

Chapter 44

Diagnosis and Management of Gestational Diabetes Mellitus: Indian Guidelines

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INTRODUCTION

“Gestational diabetes mellitus” (GDM) is defined as carbohydrate intolerance with onset or recognition during pregnancy. Women diagnosed to have GDM are at increased risk of future diabetes predominantly type 2 diabetes mellitus (DM) as are their children. Thus, GDM offers an important opportunity for the development, testing and implementation of clinical strategies for diabetes prevention. Timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition may prevent in all probability, the vicious cycle of transmitting glucose intolerance from one generation to another.¹

EPIDEMIOLOGY

The prevalence of GDM in India varied from 3.8 to 21% in different parts of the country, depending on the geographical locations and diagnostic methods used. GDM has been found to be more prevalent in urban areas than in rural areas.² For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of impaired glucose tolerance (IGT) (in nonpregnant adult) within that given population.³

SCREENING AND DIAGNOSIS

Compared to selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis.⁴ 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.⁵

World Health Organization Procedure

To standardize the diagnosis of GDM, the World Health Organization (WHO) recommends using a 2-hour 75 g oral glucose tolerance test (OGTT) with a threshold plasma glucose concentration of greater than 140 mg/dL at 2 hours, similar to that of IGT (> 140 mg/dL and < 199 mg/dL), outside pregnancy.⁶

American Diabetes Association Procedure

American Diabetes Association (ADA) procedure has become obsolete.

The International Association of the Diabetes and Pregnancy Study Groups⁷

Based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, International Association of the Diabetes and Pregnancy Study Groups (IADPSG) suggested the guidelines. In this HAPO study, population from India, China, South Asian countries (except city of Bangkok, Hong Kong), Middle East and Sub Saharan countries were not included. Thus, essentially HAPO study was performed in Caucasian population.

- The IADPSG recommends that diagnosis of GDM is made when any of the following plasma glucose values meet or exceed: Fasting: ≥ 5.1 mmol/L (92 mg/dL), 1-hour: ≥ 10.0 mmol/L (180 mg/dL), 2-hour: ≥ 8.5 mmol/L (153 mg/dL)⁷ with 75 g OGTT.
- The IADPSG also suggests: Fasting plasma glucose (FPG) > 7.0 mmol/L (126 mg/dL)/A1C $> 6.5\%$ in the early weeks of pregnancy is diagnostic of overt diabetes. Fasting > 5.1 mmol/L and < 7.0 mmol/L is diagnosed as GDM.⁷

Disadvantages of the IADPSG suggestions are:

- Most of the time pregnant women do not come in the fasting state because of commutation and belief not to fast for long hours. The dropout rate is very high when a pregnant woman is asked to come again for the glucose tolerance test.⁸ Attending the first prenatal visit in the fasting state is impractical in many settings.⁷
- In all GDM, FPG values do not reflect the 2-hour post glucose with 75 g oral glucose [2-hour plasma glucose (PG)], which is the hallmark of GDM.⁹ Ethnically Asian Indians have high insulin resistance and as a consequence, their 2-hour PG is higher compared to Caucasians.¹⁰ The insulin resistance during pregnancy escalates further¹¹ and hence FPG is not an appropriate option to diagnose GDM in Asian Indian women. In this population by following FPG > 5.1 mmol/L as cut-off value, 76% of pregnant women would have missed the diagnosis of GDM made by WHO criterion.¹²

- Asian and South Asian ethnicity are both independently associated with increased insulin resistance in late pregnancy. A diagnostic FPG was present in only 24% of those with GDM in Bangkok and 26% in Hong Kong.¹³
- Center to center differences occur in GDM frequency and relative diagnostic importance of fasting, 1-hour and 2-hour glucose levels. This may impact strategies used for the diagnosis of GDM.¹³
- The A1C is not possible to perform in the less resource countries, not only because it is expensive but also due to lack of technically qualified staff. The cost and standardization of A1C testing are issues for consideration.⁷

Evidence-based WHO Criterion

Short-term Outcome

- Economical test:
 - This procedure requires one blood sample drawn at 2 hours after 75 g oral glucose load for estimating plasma glucose. Even if the test is to be repeated in each trimester, the cost in performing the procedure will be 66% less than the cost of performing IADPSG recommended procedure. Thus, WHO procedure is feasible, sustainable, cost-effective and high impact best buy for less resource settings.
- Evidence-based:
 - A study performed by Crowther et al. found that treatment of GDM diagnosed by WHO criterion reduces serious perinatal morbidity and may also improve the women's health-related quality of life.¹⁴
 - Diagnosis of GDM with OGTT 2-hour PG ≥ 7.8 mmol/L (140 mg/dL) and treatment in a combined diabetes antenatal clinic is worthwhile with a decreased macrosomia rate and fewer emergency cesarean sections. The treatment of GDM women as defined by WHO criterion was associated with reduced risk of pregnancy outcome.¹⁵
 - Wahi et al. observed in their randomized controlled study, the advantage of adhering to a cut-off level of 2-hour PG ≥ 7.8 mmol/L in diagnosis and management of GDM for a significantly positive effect on pregnancy outcomes both in relation to mother as well the child.¹⁶
 - Perucchini et al. also suggest one-step diagnostic procedure (2-hour PG ≥ 7.8 mmol/L) to diagnose GDM.¹⁷

Long-term Outcome

- A long-term outcome study conducted by Franks et al. documented that when maternal 2-hour PG was ≥ 7.8 mmol/L, the cumulative risk of offspring developing type 2 DM was 30% at the age 24 years.¹⁸

A Single Test Procedure to Diagnose GDM in the Community (Diabetes in Pregnancy Study Group India)¹⁹

Note: Diabetes in Pregnancy Study Group India (DIPSI diagnostic criteria 2-hour PG ≥ 140 mg/dL is similar to WHO criteria 2-hour PG ≥ 140 mg/dL to diagnose GDM)

“A Single-step procedure” was developed due to the practical difficulty in performing glucose tolerance test in the fasting state, as seldom pregnant women visiting the antenatal clinic for the first time come in the fasting state. If they are asked to come on another day in the fasting state many of them do not return.²⁰ 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.

Procedure

In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination, has to be given a 75 g oral glucose load*, irrespective of whether she is in the fasting or nonfasting state and without regard to the time of the last meal. A venous blood sample is collected at 2 hours for estimating plasma glucose by the GOD-POD method. GDM is diagnosed if 2-hour PG is ≥ 140 mg/dL (7.8 mmol/L).

If 75 g glucose packet is not available, remove and discard 5 level teaspoons (not heaped) of glucose from a 100 g packet which is freely available. In hospitals where glucose is supplied in bulk, a cup or container of 75 g may be used. The glucose marketed is in anhydrous form.

Performing this test procedure in the nonfasting state is rational, as glucose concentrations are affected little by the time since the last meal in a normal glucose tolerant woman, whereas it will, in a woman with gestational diabetes.²¹ After a meal, a normal glucose tolerant woman would be able to maintain euglycemia despite glucose challenge due to brisk and adequate insulin response, whereas, a woman with GDM who has impaired insulin secretion,²² her glycemic level increases with a meal and with glucose challenge, the glycemic excursion exaggerates further.²³ This cascading effect is advantageous as this would not result in false-positive diagnosis of GDM.

Advantages of the DIPSI procedure are:

- Pregnant women need not be fasting¹⁸
- Causes least disturbance in a pregnant woman's routine activities
- Serves as both screening and diagnostic procedure.

This single-step procedure has been approved by Ministry of Health, Government of India²⁴ and also recommended by WHO.

Gestational Weeks at which Screening is Recommended

By following the usual recommendation for screening between 24 weeks and 28 weeks of gestation, the chance of detecting unrecognized type 2 diabetes before pregnancy (pre-GDM) is likely to be missed.²⁵ If the 2-hour PG is > 200 mg/dL in the early weeks of pregnancy, she may be a pre-GDM and A_{1C} of ≥ 6.5 is confirmatory.²⁶ A pregnant woman found to have normal glucose tolerance (NGT), in the first trimester, should be tested for GDM again around 24th–28th week and finally around 32nd–34th week.²⁷

MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

Treatment

Target

Maintaining a mean plasma glucose (MPG) level ~ 105 – 110 mg/dL is desirable for a good fetal outcome.²⁸ This is possible if FPG and 2-hour postprandial peaks are ~ 90 mg/dL and ~ 120 mg/dL, respectively.

Medical Nutrition Therapy

All women with GDM should receive nutritional counseling. The meal pattern should provide adequate calories and nutrients to meet the needs of pregnancy. The expected weight gain during pregnancy is 300–400 g per week and total weight gain is 10–12 kg by term.

Initiating Insulin Therapy

Once diagnosis is made, medical nutritional therapy (MNT) is advised initially for 2 weeks. If MNT fails to achieve control, i.e. FPG ~ 90 mg/dL and/or post-meal glucose ~ 120 mg/dL, insulin may be initiated.

1. Preferable to start with Premix insulin 30/70 of any brand*
Starting dose: 4 units before breakfast
↓
Every 4th day increase 2 units till 10 units
↓
If FPG remains > 90 mg/dL advise → 6 units before breakfast and 4 units before dinner
↓
Review with blood sugar test → Adjust dose further
Total insulin dose per day can be divided as two-thirds in the morning and one-third in the evening.
*Initially if post-breakfast plasma glucose is high → Start Premix 50/50
2. If GDM is diagnosed in the third trimester; MNT is advised for a week. Insulin is initiated if MNT fails.
3. If 2-hour PG > 200 mg/dL at diagnosis, a starting dose of 8 units of Premixed insulin could be administered straightaway before breakfast and the dose has to be titrated on follow-up. Along with insulin therapy, MNT is also advised.

Insulin Analogs

If postprandial glucose is still not under control—consider using rapid-acting insulin analogs.

Monitoring Glycemic Control

The success of the treatment for a woman with GDM depends on the glycemic control maintained with meal plan or pharmacological intervention. Studies suggest 1, 1.5 and 2-hour post-meal for monitoring glycemic control.²⁹ 2-hour post-meal monitoring is preferred as the diagnosis of GDM is also based on 2-hour PG. It is easier to remember this timing, as the time for diagnosis and also for monitoring is the same, i.e. 2 hours. However, whichever time is targeted for monitoring glycemic control and adjusting insulin dose, blood tests must be performed at the same time at each visit. They should be advised to perform self-monitoring of blood glucose (SMBG) on a daily basis, failing which, at least weekly monitoring should be encouraged. If self-monitoring is not possible, laboratory venous plasma glucose has to be estimated for adjusting the dose of insulin.

Oral Antidiabetic Drugs

Insulin secretagogue (glibenclamide) is being used in a few centers in India and abroad, but not yet approved by drug controller of India.

Metformin

Metformin (alone or with supplemental insulin) was not associated with increased perinatal complications as compared with insulin.³⁰ Metformin has been found to be useful in women with polycystic ovarian disease (PCOD) who failed to conceive.³¹

Measuring Other Parameters

Maternal

The blood pressure has to be monitored during every visit. If blood pressure is found to be more than 130/80, advise alpha-methyldopa 125 mg and dose to be adjusted on follow-up. Examination of the fundus and estimation of microalbuminuria, every trimester is recommended particularly in women with pregestational diabetes.

Fetal

Fetal surveillance: Ultrasound fetal measurement: Ultrasound monitoring is recommended at least every trimester.

Timing of delivery: Delivery before full term is not indicated unless there is evidence of macrosomia, polyhydramnios, poor

metabolic control or other obstetric indications (e.g. pre-eclampsia or intrauterine growth retardation). A few obstetricians prefer to terminate pregnancy around 38 gestational weeks to avoid stillbirth.

Delivery: During labor, it is essential to maintain good glycemic control, while avoiding hypoglycemia. Lower insulin requirements are common during labor (often no insulin is necessary). Maternal blood glucose level should be monitored after delivery, 24 hours postpartum and if found to be high, checked again on follow-up. A neonatologist's presence at the time of delivery is ideal, more so if significant neonatal morbidity is suspected.

FOLLOW-UP OF GESTATIONAL DIABETES MELLITUS

Gestational diabetic women require follow-up. An OGTT with 75 g oral glucose, using WHO criteria for the nonpregnant population should be performed at 6–8 weeks postpartum. If found normal, glucose tolerance test is repeated after 6 months and every year to determine whether the glucose tolerance has returned to normal or progressed. A considerable proportion of gestational diabetic women may continue to have glucose intolerance. It is important that women with GDM be counseled with regard to their increased risk of developing permanent diabetes.

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