Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical conditions in pregnancy and prevalence is growing with increasing rates of women of advanced age becoming pregnant. The increasing prevalence of maternal obesity and inactivity is also responsible for the higher incidence. Asians and moreover Indians are at a greater risk of Diabetes Mellitus and hence, pregnant women are at higher risk of Gestational Diabetes. GDM is associated with an increased risk of maternal and fetal short- term and long-term ill-health. There is a positive linear association between increasing maternal glucose at oral glucose tolerance testing and risk of important perinatal outcomes including cesarean section, large for gestational age babies and infant adiposity.

Physiology

Normal pregnancy is associated with insulin resistance similar to that found in type-2 diabetes. This physiological resistance to insulin action during pregnancy becomes more apparent in the second trimester and insulin resistance increases progressively to term. Changes in insulin resistance occur to facilitate transport of glucose across the placenta to ensure normal fetal growth and development. Transfer of glucose across the placenta
stimulates fetal pancreatic insulin secretion and insulin acts as an essential growth hormone.

If resistance to maternal insulin action becomes too pronounced, maternal hyperglycemia occurs and gestational diabetes mellitus (GDM) may be diagnosed. GDM is associated with an increased risk of adverse perinatal outcomes, including large for gestational age (LGA) babies, macrosomia (usually defined as birthweight 4 kg or 4.5 kg), induction of labor and cesarean section.

There is also growing evidence that GDM is associated with an increased risk of long-term ill-health outcomes in the mother (type 2 diabetes mellitus and cardiovascular disease) and offspring (obesity and associated cardio-metabolic risks).

**What is GDM?**

GDM is defined as carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy.

GDM defined in this way includes women with undiagnosed preexisting diabetes, as well as women with first-onset hyperglycemia during pregnancy.

In the past, less severe GDM was referred to as ‘impaired glucose tolerance’ and more severe as ‘GDM’; but now, the whole higher end of the glucose spectrum is more simply referred to as GDM.

**FIGO recommends** the term *Hyperglycemia in pregnancy* whether the Diabetes is before pregnancy, during pregnancy or because of the pregnancy.

**Maternal & Fetal Complications –**

**Maternal risks of GDM** include polyhydramnios, pre-eclampsia, prolonged labor, obstructed labor, caesarean section, uterine atony, post-partum hemorrhage, infection and progression of retinopathy, which are the leading global causes of maternal morbidity and mortality.

**Fetal risks** include spontaneous abortion, intra-uterine death, stillbirth, congenital malformation, shoulder dystocia, birth injuries, neonatal hypoglycemia and infant respiratory distress syndrome. Long-term clinical effects of GDM are important contributors to the burden of non-communicable diseases in many countries.

**Identification of GDM: screening and testing**

A screening/diagnostic test is any approach used to gather clinical information for the purpose of making a clinical decision and is a process that helps determine the presence or absence of a condition.
For GDM, the oral glucose tolerance test (OGTT) is generally the diagnostic test of choice; this test is usually administered at the first antenatal visit and between 24 and 28 weeks of gestation.

A plasma blood sample is obtained following an overnight fast and then a 75 g or 100 g glucose load is given and further plasma blood sample is obtained after 1, 2, or 3 hours. GDM is diagnosed (depending on the criteria used) if one, two, or more glucose levels are equaled or exceeded.

| Table 1 Current and previous criteria recommended to diagnose GDM (plasma glucose levels in mmol/L) |
|---------------------------------|------------------|------------------|------------------|------------------|
| Criteria                        | Fasting          | 1 hour postload  | 2 hours postload | 3 hours postload |
| 75 g OGTT (plasma glucose)      | ≥5.1             | ≥10.0            | ≥8.5             | –                |
| IADPSG* (2010), ADIPS* (2013), and WHO** (2013) | ≥6.1 | –                | ≥7.8             | –                |
| WHO** (1999)                    | ≥5.3             | ≥10.0            | ≥8.6             | –                |
| ADA* (2006)                     | ≥5.5             | –                | ≥8.0             | –                |
| ADIPS* (1998)                   | ≥5.3             | ≥10.0            | ≥8.6             | –                |
| 100 g OGTT (plasma or serum glucose) | ≥5.3             | ≥10.0            | ≥8.6             | ≥7.8             |
| ACOG†/C&C (2013)                | ≥5.8             | ≥10.6            | ≥9.2             | ≥8.0             |
| NDDG‡ (1979)                    | ≥5.0             | ≥9.2             | ≥8.1             | ≥6.9             |

Notes: *One threshold should be met or exceeded for GDM to be diagnosed. †Two thresholds should be met or exceeded for GDM to be diagnosed.

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; ADA, American Diabetes Association; ADIPS, Australasian Diabetes in Pregnancy Society; C&C, Carpenter and Coustan; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes in Pregnancy study Groups; NDDG, National Diabetes Data Group; OGTT, oral glucose tolerance test; WHO, World Health Organization.

The American College of Obstetricians and Gynecologists (ACOG) and UK National Institute for Health and Care Excellence (NICE) recommend that women who have had GDM in a previous pregnancy should be offered diagnostic testing.

ACOG also recommends early testing in obese women or women with impaired glucose metabolism as early as possible to identify undiagnosed type 2 diabetes.

The Australasian Diabetes in Pregnancy Society (ADIPS) recommends risk factor assessment in early pregnancy; risk factors are ranked by severity and either one “high” risk factor or two “moderate” risk factors are needed before an OGTT is offered.
<table>
<thead>
<tr>
<th>Agency</th>
<th>Nature of screening strategy</th>
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| **NICE**<sup>4</sup> (UK) | Offer OGTT only to women with at least one of the following:  
• BMI ≥30 kg/m<sup>2</sup>  
• Previous macromomic baby (>4.5 kg)  
• Previous GDM  
• Family history of diabetes  
• Family minority ethnic origin with a high prevalence of diabetes  
Testing at first antenatal visit should be undertaken to identify undiagnosed type 2 diabetes (universal OGTT testing is recommended at 24–28 weeks) in all pregnant women who are overweight (BMI ≥25 kg/m<sup>2</sup>) and have additional risk factors:  
• Physical inactivity  
• First-degree relative with diabetes  
• High-risk race/ethnicity (eg, African-American, Latino, Native American, Asian-American, and Pacific Islander)  
• Women who delivered a baby weighing >4 kg or were diagnosed with GDM  
• Hypertension (≥140/90 mmHg or on therapy for hypertension)  
• HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)  
• Women with polycystic ovarian syndrome  
• A1C ≥5.7%, IGT, or IFG on previous testing  
• Other clinical conditions associated with insulin resistance (eg, severe obesity and acanthosis nigricans)  
• History of CVD  |
| **ADA**<sup>13</sup> | Women who are from a high-risk ethnic background or have a BMI of 25–35 kg/m<sup>2</sup> as their only risk factor should be considered “moderate risk” and should initially be screened with either a random or a fasting glucose test in early pregnancy, followed by an OGTT if clinically indicated. ADIPS suggests that the thresholds for further action are not clear currently and clinical judgment should be exercised.  
Women at “high risk” of GDM (one high-risk factor or two moderate-risk factors) should be offered a 75 g OGTT, with venous plasma samples taken at fasting, 1 hour and 2 hours at the first opportunity after conception. Women at moderate or high risk with normal glucose should be offered an OGTT at 24–28 weeks:  
• Moderate-risk factors for GDM  
• Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, and non-white African  
• BMI: 25–35 kg/m<sup>2</sup>  
• High-risk factors for GDM  
• Previous GDM  
• Previously elevated blood glucose level  
• Maternal age ≥40 years  
• Family history of DM (first-degree relative with diabetes or a sister with GDM)  
• BMI >35 kg/m<sup>2</sup>  
• Previous macromomiria (BW >4,500 g or >90th percentile)  
• Polycystic ovarian syndrome  
• Medications: corticosteroids, antipsychotics |
Protocol for investigation
Testing for GDM is recommended twice during ANC.
The first testing should be done during first antenatal contact as early as possible in pregnancy.
The second testing should be done during 24-28 weeks of pregnancy if the first test is negative. It is important to ensure second test as many pregnant women develop blood sugar intolerance during this period (24-28 weeks).
Moreover, only one third of GDM positive women are detected during first trimester. There should be at least 4 weeks gap between the two tests.
The test is to be conducted for all pregnant women even if she comes late in pregnancy for ANC at the time of first contact.
If she presents beyond 28 weeks of pregnancy, only one test is to be done at the first point of contact.

Methodology: Test for diagnosis-
DIPSI METHOD-
Single step testing using 75 gm oral glucose & measuring blood sugar 2 hours after ingestion.
75 gm glucose is to be given orally after dissolving in approximately 300 ml water whether the pregnant women comes in fasting or non-fasting state, irrespective of the last meal.
The intake of the solution has to be completed within 5-10 minutes.
A plasma standardized glucometer should be used to evaluate blood sugar 2 hours after the oral glucose load.
If vomiting occurs within 30 minutes of oral glucose intake, the test has to be repeated the next day or else refer to a facility.
If vomiting occurs after 30 minutes, the test continues.
The threshold blood sugar level of $\geq 140$ mg/dL (more than or equal to 140) is taken as cut off for diagnosis of GDM.
Management of GDM
Guiding Principles

All Pregnant women who test positive for GDM for the first time should be started on Medical Nutrition Therapy (MNT) and physical exercise for 2 weeks.
   The woman should walk/exercise for 30 mins a day.
   After 2 weeks on MNT and physical exercise, 2 hours PPBS (post meal) should be done.

Thus, GDM is managed initially with MNT and physical exercise and if it is not controlled with MNT (lifestyle changes), Metformin or Insulin therapy is added to the MNT.

If 2hr PPBS is <120 mg/dL, repeat test every month during 2nd and 3rd trimester. More follow-up tests can be done as recommended by the treating physician.
If 2hr PPBS is ≥120 mg/dL, medical management (metformin or insulin therapy) to be started as per guidelines.

Medical Nutrition Therapy (MNT)
Principles of MNT  - Healthy eating during pregnancy
All pregnant women with GDM should get Medical Nutrition Therapy (MNT) as soon as diagnosis is made.
MNT for GDM primarily involves a carbohydrate controlled balanced meal plan which promotes Optimal nutrition for maternal and fetal health.
Adequate energy for appropriate gestational weight gain achievement and maintenance of normo-glycemia.

The importance of the individualized nutrition assessment in GDM
Nutrition assessment in GDM should be individualized to allow an accurate appraisal of the woman’s nutritional status.
This assessment includes defining her Body Mass Index (BMI) or percentage of desirable pre-pregnancy body weight and optimal pattern of weight gain during pregnancy.
Calories and GDM Individualization is important when determining energy requirement, and adjustments should be made based on weight change patterns.
Energy requirement during pregnancy includes the normal requirement of adult and an additional requirement for fetal growth plus the increase in the body weight of pregnant woman.
Energy requirement does not increase in the first trimester unless a woman is underweight.
Energy requirement increases during second and third trimester. Energy intake should be adequate enough to provide appropriate weight gain during pregnancy. As per Indian ICMR guidelines, for an average weight gain of 10-12 Kg, an addition of 350 kcal/day above the adult requirement is recommended during second and third trimester. Severe caloric restriction is not recommended as it may result in ketonemia and ketonuria and impair physical and mental development in offspring.

<table>
<thead>
<tr>
<th>Level of Activity</th>
<th>Energy requirement during pregnancy</th>
<th>Total energy requirement (kcal/Day)</th>
</tr>
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<tbody>
<tr>
<td>1 Sedentary work</td>
<td>1900+350</td>
<td>2250</td>
</tr>
<tr>
<td>2 Moderate work</td>
<td>2230+350</td>
<td>2580</td>
</tr>
<tr>
<td>3 Heavy work</td>
<td>2850+350</td>
<td>3200</td>
</tr>
</tbody>
</table>

Or we can calculate calories as follows:
- 35 Kcal/kg for low BMI
- 30Kcal/kg for normal BMI
- 25Kcal/kg for High BMI

Hypocaloric diets in obese women with GDM can adversely impair fetal growth besides ketonemia and ketonuria. However, moderate caloric restriction (reduction by 30% of estimated energy needs) in obese women with GDM may improve glycemic control without ketonemia and reduce maternal weight gain.
Diet should be balanced as follows:

- Carbohydrates – 50 to 60%
- Protein – 20 to 25%
- Fat – 25%

Select Carbohydrates Carefully

Complex carbohydrates like, whole-grain cereals as oats, bajra, jowar and ragi. Whole pulses, vegetables and fruits with skins should be preferred over simple carbohydrates.

Food with lots of added sugar or honey, or foods that are made from refined white flour should be avoided. Some examples of simple carbohydrates include sweets, cakes, puddings, sweet biscuits, pastry, juice, soft drinks, chips, white bread, naan, pizza etc.

Counting the number of carbohydrate serves that a mother eats during the day will help her to eat the right amount of carbohydrate.

As a guide, aim should be for 2–3 carbohydrate serves at each major meal and 1–2 carbohydrate serves at each snack.

Understanding Fat Intake during Pregnancy

Saturated fat intake (sources - ghee, butter, coconut oil, palm oil, red meat, organ meat, full cream milk etc.) should be less than 10 % of total calories.

Dietary cholesterol should be less than 300 mg/dL.

In obese and overweight patients, a lower-fat diet overall can help slow the rate of weight gain.

Protein: Protein requirement in pregnancy is increased (additional 23 g/day) to allow for fetal growth.

At least 3 serving of protein foods are required every day to meet the increased demand.

Sources of protein are milk and milk products, egg, fish, chicken, pulses (dal), nuts etc.

Fiber: High fiber foods especially soluble fiber may help control blood sugar by delaying gastric emptying, retarding the entry of glucose into the blood stream and lessening the postprandial rise in blood sugar.

Soluble fiber in flax seed, psyllium husk, oat bran, legumes (dried beans of all kinds, peas and lentils), and pectin (from fruit, such as apples) and forms in root vegetables (such as carrots) are helpful.
Medical Management (Oral Antidiabetic Drug-Metformin; and Insulin Therapy)

Metformin or Insulin therapy is the accepted when sugar levels of pregnant women with GDM is not controlled on MNT.

Insulin is the drug of first choice and Metformin can be considered after 20 weeks of gestation for medical management of GDM.

Insulin can be started any time during pregnancy for GDM management

If the woman's blood sugar is not controlled with the maximum dose of metformin (2 gm/day) and MNT, Insulin is to be added.

The dose of metformin is 500 mg twice daily orally up to a maximum of 2 gm/day. Hypoglycemia and weight gain with metformin are less in comparison to Insulin.

The common side-effect that occur with Metformin include diarrhea, nausea, stomach pain, heartburn, gas and the serious side-effects are lactic acidosis and low blood sugar.

**Dosage of Insulin**: Actrapid or Mixtard linsulin can be given in pregnancy.

In a simplified form dose requirement can be decided as follows:
1\textsuperscript{st} Trimester - 0.7 unit/kg  
2\textsuperscript{nd} Trimester - 0.8 unit/kg  
3\textsuperscript{rd} Trimester - 0.9 unit/kg  
At Term - 1 unit/kg

If difficulty in calculation we can start with 4 units 3 times daily of Actrapid Insulin (Breakfast, Lunch, Dinner) & then titrate twice a week and adjust the dose.

**Mixtard Insulin** –  
30\% Rapid Acting Insulin, 70\% Isophane Insulin.  
2/3\textsuperscript{rd} of the dose is given in the morning with Breakfast  
1/3\textsuperscript{rd} of the dose is given in at night with Dinner
Hypoglycemia

Any Pregnant women on insulin can develop hypoglycemia at any time. Hypoglycemia is diagnosed when blood sugar level is < 70 mg/dL. It is important to recognize symptoms of hypoglycemia & treat immediately.

How to recognize hypoglycemia?

**Early** symptoms - Tremors of hands, sweating, palpitations, hunger, easy fatigability, headache, mood changes, irritability, low attentiveness, tingling sensation around the mouth/lips or any other abnormal feeling

**Severe** - Confusion, abnormal behavior or both, visual disturbances, nervousness or anxiety.

**Uncommon** - Seizures and loss of consciousness

How to manage hypoglycemia?

Ask pregnant women to take 3 TSF of glucose powder (15-20 grams) dissolved in a glass of water.

If glucose is not available, take one of the following: Sugar - 6 TSF in a glass of water/ ssfruit juice/honey/anything which is sweet/any food.

After taking oral glucose, she must take rest & avoid any physical activity.

15 minutes after taking glucose, she must eat one chapati with vegetable/rice/one glass of milk/idli/fruit/anything eatable which is available.

If hypoglycemia continues, repeat same amount of glucose and wait.

If pregnant women develops >1 episode of hypoglycemia in a day, she should consult any doctor immediately.

Special obstetric care for pregnant women with GDM

**Antenatal care**

In cases diagnosed before 20 weeks of pregnancy, a fetal anatomical survey by USG should be performed at 18-20 weeks.

For all pregnancies with GDM, a fetal growth scan should be performed at 28-30 weeks gestation & repeated at 34-36 weeks gestation.

There should be at least 3 weeks gap between the two ultrasounds and it should include fetal biometry & amniotic fluid estimation.
Preconception

Recommendations

• Women with preexisting diabetes who are planning a pregnancy should ideally be managed beginning in preconception in a multidisciplinary clinic including an endocrinologist, maternal-fetal medicine specialist, Registered dietitian nutritionist, and diabetes care and education specialist when available.

• In addition to focused attention on achieving glycemic targets, standard preconception care should be augmented with extra focus on nutrition, diabetes education, and screening for diabetes comorbidities and complication.

• Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care provider.

Glycemic Targets in Pregnancy

Recommendations

• Fasting and postprandial self-monitoring of blood glucose are recommended in both gestational diabetes mellitus and preexisting diabetes in pregnancy to achieve optimal glucose levels. Glucose targets are fasting plasma glucose <95 mg/dL (5.3 mmol/L) and either 1-hour postprandial glucose <140 mg/dL (7.8 mmol/L) or 2-hours postprandial glucose <120 mg/dL (6.7 mmol/L). Some women with preexisting diabetes should also test blood glucose pre-prandial.

• Due to increased red blood cell turnover, A1C is slightly lower in normal pregnancy than in normal non-pregnant women. Ideally the A1C targets in pregnancy is <6% (42 mmol/mol) if this can be achieved without significant hypoglycemia, but the target may be relaxed to <7% (53 mmol/mol) if necessary to prevent hypoglycemia.

• When used in addition to pre- and postprandial self-monitoring of blood glucose. Continuous glucose monitoring can help to achieve A1C targets in diabetes and pregnancy.
• When used in addition to self-monitoring of blood glucose targeting traditional pre- and postprandial targets, continuous glucose monitoring can reduce macrosomia and neonatal hypoglycemia in pregnancy, complicated by type 1 diabetes.

• Continuous glucose monitoring metrics may be used as an adjunct, but should not be used as a substitute for self-monitoring of blood glucose to achieve optimal and postprandial glycemic targets.

**Fetal surveillance in pregnant women with GDM:**

Pregnant women with GDM are at an increased risk for fetal death in utero and this risk is increased in pregnant women requiring medical management. Hence vigilant fetal surveillance is required.

Fetal heart should be monitored by auscultation on each antenatal visit. Pregnant women should be explained about Daily Fetal Activity Assessment. One simple method is to ask her to lie down on her side after a meal and note how long it takes for the fetus to kick 10 times. If the fetus does not kick 3 times within 1hr or a minimum of 1 time in 1 hour she should consult her doctor.

**Labor & Delivery**

Pregnant women with GDM with good control of blood sugar (2 hr PPBS <120 mg/dL) levels may be delivered at their respective health facility. Ideally she should have institutional delivery.

Pregnant women with GDM on insulin therapy with uncontrolled blood sugar levels (2 hr PPBS>120 mg/dL) on MNT and physical exercise and metformin or insulin requirement >20 U/ day should deliver at higher center.

**Timing of delivery:** GDM pregnancies are associated with delay in lung maturity of the fetus; so routine delivery prior to 39 weeks is not recommended.

If a pregnant women with GDM with well controlled blood sugar has not already delivered spontaneously, **induction of labor** should be scheduled at or after **39 weeks** pregnancy.

In pregnant women with GDM with poor blood sugar control, those with risk factors like hypertensive disorder of pregnancy, previous still birth & other complications should be delivered earlier.

The timing of delivery should be individualized by the obstetrician accordingly.
Vaginal delivery should be preferred and LSCS should be done for obstetric indications only. 
In case of fetal macrosomia (estimated fetal weight >4 kg) consideration should be given for an elective cesarean section at 39 weeks to avoid shoulder dystocia.

**Special precaution during labor**

Pregnant women with GDM on medical management (metformin or insulin) require blood sugar monitoring during labor by a glucometer. The morning dose of insulin/metformin is withheld on the day of induction/labour and the pregnant women should be started on 2 hourly monitoring of blood sugar. IV infusion with normal saline (NS) to be started & regular insulin to be added according to blood sugar levels as per the table below:

<table>
<thead>
<tr>
<th>Blood sugar level</th>
<th>Amount of Insulin added in 500 ml NS</th>
<th>Rate of NS Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-120 mg/dL</td>
<td>0</td>
<td>100 ml/hr (16 drops/min)</td>
</tr>
<tr>
<td>120-140 mg/dL</td>
<td>4 U</td>
<td>100 ml/hr (16 drops/min)</td>
</tr>
<tr>
<td>140-180 mg/dL</td>
<td>6 U</td>
<td>100 ml/hr (16 drops/min)</td>
</tr>
<tr>
<td>&gt;180 mg/dL</td>
<td>8 U</td>
<td>100 ml/hr (16 drops/min)</td>
</tr>
</tbody>
</table>

**Immediate neonatal care for baby of mother with GDM**

All neonates should receive immediately essential newborn care with emphasis on early breastfeeding to prevent hypoglycemia.

**Post-delivery follow up of pregnant women with GDM**

Immediate postpartum care of women with GDM is not different from women without GDM but these women are at high risk to develop Type 2 Diabetes Mellitus in future. Maternal glucose levels usually return to normal after delivery. Subsequently, 75 gm OGTT (fasting and 2 hr PP) at 6 weeks postpartum to evaluate glycemic status of woman.

Pregnant women with GDM and their offspring’s are at increased risk of developing Type II Diabetes mellitus in later life. They should be counseled for healthy lifestyle and behavior, particularly role of diet & exercise.
Conclusion:

- Gestational diabetes mellitus (GDM) can be easily controlled by diet (MNT) and exercise.
- Only in few women in whom blood sugar is not controlled by diet and physical exercise, oral antidiabetic (metformin) or insulin injections are required.
- GDM can be treated with oral metformin tablets as they do not harm the fetus.
- Insulin injections are required (at times) only during pregnancy.
- Insulin will be stopped in most of the cases after pregnancy.
- Injecting insulin over abdomen is 100% safe.
- Modification of diet is very easy. Sweets should be avoided at all times during pregnancy.
- If blood sugar is controlled, patient and her baby both are safe and healthy.
- Pregnant women with GDM should deliver at health facilities.
- It will help in management of any complications which can be countered during delivery.

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