DIAGNOSIS AND MONITORING

Screening and diagnosis of gestational diabetes mellitus

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Abstract

American Diabetes Association defines gestational diabetes mellitus (GDM) as diabetes which is diagnosed in the 2nd or 3rd trimester of pregnancy and is not clearly overt diabetes. GDM, if missed or not treated properly can result in maternal and foetal complications, short as well as long term. Screening for overt diabetes, especially for high risk women should be done at the earliest in pregnancy and for GDM, universally at 24-28 weeks of gestation. One step screening by IADPSG (75 gram OGTT), has been recently adopted by most of professional bodies to achieve uniformity. IADPSG criteria have resulted in increase in prevalence of GDM, and consequently increase pressure on health care services as well as on patients. This has resulted in discordance of view on universal adoption of the criteria. Many feel this criteria results in over diagnosis without clear benefits. This brief review will provide the answers to some of the important questions pertaining to screening for GDM.

Keywords: Gestational diabetes, Diagnosis, Diabetes, Pregnancy, Screening.

Introduction

Gestational diabetes mellitus (GDM) was defined previously as any glucose intolerance first identified during pregnancy. However, many cases may be of pre-existing diabetes and may have been missed in pre-conception period. Also, classically the GDM has its onset during pregnancy. To clear this confusion, ADA has adopted a new definition, which extrapolates GDM as "Diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes".[1] The global prevalence of hyperglycaemia in pregnancy in women (20-49 years) is 16.9%.[2] Due to this huge number, coupled with opportunity to improve maternal and foetal outcomes, both short and long term, diagnosis and treatment of GDM has become important. The positive step in this regard is recommendation for universal screening at 24-28 weeks of gestation, by all major professional organizations.[3] However, screening for GDM is still a controversial area. We take some of the issues, in the form of questions, which come to the mind when we think about screening and diagnosis for GDM in pregnancy.

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Screening for GDM: Is it Important?

GDM is associated with maternal and foetal complications.[4] There is 50% increase risk of preeclampsia. Caesarean sections are also more in women with GDM. GDM may lead to foetal complications including foetal hypoglycaemia, hypocalcaemia, respiratory distress, stillbirth and macrosomia, sometimes associated with birth trauma. Foetal malformation may occur when hyperglycaemia is present in early pregnancy (first trimester) particularly in unknown pre-GDM.

GDM is also a warning sign and predicts future T2DM in women, it also may lead to atherogenic dyslipidaemia, and cardiovascular disease. Intrauterine exposure to maternal hyperglycaemia is associated with metabolic diseases in offspring.

Since early diagnosis and treatment of women with GDM can help in alleviating or reducing the risk of these complications, screening for GDM is imperative. There is clear evidence to show that identification and treatment of women with GDM reduces these complications.[3,4]

Should it be Universal or Selective screening?

In view of adequate evidence that screening for and treatment of GDM can significantly reduce the risk for preeclampsia, foetal macrosomia, and shoulder dystocia, all major professional organizations have adopted

universal screening strategy for GDM. This means every woman during pregnancy should be screened for gestational diabetes.[5]

What is ideal time for screening for GDM?

The recommendations are to universally screen for women at 24-28 weeks of gestation.[3,5]

Can GDM be diagnosed in first trimester?

Initially IADPSG recommended that FPG from 92 to 125 mg% before 24 weeks can be taken as diagnostic for GDM.[9] However, recently IADPSG group suggested that the use of the fasting glucose threshold of ≥92 mg% for the identification of GDM in early pregnancy is not justified by current evidence. They also feel that the data is insufficient to confidently recommend cutoff points for oral glucose tolerance testing in early pregnancy (e.g., prior to 20 weeks' gestation).[6]

Should we screen women for hyperglycaemia before 24 weeks of gestation?

The aim of screening before 24 weeks is to identify pre-existing diabetes. Due to increase prevalence of obesity, hyperglycaemia in young adults, most guidelines recommend screening at first antenatal visit for pre-existing diabetes (called as overt diabetes, if diagnosed for first time in pregnancy only).[1,3,5] Early pregnancy hyperglycaemia has associated risk of congenital malformations, abortions, and development/worsening of maternal complications like retinopathy and nephropathy. Early diagnosis helps in decreasing the brunt of undetected hyperglycaemia. As we, in South Asia are already struggling for improving maternal and foetal outcomes, any opportunity to do so like this, should not be missed. Moreover, South Asians stand at high risk of having hyperglycaemia in pregnancy, due to background prevalence of diabetes and its risk factors.

How can overt diabetes be diagnosed?

If FPG is ≥ 126 mg/dL; random plasma glucose (RPG) is ≥200 mg/dL; post 75 gram glucose challenge plasma glucose is ≥ 200 mg%; or HbA1c is ≥ 6.5%, the woman is diagnosed to have overt diabetes.[7] The abnormal value ideally should be repeated to confirm the diagnosis, except for RPG, in which case other 3 tests can be done. However, HbA1c has not been adopted by WHO for this purpose. As per the Australasian Diabetes in Pregnancy Society (ADIPS) recommendation, Asian overweight or obese women should be evaluated by OGTT. OGTT is recommended at the first opportunity after conception for women having any of the high-risk factors for GDM listed in Table.[8]

Table: Risk factors for having Overt diabetes in first antenatal visit before 24 weeks or Gestational diabetes after 24 weeks.

◆ Previous history of gestational diabetes mellitus
◆ Previously elevated blood glucose level
◆ Maternal age > 40 years
◆ Family history of diabetes mellitus (first degree relative with diabetes or a sister with gestational diabetes mellitus)
◆ Body mass index > 35 kg/m2
◆ Previous macrosomia (baby with birth weight > 4,500 g or > 90th centile)
◆ Polycystic ovary syndrome
◆ Medications: corticosteroids, antipsychotics

Which screening strategy is better for GDM: Two step vs one step?

Two step strategy: In the two-step screening approach, glucose challenge test (GCT) is done by a 50 gram glucose. If it is positive, than 100-g 3-hour OGTT is done. The threshold for positive GCT can be taken as 140 mg/dL or 130 mg/dL. In100-g glucose tolerance test (OGTT), four blood samples are taken, fasting and then every hour for next 3 hours. If two or more abnormal values are there, woman is diagnosed to have GDM. The thresholds of values on OGTT are: (fasting) ≥95 mg/dL; (1 hour) ≥ 180 mg/dL; (2 hours) ≥155 mg/dL; and (3 hours) ≥140 mg/dL. American College of Obstetricians and Gynecologists (ACOG) and NIH still follows this two-step strategy for screening for GDM. The advantage cited for this strategy is that woman is diagnosed to have GDM after failing 2 tests, GCT then OGTT. So, the assurance of having GDM is more. This advantage is not there with one step screening procedure, especially with newer IADPSG criteria, which takes single value as abnormal even on OGTT. Poor reproducibility in such cases is another major concern.

However, the disadvantage is that we are un-necessarily delaying the diagnosis of GDM, which may have its own adverse consequences.[9] A systematic review compared sensitivity and specificity of the GCT with OGTT (either 75 or 100 g).[10] It found sensitivity of 74% and specificity of 85%. However, 26% of potential GDM cases are missed by this strategy. GCT screening also misses GDM with a modestly elevated fasting glucose, which is additional drawback of this strategy.

Summarizing, one step strategy is better, as it avoids missing cases, as well as delay in treatment. But as IADPSG criteria is more stringent, more cases are diagnosed with GDM. Of these, 80-90% of them may only be managed by diet and exercise. The wise handling of this increase load in itself is a challenge. As per WHO, a 2-step procedure requiring attendance on 2 separate occasions is often not feasible in many low and middle income countries.[11]

In one step strategy which test is better? 100 gram OGTT or 75 gram OGTT

100 gram OGTT is same, which is done as second step in 2 step strategy mentioned above. One step 75 gm OGTT for GDM is based on results of HAPO study. The test is positive for GDM if FPG is $\geq$ 92 mg/dL), or 1-hour level $\geq$ 180 mg/dL, or a 2-hour value is $\geq$ 153 mg/dL.[7]

100 gram OGTT helps in identification of severe cases of GDM which clearly benefit from treatment. 75 gram OGTT helps in identification of additional cases of GDM, which are mild, but benefit from treatment, though efforts may be more to gain a reward.

What is alternative to full OGTT test?

In many parts of the world, pregnant women, may not be able to reach the laboratory in a fasting state for a blood test because of the long travel distance or increase tendency to nausea. Consequently nonfasting testing may be the only practical option.

One step DIPSI criteria: 2 hour glucose value $\geq$ 140 mg% after 75 gram glucose load irrespective of time and meal is one alternative. Anjalakshi et al.[12] compared the 75 g oral glucose load given irrespective of the time of the last meal with a 2-h 75 g OGTT given 72 h later in the fasting state (WHO 1999 criteria), in 800 pregnant women. There was no statistically significant difference in the glycaemic response between the non-fasting and standard OGTT in diagnosing GDM. All women diagnosed with GDM, according to the 1999 WHO criteria using the 75 g load irrespective of the timing of the last meal also satisfied the diagnostic criteria of the standard fasting 75 g OGTT.[12] However, a recent study by Mohan et al,[13] found that DIPSI non-fasting OGTT had a very low sensitivity when compared to WHO 1999 criteria (27.7%) and IADPSG criteria (22.6%) Circadian variation to GCT may be responsible for these results. A woman with a positive test in the afternoon tested in a non-fasting state has a better metabolic function and a lower risk of GDM on subsequent OGTT, as per one of the study.[14]

Can HbA1c or Random blood glucose be used to diagnose GDM?

HbA1c, though helpful in management, is not recommended for screening of GDM, by any professional organization. Data scarcity and physiological changes in red cell mass and turnover makes interpretation of HbA1c difficult in pregnancy in relation to glycaemic levels.

Random glucose testing is not included in guidelines as a means of screening for GDM.[11]

Conclusion

GDM has immediate and longer term implications for the mother and child. The OGTT remains the standard diagnostic test. The choice of OGTT depends upon health care facilities and health professional expertise. Universal screening for GDM at 24-28 weeks, and for overt diabetes at first antenatal visit should be done.

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