develops. women who are underlying or hidden glucose intolerance they will be discovered or exposed when they get pregnant, bc the response will not be as good as other women and then she will develop GDM.

Effect of Diabetes on Pregnancy

- Gestational diabetes usually does not cause birth defects or deformities.why GDM does not cause birth deformities ? because it doesn't happen in the beginning (24 weeks of pregnancy) so it doesn't affect the embryogenesis. We detect GDM in 24-28
- Most developmental or physical defects happen during the first trimester of pregnancy, between the 1st and 8th week, and gestational diabetes typically develops around the 24th week of pregnancy.
- Therefore, women with gestational diabetes typically have normal blood sugar levels during the first trimester, allowing the body and body systems of the fetus to develop normally.

A. Maternal effects: IMP

I. Obstetric complications:
   - Polyhydramnios, poor control. is a sign of uncontrolled diabetes
   - Infections, e.g., urinary tract infection is more common and candidiasis
   - Preeclampsia
   - Cesarean delivery
   - Genital trauma

II. Spontaneous abortion(loss of pregnancy before 20 weeks), higher in poorly controlled. sometimes we discover diabetes by spontaneous aborion (it has a higher risk)

III. Preterm labor, twice as common (20% risk) because she may have developed polyhydramnios (means there is distension of the uterus which leads to early rupture of the membrane= leakage of fluid).

IV. Diabetic emergencies: Hypoglycemia, Diabetic coma, and Ketoacidosis
V. Vascular and end-organ involvement or deterioration (in patients with pregestational diabetes mellitus): Cardiac,Peripheral vascular, renal underlying renal problems bc of DM (nephropathy) and she gets pregnant, then the load of pregnancy with the hormonal changes it will get her renal function even worse and that's why always we instruct her to control things before get pregnant, and ophthalmic that's why we refer her to ophthalmologist when she gets pregnant
VI. Neurologic :Peripheral neuropathy and gastrointestinal disturbance
VII. Long-term outcome: type 2 diabetes, metabolic syndrome, obesity , and Cardiovascular disease

B. **Fetal and Neonatal Effects:**
I. Delayed organ maturity
- Pulmonary,hepatic, and neurologic
- RDS (delayed lung maturity): Caused by delayed pulmonary surfactant production.
  - Hyperglycemia+Hyperinsulinaemia⟶ Inhibition of surfactant synthesis⟶ Delayed pulmonary maturation ⟶RDS
- Neonatal Hypocalcemia
  - Occurs at increased rate in IDM
  - Failure to increase normal parathyroid hormone synthesis following birth

II. Increased Stillbirth (died fetus) Rate (Insult must act before 7th week of pregnancy) because of increased risk of congenital anomalies.(embryogenesis defect)
- Causes of IUFD in GDM patient:
- Pre-eclampsia (8% of cases): Diabetes⟶Narrowing & vasospasm of spiral arteriors⟶↓Flow through intervillous space⟶ Intrauterine hypoxia⟶ ↑IUGR, IUFD
- Diabetic Ketoacidosis: Diabetes⟶Dehydration ⟶Hypovolemia⟶ Hypotension⟶ Intrauterine hypoxia⟶ ↑IUGR, IUFD
- Derangement in maternal metabolism: Diabetes⟶abnormal embryogenesis ⟶congenital malformation (3 times expected rate)⟶ 30-50% of perinatal mortality NND exceeds SB⟶ ↑IUGR, IUFD
- Fetal Hyperinsulinemia:
  - Glucose crosses the placenta, causing fetal hyperglycemia, which stimulates β-cells in the pancreas that result in fetal hyperinsulinism.
  - Diabetes⟶↑Fetal metabolic rate⟶↑O2 consumption⟶ ↓Arterial O2 content ⟶Intrauterine hypoxia⟶ ↑IUGR, IUFD
- Alterations in red blood cell oxygen release & placental blood flow:
  - Diabetes⟶Diabetic vasculopathy ⟶ ↓uterine blood flow⟶Intrauterine hypoxia ⟶ ↑IUGR, IUFD
  - Hypoxia can result from fetal side, decreased uterine blood flow, and ketoacidosis (ketoacidosis will result in dehydration, hypovolemia

hypotension, decreased blood flow in intervillous space in placenta= hypoxia, IUGR, IUFD

III. Fetal malformation
- HbA1C < 8.5% is associated with a malformation rate of 3.4%
- HbA1C > 9.5% is associated with a malformation rate of nearly 22%
- That's why we care about **HbA1C** In preconception care

IV. Macrosomia
- Maternal Hyperglycemia→Placenta (facilitated diffusion)→ Fetal hyperinsulinemia→Fat cell hypertrophy→Total body and muscle fat increase & organomegaly (brain growth is not increased) →Predispose to: Shoulder dystocia, Traumatic birth injury, Asphyxia and Erb's' palsy

V. Hyperbilirubinemia (25% >170 MMOL/L)
- Predisposing factors: Bruising , Polycythemia,RDS , Prematurity
- Reducing Incidence: Early feeding ,Vit K, Phenobarbitone,Exchange transfusion

VI. Neonatal Hypoglycemia (< 2.2 mmol/L)
- Influenced by:
  1. Maternal glucose control during the latter half of pregnancy
  2. Maternal glycemic control during the labour & delivery (<5mmol/L)
- Fetal Hyperinsulinemia →Suppression of free Fatty acids levels → ↑Glycogenolysis → Neonatal hypoglycemia
- Clamping Umbilical cord→Rapid drop in Plasma Glucose→Neonatal hypoglycemia
- Infant feeding should begin by 2h of age and continue at 3-4h interval.

Congenital malformations in infants of diabetic mothers

Cardiovascular	• Transposition of the great vessels • Ventricular septal defect • Atrial septal defect • **Hypoplastic left ventricle** (poor prognosis) • Situs inversus • Anomalies of the aorta
Central nervous system	• Anencephaly* • Encephalocele* • Meningomyelocele* • Holoprosencephaly • Microcephaly *very lethal, which is not compatible with surviving as well

Skeletal	• Caudal regression syndrome • Neural tube defects like Spina Bifida
Genitourinary	• Absent kidney (Potter syndrome)not associated with survival at all • Polycystic kidneys • Double ureter
Gastrointestinal	• Tracheo - esophageal fistula • Bowel atresia • Imperforate anus

Risk factors for Gestational Diabetes

- Family history of type 2 diabetes.
- Previous diagnosis of GDM.
- Previous delivery of a macrosomic infant, stillbirth, or neonatal death.
- Member of high-risk population (e.g. woman of Hispanic,South Asian, Asian or African descent).
- Age ≥ 35 years.
- Obesity (BM ≥ 30g/m2).
- Polycystic ovary syndrome and/or hirsutism.
- Acanthosis nigricans.
- Corticosteroid use.
- Polyhydramnios.
- Recurrent abortion.

Screening of Diabetes in Pregnancy

- All pregnant women must be screened for GDM, whether by: History and clinical risk factors, or a laboratory screening test

Screening for gestational diabetes is generally performed between 24 and 28 weeks of gestation with:	
50 gm one-hour oral glucose challenge test (GCT)	• It's given without regard to last oral intake. • An abnormal blood glucose level > 130-140 mg/dl is followed by a diagnostic test.

100-g,three-hour oral glucose tolerance test (oGTT)	• This involves checking the fasting blood glucose after an overnight fast, drinking a 100-g glucose drink, and checking glucose levels hourly for 3 hours. • The patient is diagnosed with GDM when two or more values are abnormal the 3-hour GTT • If the 1-hour screening (50-g oral glucose) plasma glucose exceeds 200 mg/dL, a glucose tolerance test is not required and may dangerously elevate blood glucose values. • A fasting blood glucose or a 75-g oral glucose tolerance test should be performed at 6 to 12 weeks postpartum.

Management of Diabetes in Pregnancy

- The diabetic team :strategies to achieve maternal euglycemia,and avoidance of fetal-neonatal compromise.

Achieving euglycemia

- strict metabolic control before and during pregnancy to decrease the incidence of congenital anomalies, perinatal morbidity .
- FBS should be <95 mg/dL , 1 h PPG <140 mg/dL . and 2 h PPG <120 mg/dL
- Diet
- Caloric requirements are calculated on the basis of ideal body weight

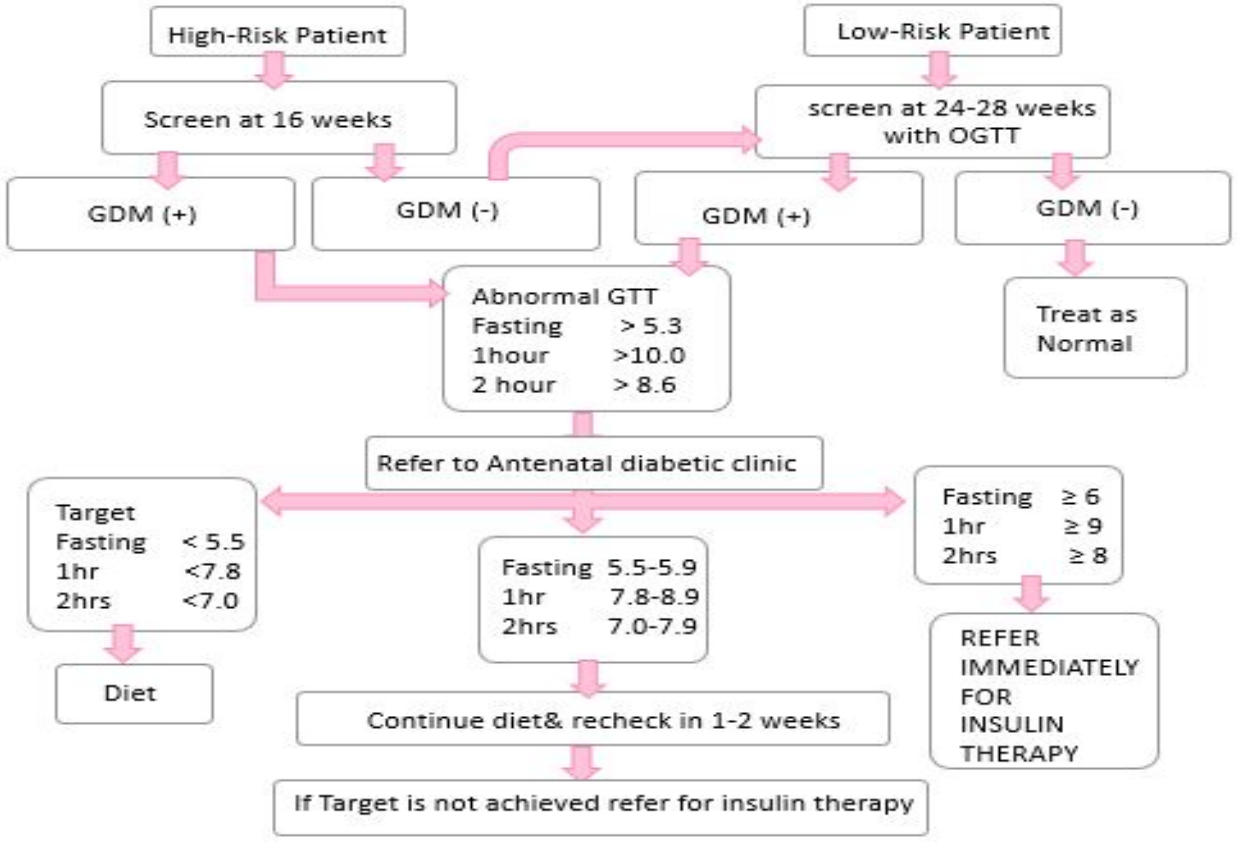
30 kcal/kg for 80% to 120% of ideal body wt.
35-40 kcal/kg for less than 80%of ideal body wt
24 kcal/kg for 120% to 150% of ideal body wt

- A healthy diet comprises:

50 % carbs 20 % proteins 20 % Fat Generous amount of fiber

- Exercise: Diabetic patients should be encouraged to engage in mild to moderate aerobic exercise (e.g., brisk walking) for about half an hour after meal
- Oral hypoglycemic agents
- They are not recommended for pregnant women because of the risks for teratogenesis and neonatal hypoglycemia
- Glyburide can treat GDM after the first trimester since it doesn't appear to enter the fetal circulation in large amounts.
- Insulin (The gold standard to maintain euglycemia in pregnancy)
- Total daily insulin units = actual body weight in kilograms × 0.6 (first trimester), 0,7 (second trimester), or 0.8 (third trimester)

- Dosage schedule: give 2/3 in am and 1/3 in pm
- Before breakfast: 2/3 NPH, 1/3 regular or lispro
- Before dinner: 1/2 NPH, 1/2 regular or lispro (if on lispro, administer additional dose before bedtime snack)



Summary for the management :
First thing we always start with a diet, if the diet didn't control it in 2 weeks, then I need to give her something, because that means she either has low production or high resistance, so I give her oral hypoglycemic . If oral hypoglycemics didn't work, then I go to insulin .
I will be adjusting her doses based on her readings and results.

Oral hypoglycemic used to be contraindicated during pregnancy,but a lot of studies showed that pregnant women can be given oral hypoglycemic in mild cases.
So not all hypoglycemics are contraindicated , we give glucophage which affects the absorption and has no effect on the fetus.

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Case : Sarah is a 35 years old, Para 6 known DM, on oral hypoglycemic, seen in ANC with I 0 weeks amenorrhoea. Discuss, antenatal, intrapartum and postpartum management?

Antenatal	Intrapartum	Postpartum

• History
• Stop oral hypoglycemic
• BSS either at home or in hospital
• The HbA1C should be obtained at the first prenatal visit, which is preferably scheduled early in the first trimester. Individuals with significantly elevated values (>8.5%) should be particularly targeted for careful ultrasonic assessment for congenital anomalies.
• Start insulin
• First-trimester dating ultrasound followed by:
  ○ a detailed obstetric ultrasonic study
  ○ fetal echocardiogram
  ○ Maternal serum alpha-fetoprotein level should be obtained at 16 to 20 weeks to check for congenital malformations.
  • Maternal renal, cardiac, and ophthalmic functions must be closely monitored.
  • Give diet advice and refer to dietitian
  • Confirm fetal viability and gestational age, follow up scan for growth and wellbeing
  • Timing and Mode of Delivery:
  ○ If the maternal state is stable, blood glucose is in the euglycemic range, and fetal studies indicate a healthy baby, spontaneous onset of labor at term may be awaited.
  ○ Cesarean delivery may be elected for large fetuses (>4250 to 4500 g)
	• Deliver at between 38 and 40 weeks if well controlled with no complications
	• Aim at vaginal delivery if no contraindications
	• If for CS give evening insulin and omit morning one
	• Intrapartum management of a diabetic patient requires the establishment of maternal euglycemia during labor .This may be achieved by giving a continuous infusion of regular insulin. Plasma glucose levels are measured frequently, and insulin dosage is adjusted accordingly to maintain a plasma glucose level between 80 and 120 mg/dL
	• Not all insulin-dependent patients require exogenous insulin during labor
	• Continuous electronic fetal heart rate monitoring is recommended for all diabetic patients
	• Give epidural
	• Give baby to the pediatrician for early feeding and check for neonatal complications
		• Stop insulin
		• continue BSS
		• Encourage breastfeeding
		• Give contraceptive advice (A void Oestrogen containing preparations in mothers with vascular disease)
		• After delivery of the fetus and placenta, insulin requirements drop sharply because the placenta, which is the source of many insulin antagonists, has been removed
		• Plasma glucose levels should be monitored and lispro or regular insulin given when plasma glucose levels are elevated.
		• A fasting blood glucose or a 75-g oral glucose tolerance test should be performed at 6 to 12 weeks postpartum

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