Gestational Diabetes Mellitus

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2/5/2012
Definition of DM

- Metabolic disorder of multiple etiology characterized by chronic hyperglycemia due to defective insulin secretion or action or both.
Common Types of DM

- Type One Diabetes
- Type Two Diabetes
- Diabetes in Pregnancy

Preexisting Diabetes
Gestational Diabetes
Type One Diabetes Mellitus

- IDDM also known as juvenile onset DM, it’s the commonest in childhood.
- It occurs due to defective insulin secretion as a result of B cell destruction (immune mediated) usually leading to absolute insulin deficiency.
Type Two Diabetes Mellitus

- NIDDM also known as adult onset DM, it’s the commonest in adulthood.
- It occur due to insulin resistance with relative insulin deficiency.
Type 2 Diabetes RISK FACTOR

- Family history
- Age
- Gestational diabetes
- Obesity
Gestational Diabetes

- This diagnosis is given when a woman, who has never had diabetes before, gets diabetes or has high blood sugar, when she is pregnant.

- Its medical name is *gestational diabetes mellitus* or GDM.

- It is one of the most common health problems for pregnant women.

- The word “gestational” actually refers to “during pregnancy.”
Gestational Diabetes

- It occurs in about 5% of all pregnancies, which is around 200,000 cases each year.

- If not treated, gestational diabetes can cause health problems for the mother and the fetus.
Pathophysiology:

- Caused by placental production of human placental lactogen (HPL) and progesterone.
- Other hormones that may contribute include prolactin and cortisol.
Pathophysiology-cont:

- Early in pregnancy, relatively higher levels of estrogen enhance insulin sensitivity.
- As placenta develops, estrogen decreases as HPL and progesterone rise, resulting in increased insulin resistance at the end organs.
- Insulin resistance is most marked in the third trimester at which time GDM most often occurs.
Pathophysiology-cont:

**Insulin**

- is the major fetal growth hormone.
- produces excessive fetal growth particularly in fat, the most insulin-sensitive tissue.
Growth Abnormalities(1)
Two Extremes Of Growth Abn:

Figure 1. Two extremes of growth abnormalities seen in infants of diabetic mothers. The small growth-restricted infant on the left weighed 470 g and is the offspring of a woman with nephropathy, hypertension, and severe preeclampsia delivered at 28 weeks’ gestation. The neonate on the right is the 5100-g baby of a woman with suboptimally controlled diabetes. Reprinted from Landon MB, Catalano PM, Gabbe SG. Diabetes mellitus. In: Gabbe SG, Niebyl JR, Simpson JL, eds. Obstetrics: Normal and problem pregnancies. Philadelphia: Churchill Livingstone, 2002:1099–100, with permission from Elsevier, Inc.

EFFECT OF PREGNANCY ON DM

- Insulin requirement ↑↑ in pregnancy reaching a max at term & being at least 2 X the pre-pregnancy requirement

- Pt with diabetic nephropathy ➔ deterioration in renal function with ↓ in creatinine clearance & proteinuria
  ➔ this deterioration in renal function is usually reversed after delivery
EFFECT OF PREGNANCY ON DM

- 2 X ↑↑ in retinopathy
  - rapid improvement in glycemic control ➔
  - worsening retinopathy due to ↑↑ retinal blood flow

- ↑↑ incidence of hypoglycemia

- Ketoacidosis is rare unless associated with hyperemesis, infections, tocolytic & corticosteroid Rx
EFFECTS OF DM ON PREGNANCY

- ↑↑ incidence of congenital abnormalities
- The risk is related to the degree of glycemic control ➔ 5% with Hb A1c > 8%
  ➔ 25% with Hb A1c > 10% with ↑↑ risk of abortions
- Sacral agenesis, congenital heart defects, skeletal abnormalities & neural tube defects
- Perinatal & neonatal mortality ↑↑ 2-4 X
- Unexplained IUFD at term / more in macrosomic babies
Skeletal abnormality

Proband C

Proband D
Sacral agenesis
EFFECTS OF DM ON PREGNANCY

- Macrosomia ➞ the incidence is ↑↑ with poor diabetic control
  ➞ not eliminated by tight control
  ➞ associated with ↑↑ risk of operative delivery, birth trauma, & shoulder dystocia

- Hyperglycemia ➞ fetal polyuria ➞ polyhydramnios ➞ PROM, preterm delivery

- Prematurity pose an added problem as pulmonary surfactant production is slightly delayed in babies of diabetic mothers
1- mother's blood brings extra glucose to the fetus

2- fetus makes more insulin to handle extra glucose

3- extra glucose gets stored as fat and fetus becomes larger than normal
MACROSOMIA
EFFECTS OF DM ON PREGNANCY

- Postnatally, babies are at risk of hypoglycemia & jaundice
- ↑↑ risk of PET especially in pt with pre-existing hypertension & nephropathy where it reaches almost 30%
Risk assessment
Low-risk status requires no glucose testing, but this category is limited to those women meeting all of the following characteristics:

- Age <25 years.
- Weight normal before pregnancy.
- Member of an ethnic group with a low prevalence of gestational diabetes mellitus.
- No known diabetes in first-degree relatives.
- No history of abnormal glucose tolerance.
- No history of poor obstetric outcome.
Risk assessment

A high risk of gestational diabetes mellitus:

- marked obesity.
- personal history of gestational diabetes mellitus.
- Glycosuria.
- a strong family history of diabetes.
Risk assessment

- High risk patients should undergo glucose testing.

A fasting plasma glucose level \( >125 \text{mg/dL} \) or a casual plasma glucose \( >200 \text{mg/dL} \) meets the threshold for the diagnosis of diabetes.

In the absence of this degree of hyperglycemia, evaluation for gestational diabetes mellitus in women with average or high-risk characteristics is by glucose tolerance test.
The screening test for GDM, a 50-g oral glucose challenge, may be performed in the fasting or fed state. Sensitivity is improved if the test is performed in the fasting state.

A plasma value above 130 - 140 mg/dl one hour after is commonly used as a threshold for performing a 3-hour OGTT.

If initial screening is negative, repeat testing is performed at 24 to 28 weeks.
3 hour Oral glucose tolerance test

**Prerequisites:**
- Normal diet for 3 days before the test.
- No diuretics 10 days before.
- At least 10 hours fast.
- Test is done in the morning at rest.

**Giving 75 gm (100 gm by other authors) glucose in 250 ml water orally**

**Criteria for glucose tolerance test:**
The maximum blood glucose values during pregnancy:
- fasting 90 mg/dl,
- one hour 165 mg/dl,
- 2 hours 145 mg/dl,
- 3 hours 125 mg/dl.

If any 2 or more of these values are elevated, the patient is considered to have an impaired glucose tolerance test.
Fasting and 2 hours postprandial venous plasma sugar during pregnancy.

<table>
<thead>
<tr>
<th>Fasting</th>
<th>2h postprandial</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 mg/dl</td>
<td>&lt; 145mg/ dl.</td>
<td>Not diabetic</td>
</tr>
<tr>
<td>&gt;125 mg/ dl</td>
<td>&gt;200 mg/ dl.</td>
<td>Diabetic</td>
</tr>
<tr>
<td>100-125 mg/dl</td>
<td>125-200 mg/dl.</td>
<td>Border line indicates glucose tolerance test.</td>
</tr>
</tbody>
</table>
Monitoring
Urine glucose monitoring is not useful in gestational diabetes mellitus. Urine ketone monitoring may be useful in detecting insufficient caloric or carbohydrate intake in women treated with calorie restriction.
Monitoring

*Daily* self-monitoring of blood glucose (SMBG) appears to be superior to *intermittent* office monitoring of plasma glucose.
For women treated with insulin, preprandial monitoring is superior to postprandial monitoring. However, the success of either approach depends on the glycemic targets that are set and achieved.
Monitorings

Glycosylated haemoglobin (Hb A1)

It is normally accounts for 5-6% of the total haemoglobin mass. A value over 10% indicates poor diabetes control in the previous 4-8 weeks.

If this is detected early in pregnancy, there is a high risk of congenital anomalies.

If this is detected in late pregnancy it indicates increased incidence of macrosomia and neonatal morbidity and mortality.
The mean glucose represented by the hemoglobin A1c level can be calculated using the "rule of 8's." A value of 8 percent equals 180 mg/dl, and each 1 percent increase or decrease represents ± 30 mg/dl.
Assessment for asymmetric fetal growth by ultrasonography, particularly in early third trimester, may aid in identifying fetuses that can benefit from maternal insulin therapy.
Maternal surveillance should include blood pressure and urine protein monitoring to detect hypertensive disorders.
Treatment Options

1. DIET
2. EXERCISE
3. EDUCATION
4. MEDICATION
Medical nutrition therapy should include the provision of adequate calories and nutrients to meet the needs of pregnancy and should be consistent with the maternal blood glucose goals that have been established. Noncaloric sweeteners may be used in moderation.
Diet therapy is critical to successful regulation of maternal diabetes. A program consisting of three meals and several snacks is used for most patients. Dietary composition should be:

- 50 to 60 percent carbohydrate,
- 20 percent protein,
- 25 to 30 percent fat with less than 10 percent saturated fats, up to 10 percent polyunsaturated fatty acids, and the remainder derived from monosaturated sources.
Diabetes Food Pyramid

- Fats, oils & sweets
- Meat, meat substitutes & other proteins
- Milk
- Vegetables
- Fruits
- Breads, grains & other starches
Exercise

- Same guidelines as for women with pre-gestational diabetes
- Walking and swimming are both good options.
Education - 1

- Symptoms
- Role of diet and exercise
- Blood sugar goals
- Technique and frequency for self-monitoring of blood sugars
- How to complete blood sugar logs
- Potential adverse outcomes of uncontrolled blood sugars
Education - 2

- Frequency of visits and antepartum testing
- Potential for medication (including increasing dosages)
- Effects of stress and infection on blood glucose levels
- Risks for future diabetes
- Risk reduction strategies
- Need for lifelong follow up
When Dietary Therapy Fails:

- Insulin
- Oral Hypoglycemic Agents:
  - Glyburide
  - Metformin
insulin therapy is recommended when medical nutrition therapy fails to maintain self-monitored glucose at the following levels:

**Fasting** whole blood glucose \(<95\) mg/dL

Fasting plasma glucose \(<105\) mg/dL

or

**1-hour postprandial** whole blood glucose \(<140\) mg/dL

1-hour postprandial plasma glucose \(<155\) mg/dL

or

**2-hour postprandial** whole blood glucose \(<120\) mg/dL

2-hour postprandial plasma glucose \(<135\) mg/dL
**GOAL**

Self-blood glucose monitoring combined with aggressive insulin therapy has made the maintenance of maternal normoglycemia (fasting and premeal glucose between 50-80mg/dl and 1 hour postprandial glucose <140mg/dl)

*Insulin therapy* ..... cont.
Insulin therapy ..... cont.

Twice daily (before breakfast and before dinner) injections of a combination of short and intermediate acting insulins are usually sufficient to control most patients otherwise a subcutaneous insulin pump is used.
The total first dose of insulin is calculated according to the patient’s weight as follows:

*Insulin therapy* ..... cont.

In the first trimester ............. weight x 0.7
In the second trimester .......... weight x 0.8
In the third trimester .......... weight x 0.9
If the total dose of insulin is less than 50 units/day, it is given in a single morning dose with the ratio: Short acting (regular or Actrapid)/Intermediate (NPH or Monotard) = 1 : 2

In higher doses, As a general rule, the amount of intermediate-acting insulin will exceed the short-acting component by a 2:1 ratio. Patients usually receive two thirds their total dose with breakfast and the remaining third in the evening as a combined dose with dinner.
Insulin Dose adjustment

Home glucose monitoring with a reflectance meter by measuring fasting and preprandial glucose values 4 times a day (30-40 min) before each meal.

Preprandial glucose measuring allows adding additional regular insulin to compensate any hyperglycemia already present before meals.

All values are recorded in a daily log.
Insulin Dose adjustment

Each time the fasting or premeal glucose is measured, the patient refers to the supplemental regular insulin scale to determine if additional regular insulin is needed
supplemental regular insulin scale

<table>
<thead>
<tr>
<th>Preprandial glucose mg/dl</th>
<th>Additional units (regular insulin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>0</td>
</tr>
<tr>
<td>100-140</td>
<td>2</td>
</tr>
<tr>
<td>140-160</td>
<td>3</td>
</tr>
<tr>
<td>160-180</td>
<td>4</td>
</tr>
<tr>
<td>180-200</td>
<td>5</td>
</tr>
<tr>
<td>200-250</td>
<td>6</td>
</tr>
<tr>
<td>250-300</td>
<td>8</td>
</tr>
<tr>
<td>&gt;300</td>
<td>10</td>
</tr>
</tbody>
</table>
Insulin Dose adjustment

When the pattern for additional regular insulin supplementation is identified over 2-3 days, that amount of insulin can then be added to the planned daily dose.
In patients who are not well controlled, a brief period of hospitalization is often necessary for the initiation of therapy. Individual adjustments to the regimens implemented can then be made.
Alternative to Insulin Therapy

Glyburide:

- 2nd generation sulfonylurea
- Does not cross the placenta
Alternative to Insulin Therapy

Metformin:

- Is used as a tx for infertility in PCOS.
- Is a category B drug
- Hasn’t been well studied for use in pregnancy.
KETOACIDOSIS
KETOACIDOSIS

As pregnancy is a state of relative insulin resistance marked by enhanced lipolysis and ketogenesis, diabetic ketoacidosis may develop in a pregnant woman with glucose levels barely exceeding 200 mg/dl.

Thus, DKA may be diagnosed during pregnancy with minimal hyperglycemia accompanied by a fall in plasma bicarbonate and a pH value less than 7.30. Serum acetone is positive at a 1:2 dilution.
KETOACIDOSIS

clinical signs of volume depletion follow the symptoms of hyperglycemia, which include:

- polydipsia and polyuria.
- Malaise.
- Headache.
- Nausea.
- Vomiting.
Occasionally, diabetic ketoacidosis may present in an undiagnosed diabetic woman receiving β-mimetic agents to arrest preterm labor.

Because of the risk of hyperglycemia and diabetic ketoacidosis in diabetic women. Terbutaline and magnesium sulfate has become the preferred tocolytic for cases of preterm labor in these cases.

Sometimes Administration of antenatal corticosteroids to accelerate fetal lung maturation can cause significant maternal hyperglycemia and precipitate DKA. In diabetic patients.
An intravenous insulin infusion will usually be required and is adjusted on the basis of frequent capillary glucose measurements.

Therapy hinges on the meticulous correction of metabolic and fluid abnormalities.

Every effort should therefore be made to correct maternal condition before intervening and delivering a preterm infant.
ANTEPARTUM FETAL EVALUATION
ANTEPARTUM FETAL EVALUATION

Antepartum fetal monitoring tests are now used primarily to reassure the obstetrician and avoid unnecessary premature intervention.

These techniques have few false-negative results, allowing the fetus to benefit from further maturation in utero.
1-Ultrasound

Ultrasound is a valuable tool in evaluating fetal growth, estimating fetal weight, and detecting hydramnios and malformations.
maternal serum α-fetoprotein (MSAFP) at 16 weeks' gestation is often used in association with a detailed ultrasound study during the second trimester in an attempt to detect neural tube defects and other anomalies. Normal values of MSAFP for diabetic women are lower than in the nondiabetic population.
Ultrasound examinations should be repeated at 4- to 6-week intervals to assess fetal growth. The detection of fetal macrosomia, the leading risk factor for shoulder dystocia, is important in the selection of patients who are best delivered by cesarean section.
2-Maternal assessment of fetal activity

While the false-negative rate with maternal monitoring of fetal activity is low (~1 percent), the false-positive rate may be as high as 60 percent.

Maternal hypoglycemia, while generally believed to be associated with decreased fetal movement, may actually stimulate fetal activity.
Done weekly at 28 weeks and Twice weekly at 34 weeks

remains the preferred method to assess antepartum fetal well-being in the patient with diabetes mellitus

If the NST is nonreactive, a biophysical profile (BPP) or contraction stress test is then performed.
Doppler umbilical artery velocimetry has been proposed as a clinical tool for antepartum fetal surveillance in pregnancies at risk for placental vascular disease.

It is found that Doppler studies of the umbilical artery may be predictive of fetal outcome in diabetic pregnancies complicated by vascular disease. Elevated placental resistance as evidenced by an increased systolic/diastolic ratio is associated with fetal growth restriction and preeclampsia in these high-risk patients.
TIMING AND MODE OF DELIVERY
There is **very little evidence** to support either elective delivery or expectant management at term in pregnant women with insulin-requiring diabetes. Limited data from a single randomized controlled trial suggest that induction of labour in women with gestational diabetes treated with insulin reduces the risk of macrosomia.
When antepartum testing suggests fetal compromise, delivery must be considered.
Delivery by cesarean section usually is favored when fetal distress has been suggested by antepartum heart rate monitoring.

If a patient reaches 38 weeks' gestation with a mature fetal lung profile and is at significant risk for intrauterine demise because of poor control or a history of a prior stillbirth, an elective delivery is planned.
During labor, continuous fetal heart rate monitoring is mandatory. Labor is allowed to progress as long as normal rates of cervical dilatation and descent are documented. Arrest of dilatation or descent despite adequate labor should alert the physician to the possibility of cephalopelvic disproportion.
Insulin Management during Labor and Delivery

- Usual dose of intermediate-acting insulin is given at bedtime.
- Morning dose of insulin is withheld.
- Intravenous infusion of normal saline is begun.
- Once active labor begins or glucose levels fall below 70 mg/dl, the infusion is changed from saline to 5% dextrose and delivered at a rate of 2.5 mg/kg/min.
- Glucose levels are checked hourly using a portable meter allowing for adjustment in the infusion rate.
- Regular (short-acting) insulin is administered by intravenous infusion if glucose levels exceed 140 mg/dl.