Screening for gestational diabetes in India: Where do we stand?

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] It remains an area of controversy, in areas including selective versus universal screening, timing of testing, choice of one-step or two-step approach, and the criteria to be used to diagnose GDM. Some of these controversies have been plaguing this field for several decades and they continue to remain unresolved. Until recently, many researchers questioned the very need to screen for GDM, and its cost-effectiveness in particular.[2] Many professional bodies were convinced of the need to screen, but uncertainty existed on how to do this effectively. The work of Crowther *et al*.[3] and Landon *et al*.[4] showed that treatment of GDM reduced perinatal complications, and this finally led to the acceptance of the need to screen and treat GDM. The National Institute for Health and Clinical Excellence (NICE, 2008) guidelines concluded that "screening, diagnosis, and treatment of gestational diabetes is cost-effective."[5] The U.S. Preventive Services Task Force (USPSTF, 2013) recommended that all asymptomatic pregnant women should be screened for GDM after 24 weeks of gestation.[6]

Today, several professional bodies worldwide including the American College of Obstetricians and Gynecologists (ACOG), the American Endocrinology Society, the Canadian and Australian Diabetes Association and the Diabetes in Pregnancy Study Group of India (DIPSI) agree that screening for GDM should be universal, though the choice of screening tests varies between these agencies. Even those organizations that recommend selective screening [e.g., the American Diabetes Association (ADA) and NICE] have included Asian Indians as a high-risk ethnic group who need universal screening. A significant advantage of universal screening that is often unrecognized is that in countries like ours where the prevalence of diabetes is very high, type 2 diabetes occurs at much lower ages and urban areas have a high prevalence of it;[7,8] the chances of detecting preexisting diabetes are quite high.

The ADA and the American Congress of Obstetricians and Gynecologists (ACOG) have, until recently, recommended a two-step screening method, with a 50 g oral glucose challenge test (GCT) being used as the first step. The test is done in a nonfasting (random) state; 1 h after a 50 g glucose load, blood is drawn, and if the plasma glucose value is over 140 mg/dL, it is taken as a "positive test" and then a 3 h 100 g oral glucose tolerance test (OGTT) is recommended. The criteria to diagnose GDM for the latter test, originally, proposed by O'Sullivan and Mahan in 1964,[9] were converted to the present-day methodology of glucose estimation by Carpenter and Coustan in 1982.[10] In 1999, for the sake of logistic simplicity, the World Health Organization (WHO) introduced one-step screening and diagnostic test criteria. This was based on a single cut-point of 140 mg/dL, 2 h after a 75 g glucose load administered in the fasting state. Though arbitrary and likely based on the cut of value in impaired glucose tolerance in a nonpregnant state, this came to be widely accepted in many parts of the world because of its sheer convenience.[11]

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, one of the largest studies ever done on GDM, showed a continuum of risk between maternal glucose levels and adverse pregnancy outcomes. The HAPO Study used a 2-h 75-g glucose test as single-step screening and diagnostic test.[12] Based on this study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for GDM were developed.[13] For the IADPSG criteria, an OGTT is done in the fasting state using 75 g of glucose at 24-28 weeks, and GDM is diagnosed if any one of the following cut-points is met, i.e., fasting ≥ 92 mg/dl, or 1 hr ≥ 180 mg/dl or 2 hr ≥153 mg/dl.

The IADPSG criteria were endorsed by many professional bodies.[14] In 2013, the WHO also endorsed the IADPSG criteria as against the earlier 1999 criteria.[15] The ADA also accepted the IADPSG criteria in 2013 and it seemed as if an international consensus would finally emerge. However, in 2014, National Institutes of Health (NIH) declined to endorse the IADPSG criteria, stating that it needed more evidence prior to adoption.[16] Following the NIH report in 2014, the ADA has offered two options, i.e., either the one-step IADPSG or the two-step procedure, which involves a 50 g GCT (done in a nonfasting state), followed by 100 g 3-h OGTT (done on a fasting state) in those women who are screen positive.

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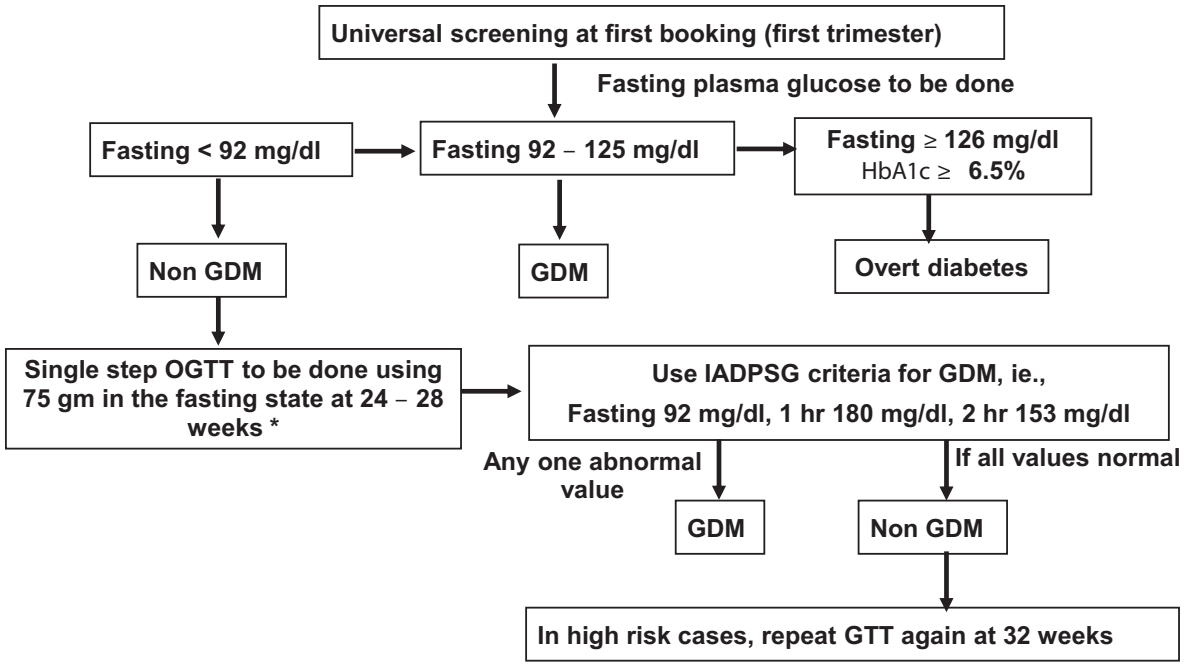
In developing countries such as India, particularly in rural areas, there are several challenges to screening for GDM. Some of these challenges include lack of trained phlebotomists, lack of standardized laboratories to do blood glucose estimations, and the problem in getting all women to visit in a fasting state. Due to these challenges, the WHO 1999 criteria, which require only a single sample (compared to three samples with the IADPSG and four samples with the Carpenter and Coustan criteria), became very popular in India.[11] DIPSI also endorsed the 1999 WHO criteria and recommended universal screening at first contact and again at 24-28 weeks using this single-step 2-h value, which the WHO (1999) criteria proposed.[17] Because there are difficulties in getting women to visit in a fasting state for the OGTT, Anjalakshi *et al*.[18] conducted a study comparing the GTT done in the fasting and the nonfasting states. They found that the nonfasting OGTT had 100% specificity and sensitivity when compared to the fasting test taken as a "gold standard." Based on this study, DIPSI adopted the nonfasting OGTT as a single-step screening and diagnostic test for GDM in India. The DIPSI guidelines recommend using 75 g glucose load, which can be given in either a nonfasting or a fasting state, and one blood sample to be drawn 2 h after glucose load, and a cut-point of 140 mg/dL as the diagnostic cut-point for GDM irrespective of whether the GTT is done in the fasting or nonfasting state.[17,18]

In 2012, the International Diabetes Federation (IDF) started a project in Chennai, India called "Women in India with GDM Strategy (WINGS)." The primary aim was to develop a model of care for GDM that would be piloted in India followed by a rollout in other developing countries. A secondary aim was to find a cost effective way of screening for GDM. WINGS therefore tried to validate the nonfasting DIPSI criteria, because if this proved to be a reliable and reproducible test, it could be more widely adopted. The study showed that DIPSI nonfasting OGTT criteria had a very low sensitivity (27.7%) compared to the WHO (1999) criteria and even lower in comparison with the IADPSG criteria (22.6%), although, admittedly, the specificity was quite high.[19] A study from Delhi similarly reported that the nonfasting DIPSI criteria results in low sensitivity.[20] Thus, two independent studies from different geographic locations showed that the DIPSI nonfasting OGTT is not suitable as a diagnostic test as it can miss a considerable number of women with GDM. One of the compelling arguments for a nonfasting test has been that most pregnant women will not come back for an OGTT in the fasting state.[21] The WINGS study however showed that 78.5% of women did report for the second OGTT done in the fasting state, even though no incentives were provided to the women.

In this issue of Journal of Postgraduate of Medicine, Gopalakrishnan *et al*.[22] report on the prevalence of GDM using the IADPSG criteria in another North Indian population studied in Lucknow and adds to the growing body of evidence on this criteria. This study reports a surprisingly high prevalence of GDM (41.9%). This is likely given the small sample size of 322 and referral bias, as this is a clinic-based study. Thus, population-based studies based on large numbers are urgently needed to determine the true prevalence of GDM in both urban and rural India.

In many parts of rural India, getting venous blood samples is next to impossible. Hence, several authors have tried to evaluate whether capillary blood glucose (CBG) testing can be



*** When a single step fasting OGTT is not possible, do a 2 step procedure, ie., 50 gm glucose challenge test (GCT) in the non fasting state followed by 3 hr OGTT in the fasting state using 100 gm Carpenter and Coustan criteria in those who screened positive in the GCT.**

Figure 1: Proposed guidelines for screening for GDM in India

used for screening for GDM. One study[23] compared capillary and venous samples using WHO 1999 criteria and showed that a CBG value at a 2-h plasma glucose level of ≥140 mg/dL had a sensitivity of 80.2% and specificity of 98.5%. We recently compared CBG with venous plasma glucose (VPG) using IADPSG criteria and we found that a 2-h CBG cut-point of 126 mg/dL (7.0 mmol/L) had sensitivity and specificity of 70.8% and 63% respectively.[24] However, as these sensitivity and specificity rates are unsatisfactory, CBG cannot replace VPG for diagnosis for GDM. However, it can be used as a screening test, maximizing the sensitivity by using lower 2 h cut-points, in low resource settings where VPG is impossible.

One of the biggest criticisms of the IADPSG criteria has been that it increases the number of women diagnosed as GDM, as it uses a rather low fasting plasma glucose cutoff. This obviously has several implications such as increasing health care costs. So, with all these new data, where do we stand with reference to diagnosis and the ideal screening strategy for GDM in India? There is no doubt that universal screening needs to be done, as seen by worldwide recommendations. Even though the old 1999 WHO criteria are simple to implement, the IADPSG are the only outcome-based criteria and close to international consensus. The low sensitivity of the nonfasting OGTT makes it ideal to choose the fasting 75 g OGTT and apply the new WHO guidelines, which recommend the IADPSG criteria. The recent NICE 2015 guidelines[25] have recommended a fasting plasma glucose value of 100 mg/dL in addition to the 2 h cut-point of 140 mg/dL after a 75 g glucose challenge. We propose in this editorial a potential guideline for screening for GDM in India [Figure 1]. Universal screening for GDM is necessary amongst Indians and at the time of the first registration. Fasting plasma glucose estimation should be done in all pregnant women. In order to obtain international standardization, we recommend that, wherever possible, a single-step fasting OGTT using 75 g glucose, and the IADPSG criteria be used, with the two-step procedure remaining a viable option.

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There are no conflicts of interest.

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