Gestational diabetes is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies whether insulin or only diet modification was used for treatment and whether or not the condition persists after pregnancy. This it does not exclude the possibility that unrecognized glucose intolerance may have antedated or being concomitantly with pregnancy.

Pregnancy that occurs in a woman who already has diabetes is termed as pregestational diabetes. It may be type 1 or type 2 diabetes. Therefore diabetes in pregnancy is classified as follows:

1. Pregestational diabetes which may be type 1 or type 2.
2. Gestational diabetes GDM can be reclassified after 6 weeks.

Both GDM and Pregestational diabetes are associated with increased maternal and fetal morbidity and mortality. However the magnitude of the problem is lesser in GDM. Pregnant women with GDM have a significantly high risk of undergoing caesarean section, preeclampsia and fetal macrosomia and increased risk hypertension and diabetes after pregnancy. GDM is a powerful predictor of Type 2 diabetes within 10 years after the index delivery. Hence women with GDM should be informed and made aware that they have a risk of developing future diabetes which could be prevented by altering their lifestyle - in terms of improved dietary habits and regular physical exercise. The hyperglycemia may also critically influence the fetal programming, leading to later development of diabetes in the fetuses during their adult life.

Women diagnosed to have GDM are at increased risk of future diabetes predominantly type 2 diabetes as are their children.

1. Thus GDM offers a unique opportunity for the development, testing and implementation of clinical strategies for diabetes prevention.
2. Timely action taken towards screening all pregnant women for glucose intolerance, identifying glucose intolerance, effectively achieving euglycaemia in them and assuring adequate nutrition may prevent in all probability the vicious cycle of transmitting glucose intolerance from one generation to another.

Prevalence of GDM varies in India widely from 2.8 - 21% in different parts of the country depending upon the geographical locations and diagnostic method used. Seshaih et al have reported a prevalence of 17.8% among the women in urban areas, 13.8% in semiurban and 9.9% in rural areas. 72% of these women were detected in the first visit and the remaining 28% in the subsequent visits. GDM has been found to be more prevalent in urban areas than in rural areas. For a given population and ethnicity the prevalence of GDM corresponds to the prevalence of impaired glucose intolerance (IGT) in the non pregnant adults.

Pregnancy induces progressive changes in maternal carbohydrate metabolisms. As pregnancy advances rise in placental hormones which are counterregulatory to insulin, result in increasing insulin resistance necessitating compensatory increase in insulin secretion. When this compensation is inadequate gestational diabetes develops. Insulin resistance in a normal pregnancy is estimated to
increase by 40%-70% predominantly in the 3rd trimester.

**Screening and diagnosis of GDM:** There is no consensus regarding the diagnostic criteria for GDM or the importance of diagnosing and treating GDM. There are several controversies in this subject like:

1. Whom to screen
2. How to screen
3. When to screen

Who is at Risk for GDM - Whom to Screen?
The expert committee on diagnosis and classification of diabetes has recommended that screening may not be necessary in women who fulfill the criteria given below:

- **‘Low Risk’** states where screening is not required
  - Age < 25 years
  - Weight normal before pregnancy
  - Member of an ethnic group with a low prevalence of GDM
  - No known diabetes in first-degree relatives
  - No history of abnormal glucose tolerance
  - No history of poor obstetric outcome

But in the Indian context, recognition of glucose intolerance during pregnancy is perhaps more relevant as Indian women have an eleven fold increased risk of developing GDM compared to white Caucasian women. It is important to detect these GDM cases, because if unrecognized, the pregnancy may end in fetal wastage or the child may be at higher risk of diabetes in adult life.

GDM is associated with a high risk of poor outcome of pregnancy, since glucose is toxic to the developing fetus. Hence, ideally all pregnant women should undergo screening for glucose intolerance but short of that screening is mandatory for high risk patients likely to develop GDM (table I)

<table>
<thead>
<tr>
<th><strong>Table I. Indications for screening</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Age &gt; 25 years</td>
</tr>
<tr>
<td>- Family history of diabetes</td>
</tr>
<tr>
<td>- Obesity (Pre-pregnancy BMI&gt;25)</td>
</tr>
<tr>
<td>- BOH - previous history of</td>
</tr>
<tr>
<td>- Unexplained perinatal loss</td>
</tr>
<tr>
<td>- IUD</td>
</tr>
<tr>
<td>- Large for gestational age infant</td>
</tr>
<tr>
<td>- Congenitally malformed infant</td>
</tr>
<tr>
<td>- Polyhydramnios</td>
</tr>
<tr>
<td>- Pre-eclampsia</td>
</tr>
<tr>
<td>- Glucose in second fasting urine sample</td>
</tr>
</tbody>
</table>

**Screening and Diagnosis**
A number of screening procedures and diagnostic criteria (ADA, WHO, CDA, NDDG and Australasian criteria) are being followed in the same as well as in different countries. American Diabetes Association (ADA) recommends screening for selective (high risk) population. But compared to selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis. Hence universal screening for GDM is essential as it is generally accepted that women of Asian origin and especially ethnic Indians, are at a higher risk of developing GDM and subsequent type 2 diabetes.

**ADA procedure** - ADA recommends two step procedures:

1. **Step 1:** A 50g glucose challenge test (GCT) is used for screening without regard to the time of last meal or time of the day. Those with a 1 hour plasma glucose value of <140 mg/dl do not require further testing.

2. **Step 2:** If 1 hour GCT value is more than 140 mg/dl, 100g oral glucose tolerance test (OGTT) is recommended and plasma glucose is estimated at 0, 1, 2 and 3 hours. GDM is diagnosed (Carpenter and Coustan criteria) if any 2 values meet or exceed the cutoff values: FPG >95 mg/dl, 1 hour PG>180 mg/dl, 2 hour PG>155 mg/dl and 3 hour PG>140 mg/dl. The drawback of this criteria is that, the glycaemic cut-off was originally validated against the future risk of these women developing diabetes and not on the fetal outcome. Further, in the community health centers, pregnant women are reluctant to undergo ADA procedures for two reasons: The number of blood samples drawn are many both for screening and for subsequent 3 - hour OGTT to confirm the diagnosis. Moreover, the women have to visit the antenatal clinic on two occasions. It was found that 18-23% pregnant women whose GCT was positive in the first visit, failed to return for the definitive OGTT. Therefore a single step procedure is preferred for the diagnosis of GDM.

International Association of Diabetes and Pregnancy Study Groups (IADPSG) based on the HAPO study outcome recommends any one or more values of FPG ≥ 92 mg/dl, 1 h PG ≥ 180 mg/dl and 2 hr PG ≥ 153 mg/dl for the diagnosis of GDM. The IADPSG recommendation would result in variation in the prevalence of GDM from one center to another, depending on the choice of cut-off value used, either fasting 1h, 2h, or any two values for diagnosis. This flexibility will compromise the uniformity and likely to pose difficulty in comparing outcome data.
WHO Procedure: In many countries the WHO criteria for Gestational Diabetes Mellitus is considered standard. The WHO bases the diagnosis of GDM on a test of impaired glucose tolerance (IGT) with a 75gm glucose load, which is the same as for IGT in non-pregnant women. This is the lowest glucose load to identify GDM. To standardize the diagnosis of GDM the World Health Organization (WHO) recommends using a 2 hour 75g OGTT with a threshold plasma glucose concentration of greater than 140mg/dl at 2 hours, similar to that of IGT (>140 and 199 mg/dl), outside pregnancy. Numerous independent studies have shown that the WHO criteria are superior to other criteria issued by other health organizations, when examining undesirable outcomes in pregnancy.

When a GTT is administered to a non-pregnant individual, the standard is to use the 75g, 2-hour OGTT. Using a different glucose challenge in pregnant versus non-pregnant persons leads to confusion in the laboratory and may result in errors in applying the proper diagnostic criteria. WHO procedure also has a shortcoming in that, the criteria was recommended for its easy adaptability in clinical practice.

Reconciliation factors between ADA and WHO - GDM based on 2 hour 75g OGTT defined by either WHO or ADA criteria predicts adverse pregnancy outcome. There was no significant difference between prevalence of GDM using Carpenter and Coustan (ADA) and WHO criteria. WHO criteria of 2 hour PG ≥ 140mg/dl identifying a large number of cases may have a greater potential for prevention of diabetes. The glycaemic criteria for diagnosis of different categories of glucose intolerance by 75g, 2-hour OGTT is listed in table 1.

Significance of 2 hour plasma glucose level of 140 mg/dl (7.8 mmol/l): Increasing maternal carbohydrate intolerance in pregnant women is associated with a graded increase in the adverse maternal and foetal outcomes though there is a continuous relationship between maternal glycaemia and neonatal outcomes, the primary outcomes of birth weight, neonatal adiposity and cord C peptide level >90th percentile tends to occur as the 2 hour PG increases >140 mg/dl (7.8mmol/l). In yet another follow up study of children born to mothers who had third trimester plasma glucose. 120-139 mg/dl, the cumulative risk of type 2 diabetes was 19% at age 24 years and this risk increased to 30% with respect to those women who had 2 hour plasma glucose 140-199mg/dl. Thus both short-term and long-term morbidity in the offspring occurs in the inflection point of maternal 2 hour plasma glucose > 140 mg/dl and as such, this level assumes clinical significance. A pregnant woman, whose 2 hour plasma glucose is 120-139 mg/dl needs follow up.

A single test procedure to diagnose gestational diabetes mellitus in the community: seldom a pregnant woman visiting the antenatal clinic for the first time comes in the fasting state. If she is asked to come on another day in the fasting state she may not return. Hence it is important to have a test that detects the glucose intolerance without the woman necessarily undergoing a test in the fasting state and it is preferable to perform the diagnostic test at the first visit itself.

In the anteratal clinic a pregnant woman after undergoing preliminary clinical examination has to be given a 75g oral glucose load, without regard to the time of the last meal. A venous blood sample is collected at 2 hour for estimating plasma glucose by the GOD-POD method. GDM is diagnosed if 2 hour glucose is ≥ 140mg/dl.

Performing this test procedure in the non-fasting state is rational, as glucose concentrations are little affected by the time since the last meal in a normal glucose tolerance woman, whereas it will, in a woman with gestational diabetes. After a meal, a normal glucose tolerant woman would be able to maintain euglycaemia despite glucose challenge due to brisk and adequate insulin response, whereas, a woman with GDM who has impaired insulin secretion, as her glycaemic level increases with a meal and with glucose challenge, the glycaemic excursion exaggerates further. Therefore this procedure assumes clinical relevance as WHO criteria based on glucose concentration 2 hour after 75g glucose load was able to correctly identify subjects with GDM. Yet another reason for recommending the single step procedure is that, the specificity of ADA screening with 50 g 1 hour GCT without regard to time of the last meal is low. Hence instead of performing screening test using 50 g 1 hour test and then the 100g OGTT, this single step procedure serves both as screening and diagnostic test for GDM, is simple, economical and feasible.

Advantages of the Single Step Diagnostic Procedure for GDM: The pregnant women need not be fasting, it causes least disturbance in a pregnant woman’s routine activities. More importantly, it serves as both a screening and diagnostic procedure.

The timing of Screening: The current recommendation is to perform screening tests between 24-28 weeks. However
there are reports that claims about 40 - 66% of women with GDM can detected during early pregnancy. Therefore some workers suggest that the ideal period to screen for GDM is around 16 weeks of gestation or even earlier in high risk groups and if the test is negative it should be repeated at 24 and 32 weeks11.

The DIPSI guideline recommend screening on the 1st antenatal visit with 75g OGTT irrespective of whether the patient fasting or not12.

Short-term and long-term implications of GDM

Short term: A large multinational study the Hyperglycemia Adverse Pregnancy Outcome Study (HAPO) recruited 23800 pregnant women from 16 different centers with the aim to define the glycaemic thresholds during 75gm glucose tolerance test that are associated with adverse pregnancy outcome.

The HAPO study observed a continuous relationship between maternal glycemia and neonatal outcomes, both for the primary (birth weight, neonatal adiposity, and cord C peptide level > 90th percentile) and secondary outcomes (premature delivery, birth injury, intensive neonatal care, hyperbilirubinemia, and preeclampsia). Of these, the primary outcomes are important, as they are more likely to have permanent impact on the future development of obesity and type 2 diabetes in the offspring, whereas the secondary outcomes, which are treatable, have transitory influence on the new born. In the HAPO study, though the composite outcomes (which includes both primary and secondary outcomes) occur from 2h PG ≥ 153mg/dl, the maternal glucose of 2 h PG > 140 mg/dl. A sub-study of DIPAP project also observed that the occurrence of the macrosomia was continuum, as the 2 h PG with 75g OGTT increased above 120mg/dl.

Long term Outcomes: Franks et al. documented in their follow up study of children born to mothers, who had third trimester 2 h PG 120-139 mg/dl, the cumulative risk of type 2 diabetes was 19% at age 24 years and this risk increased to 30% with respect to those women who had 2 h PG 140-199 mg/dl13.

Thus, both short-term and long-term morbidities in the offspring occur as maternal plasma glucose increases and this trend is perceptible from 2h PG ≥ 140mg/dl. As such, this level assumes a great clinical significance.

CONCLUSION

Gestational Diabetes Mellitus is not only associated with increasing maternal morbidity and perinatal mortality but also there is increased risk of developing diabetes in future in both the mother and the offspring. Early diagnosis and effective management not only helps in improving maternal and fetal morbidity and mortality, but also helps in prevention of diabetes in both the mother and the offspring. Although there has been lot of confusion with several screening and diagnostic tests recommended by the ADA and WHO. The introduction of the single step test for both screening and diagnostic, which is recommended in the Indian guidelines (DIPSI guideline), has made it clear and simple. The HAPO study and the subsequent IADPSG guideline also are now advocating a single abnormal value on a 75 gm OGTT. There is also consensus on screening all women and doing it early and repeating it in every trimester.

REFERENCES