Diabetes in pregnancy & its management
Begum R

Introduction
Diabetes mellitus is the most common medical complication of pregnancy and it carries a significant risk to the fetus and the mother. Congenital malformations and perinatal morbidity remain common compared with the offspring of non diabetic pregnancies. Diabetic mothers are at risk of progression of micro-vascular diabetic complications as well as early pregnancy loss, pre-eclampsia, polyhydramnios and premature labor. Glycemic control before and during pregnancy is critical and the benefit may result in a viable, healthy offspring. Gestational diabetes mellitus (GDM) which manifests for the first time during pregnancy is common and on the increase, its proper management will reduce the risk of neonatal macrosomia and hypoglycemia. Post-partum evaluation of glucose tolerance and appropriate counseling in women with GDM may help decrease the high risk of subsequent type 2 diabetes in the long-term. The article will briefly review the changes in the carbohydrate metabolism that characterise normal pregnancy and will focus on a practical approach to the care of patients with pre-existing diabetes as well as GDM.

Prevalence
Gestational diabetes mellitus (GDM) represents approximately 90% of these cases and affects 2-5% of all pregnancies and varies in direct proportion to type 2 diabetes mellitus in the background population. Pre-existing diabetes mellitus complicates 0.2% to 0.3% of pregnancies. The importance of diabetes in pregnancy stems from the fact that it carries a significant risk to both the fetus and the mother. Despite major advances in clinical management, there is still facing a higher incidence of malformations and perinatal morbidity compared to the non-diabetic population. Over the past 30 years, great strides have been made in improving the outcomes of women with type 1 diabetes who become pregnant. However, during the past decade, type 2 diabetes in pregnancy has emerged and is certain to become a prominent concern. The overall prevalence of diabetes is 6.8% and 8.2% according to FBG and 2hBG, respectively. The prevalence of type 2 diabetes is 8.1% and the prevalence for men and women is 7.7% and 8.5% respectively. The prevalence of gestational diabetes is strongly related to the patient's race and culture. Typically, only 1.5-2% of white persons from the midwestern United States develop GDM, while American Indians from the southwestern United States may have rates as high as 15%. In Hispanic, African American, and Asian populations, the rate is 5-8%.

Normal glucose regulation during pregnancy: Metabolic changes occur in normal pregnancy in response to the increase in nutrient needs of the fetus and the mother. There are two main changes which are seen during pregnancy, progressive insulin resistance that begins near mid-pregnancy and progresses through the third trimester to the level that approximates the insulin resistance seen in individuals with type 2 diabetes mellitus. The insulin resistance appears to result from a combination of increased maternal adiposity and the placental secretion of hormones (progesterone, cortisol, placental lactogen, prolactin and growth hormone). The fact that insulin resistance rapidly abates following delivery suggests that the major contributors to this state of resistance are placental hormones. The second change is the compensatory increase in insulin secretion by the pancreatic beta-cells to overcome the insulin resistance of pregnancy. As a result, circulating glucose levels are kept within

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normal. If there is maternal defect in insulin secretion and in glucose utilization, then GDM will occur as the diabetogenic hormones rise to their peak levels.

During a healthy pregnancy, mean fasting blood sugar levels decline progressively to a remarkably low value of 74 ±2.7 (standard deviation) mg/dL. On the other hand, peak postprandial blood sugar values rarely exceed 120 mg/dL. Meticulous replication of the normal glycemic profile during pregnancy has been demonstrated to reduce the rate of macrosomia. Specifically, when 2-hour postprandial glucose levels are maintained at less than 120 mg/dL, approximately 20% of fetuses demonstrate macrosomia. Conversely, if postprandial levels range up to 160 mg/dL, macrosomia rates rise to 35%.

Pathophysiology
1) Metabolic disorder characterized by hyperglycemia due to:
   • Relative pancreatic insulin production
   • Limited insulin release
   • Impaired effect of insulin at the cellular level

2) Incidence: 1-3% of all pregnant women
   0.5% overt DM Cause: - Multifactorial includes genetic & environmental factor.

3) Carbohydrate metabolism during pregnancy:
   Diabetogenic effects of pregnancy
   A. Insulin resistance:
      • Production of placental somatomammotropin
      • Increased production of estriol & progesterone
      • Increased insulin destruction by kidney & placenta
   
   B. Increased lipolysis: The mother uses fat for her calorie needs & saves glucose for fetal needs.

   C. Changes in gluconeogenesis: The fetus uses preferentially alanine & other amino acids & deprives the mother of major gluconeogenic source.

4) Effects of DM on pregnancy:
A. On mother:
   1. 1st trimester abortion
   2. ↑Pre-eclampsia 15-25%
   3. ↑ Polyhydramnious
   4. ↑ Infections ——> ↑ Chorioamnitis
   5. ↑ Post partum haemorrhage
   6. ↑ LUCS

Table 1: Risks to the mother

<table>
<thead>
<tr>
<th>Maternal complications in diabetic pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diabetic keto-acidosis</td>
</tr>
<tr>
<td>• Visual deterioration/retinopathy</td>
</tr>
<tr>
<td>• Deterioration of nephropathy</td>
</tr>
<tr>
<td>• Polyhydramnios</td>
</tr>
<tr>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td>• Miscarriage</td>
</tr>
<tr>
<td>• Pre-eclampsia</td>
</tr>
<tr>
<td>• Premature delivery</td>
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</tbody>
</table>

B. On the fetus:
   1. Abortion in 1st trimester
   2. Congenital abnormalities
   3. Macrosomia
   4. Hypoglycemia
   5. Hyperviscosity syndrome
   6. Hyaline membrane disease
   7. Hypocalcemia
   8. Apnea & bradycardia
   9. Traumatic delivery
   10. IUFD

Table 2: Risks to the fetus

<table>
<thead>
<tr>
<th>Fetal complications in diabetic pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Congenital anomalies: cardio-vascular, central nervous system, skeletal (sacral agenesis) &amp; genito-urinary</td>
</tr>
<tr>
<td>• Excessive fetal growth (macrosomia)</td>
</tr>
<tr>
<td>• Fetal growth retardation (in diabetic pregnancy complicated by nephropathy)</td>
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</tbody>
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Table 3: Risks to the neonate

<table>
<thead>
<tr>
<th>Neonatal complications in diabetic pregnancy</th>
<th><em>Traumatic delivery</em></th>
<th><em>Polycythemia</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Hypomagnesemia</em></td>
<td><em>Hypoglycemia</em></td>
</tr>
<tr>
<td></td>
<td><em>Pulmonary surfactant deficiency</em></td>
<td><em>Hypocalcemia</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hypoglycemia</em></td>
</tr>
</tbody>
</table>

5) Effects of pregnancy on DM:
   1. More insulin required to achieve metabolic control
   2. Progressive of diabetic retinopathy
   3. Worsening of DM nephropathy
   4. Risk of death for patient with DM cardiomyopathy

6) Preconception counseling on the diabetic patient:
   - Pregnancy should be planned.
   - Importance of blood glucose control patient should be informed about the outcome of pregnancy in a uncontrolled blood sugar level.
   - Importance of self-monitoring & frequent test to detect early complication & therefore management.
   - Importance of fetal surveillance during the diabetic pregnancy.

   a) The problem affecting the fetus should be explained:
      - HBA1C
      - Sr fetoprotein at 16 wk
      - Fetal anomaly scan at 20 wk
      - Fetal echocardiogram at 24 wk
      - Serial USG to detect macrosomia or IUGR

   b) Fetal well being should be monitored in last trimester by:
      - CST (Contraction Stress Test)
      - NST
      - Modified BPP (Biophysical profile)

7) Financial cost of the diabetic pregnancy:
   - Needs frequent laboratory test
   - Frequent visit to the doctor
   - May need hospitalization for control of DM
   - May need to terminate the pregnancy earlier
   - Maximum will be ended with LUCS
   - Baby may need NICU care, which cost lot.

Diagnosis
Screening for diabetes before the discovery of insulin in 1921, pregnancy in the diabetic women was uncommon & accompanied by high maternal & fetal mortality rates. But after the discovery of insulin & better understanding of the disease the mortality rate comes down from 65% to 2-5% if blood glucose controlled meticulously. So it is necessary to diagnose DM in pregnancy properly. So necessity for screening is very important.

Why screening is important
1) Risk of developing NIDDM/ IDDM at later age (off spring 1.5% at 25 yrs of age).
2) GDM is seldom symptomatic.
3) Impact of GDM on pregnancy similar to progestational diabetes mellitus though complications are fewer less severe.
4) To improve perinatal outcome.
5) To decrease the maternal morbidity & mortality.
6) To intervene in proper time.

When to screen
1. All pregnancies should be screened for GDM between 24-28 wks.
2. High risk group-
   - On first visit
   - If not on 28 wks
   - If not on 32 wks

Blood flow may be the factor involved with IUGR and fetal death. They suggested that there is a relationship between maternal hyperglycemia and reduced uteroplacental blood flow. This is seen in cases of ketoacidosis and pre-eclampsia, two conditions associated with IUD. Alterations in fetal carbohydrate metabolism and fetal

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hyperinsulinemia leading to hypoxia and fetal death.

Goals to antepartum fetal surveillance
1. Avoidance of intrauterine death
2. Early detection of fetal compromise
3. Prevention of unnecessary premature delivery

Fetal surveillance test
1. Contraction Stress Test (CST)
2. Non-Stress test
3. fetal Biophysical Profile (FBP)
4. Maternal assessment of fetal activity (or kick count)
5. Doppler study

Prevention of respiratory distress syndrome: In diabetic pregnancies there is a delayed production of surfactant and lung maturity.

Education of the patient with newly diagnosed diabetes: Patient who newly detected has little idea about diet and blood glucose monitoring. Nutritionist will give the idea-

  a) Calorie
  b) Meal time
  c) Balanced diet
  d) Value of diet

So patient needs 3D
  a) Education about diet.
  b) Discipline life.
  c) Drug if needed - insulin education about self administration of insulin.
  d) If possible home monitoring of blood glucose & to educate when to see the advice of doctor what is the level of blood glucose to be maintained.
  e) The patient must be able to recognize & treat hypoglycemia instructions to be given to carry candy or sugar with them to combat hypoglycemia.
  f) Instruction to be given if any infection immediately reports to the physician.
  g) In last trimester patient asked for maintaining KICK count.

Management
The role of ultrasonography in the management of diabetic pregnancy:
1. Estimation of gestational age.
4. Diagnosis of congenital anomalies.

Insulin therapy during pregnancy
a) The American Diabetes Association recommends the use of human insulin for pregnant women with diabetes & diabetes considering pregnancy. Insulin in available in 3 different forms which may be mixed in one syringe or injected separately. Short acting insulin (regular & semi lente) have peak action at 2 to 4 hours post injection. Intermediate acting insulins (Lente & NPH) have peak action at 5 to 12 hours. Long acting insulins (Protagne Zinc & Ultra Lente) have peak action of 12 to 24 hours.

b) Insulin requirements increased throughout pregnancy
   6-18 weeks : 0.7 U/kg body wt
   18-26 weeks : 0.8 U/kg body wt
   26-36 weeks : 0.9 U/kg body wt
   36-41 weeks : 1.0 U/kg body wt

c) Regimens: Recommended regimens should be considered starting places & must be adjusted to each patients' specific needs. Generally for a patient who is familiar with here diabetes, it is best to maintain the form of administration that she used before pregnancy, if possible.
   2- injection regimen
   3- injection regimen
   4- injection regimen

Continuous subcutaneous insulin infusion
1) Two- injection regimen: Two- thirds of the total daily dose is given in the morning (2:1 ratio of NPH to regular insulin) & one- third in the evening (1:1 ratio of NPH to regular).
2) Three- injection regimen: Administration of NPH or lente insulin at bedtime, rather than with dinner, has been found to prevent
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nocturnal hypoglycemia & result in improved control of fasting morning glucose levels.
3) Four-injection regimen: 50% to 60% of the total daily insulin requirement is given as ultralente, together with regular insulin premeal times.
4) Continuous subcutaneous insulin infusion: A pump system, which is usually attached to the patient's abdominal wall, delivers regular insulin continuously to maintain basal blood glucose levels, with additional bolus administered at mealtimes. The same total insulin dose that would be administered in multiple injection therapy is administered as the basal rate infusion, with the remainder administered as boluses before meals. Breakfast usually requires a larger bolus than other meals.

Insulin adjustment by neutralizing dose

<table>
<thead>
<tr>
<th>Blood sugar mmol/L</th>
<th>Insulin in drip 500cc 5% DA or DNS</th>
</tr>
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<tbody>
<tr>
<td>6-9</td>
<td>6 unit Actrapid</td>
</tr>
<tr>
<td>9-11</td>
<td>8</td>
</tr>
<tr>
<td>11-13</td>
<td>10</td>
</tr>
<tr>
<td>13-17</td>
<td>12</td>
</tr>
<tr>
<td>17-21</td>
<td>12+4 unit s.c</td>
</tr>
<tr>
<td>&gt;21</td>
<td>12+8 unit s.c (consult the concern person)</td>
</tr>
</tbody>
</table>

Timing of delivery in diabetic pregnancy: Obstetric management has undergone tremendous changes in managing a diabetic pregnancy. Till 1960, all patients were induced at or before 36 weeks to avoid IUD. Later on inductions were carried out at 37-38 weeks to reduce RDS in the newborn.

However, now a day's with the availability of sophisticated methods for antenatal fetal surveillance, and with a policy of intensive insulin administration and strict metabolic control using frequent glucose estimations, pregnancy is continued up to term and onset of spontaneous labour is awaited in all cases, provided the patient's diabetes is well controlled and the fetus is not a risk. Patients with vascular disease are delivered early if hypertension worsens or if there is IUGR.

When antepartum testing suggests fetal compromise, immediate delivery is indicated, if pulmonary maturity is confirmed.

Factors influencing timing of delivery in diabetic pregnancy
A. Maternal factors:
* Vascular disease complications
* Control of diabetes
* Condition of cervix
* Previous obstetric history
* Early elderly patient

B. Fetal factors:
* Fetal weight
* Fetal distress

Route of delivery: Primary cesarean section (LSCS) rate in diabetes pregnancies is as high as 30-40%.

Indication for LSCS in diabetic pregnancy
1. Pregnancy complicated by PIH
2. Malpresentations
3. Previous LSCS
4. Macrosomia
5. Proliferative retinopathy
6. Fetal distress prior to or during labor

Conclusion
Abnormalities of glucose tolerance during pregnancy are a potential threat to the mother and the growing fetus. Not only that it is already established that mothers who developed GDM many of them develop frank DM/IGT later on. Therefore epidemiological studies are important to predict nature of distribution, progression of this particular disease. High risk group of patient can deliver healthy baby if screened for GDM with good glycemic control with proper antenatal care. It is evident that international comparison of the prevalence of GDM is not possible accurately due

* a) Wide differences in screening protocol
* b) Different cut off points of diagnostic criteria.
So, our recommendation is, population or community based studies are to be undertaken by unified-screening and diagnostic criteria.

References