

Gestational diabetes mellitus: Get, set, go From diabetes capital of the world to diabetes care capital of the world

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ABSTRACT

Screening and diagnosis for gestational diabetes mellitus (GDM) as well as interventions for its management evoke considerable controversy. There are different types of screening methods: universal or risk-based, one step or two step. Different thresholds for diagnosis of GDM have been in vogue. Previous definition and diagnostic criteria had no place for diagnosis of overt diabetes in pregnancy. Following Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study and International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations, new screening and diagnostic criteria around the world seem to be gaining consensus. The present recommendation given by IADPSG for screening and diagnosis of diabetes mellitus in pregnancy has two discrete phases. The first is detection of women with overt diabetes not previously diagnosed or treated outside of pregnancy. Universal early testing in populations is recommended at the first prenatal visit. The second phase is a 75-g OGTT at 24–28 week gestation in all women not previously found to have overt diabetes or GDM. ACHOIS and MFMU Network trials have proven benefit in treating hyperglycemias less than what is diagnostic for diabetes. DIPSI has shown the alternative way for resource-challenged communities. Efforts from all stake holders with interest in GDM are required to make the diabetes capital of the world into the diabetes care capital of the world.

Key words: Diabetes in Pregnancy Study Group India, gestational diabetes mellitus, gestational diabetes mellitus, guidelines, Hyperglycemia and Adverse Pregnancy Outcomes study, International Association of Diabetes and Pregnancy Study Groups, screening

INTRODUCTION

Gestational diabetes mellitus (GDM) is a topic of considerable controversy. It is so especially when it comes to its screening and diagnosis and at times even to justify interventions for its management and their cost-effectiveness adds to the controversy. It is more controversial whether maternal hyperglycemias less severe than that in diabetes mellitus are associated with increased risks of adverse pregnancy outcomes. A fair trial to demystify the entire spectrum of this disease: what is GDM,

its relevance, how and when to screen pregnant women for GDM, diagnostic criteria for GDM, its management, and its effects on mother and baby, shall be made in a series of review articles. Also, equally important is to discuss why GDM requires efforts on the part of clinicians to screen and manage women for it? The present review article shall concentrate on defining GDM, its present day relevance, screening, and diagnostic criteria.

RELEVANCE IN INDIA

India leads the world with largest number of diabetic subjects earning the dubious distinction of “*the diabetes capital of the world.*” It was estimated to have had 31.7 million people having diabetes in year 2000 which is projected to be 79.4 million by year 2030.^[1] Both the figures are highest in the world. During the next 2 decades, the world population is expected to increase by 37%, but the prevalence of diabetes will increase by 114%. More bothersome is a 151% projected increase in number of people with diabetes vis

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a vis just a 40% projected increase in population of India during the same period. According to the Diabetes Atlas 2009 published by the International Diabetes Federation, the number of people with diabetes in India in year 2010 was reported to be around 50.8 million which is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken.^[2] The so-called Asian Indian Phenotype refers to certain unique clinical and biochemical abnormalities in Indians which includes but is not limited to increased insulin resistance, greater abdominal adiposity i.e., higher waist circumference despite lower body mass index. This phenotype makes Indians more prone to diabetes. Although genes are there to be blamed, but the primary driver of the epidemic of diabetes is the rapid epidemiological transition associated with changes in dietary patterns and decreased physical activity as evident from the higher prevalence of diabetes in the urban population.

It is strongly felt by the author that screening for GDM is to type 2 diabetes mellitus what a pap smear is to cervical cancer. Both are modalities of secondary prevention of diseases. Cervical cancer may be perceived to be more deadly but it is the GDM which has already reached a magnitude which has brought it to the proportions of an international epidemic. It is further going to increase by leaps and bounds in times to come, more so in light of a global increase of obesity in the women of reproductive age group. Whereas screening for cancer of cervix benefits this generation, the same in case of GDM also helps the future generations by reducing the incidence of type 2 diabetes mellitus in later generations.

Definition

GDM is defined as “glucose intolerance with onset or first recognition during pregnancy.”^[3,4] Criteria for the diagnosis were initially established more than 40 years ago^[5] and, with minor modifications, remain in use today. These criteria were not designed to identify pregnant women who are at an increased risk for adverse pregnancy outcomes but rather women who are at a high risk for the development of diabetes after pregnancy^[5,6] or they are the criteria used for the general population.^[7]

DIAGNOSTIC CRITERIA

Overt diabetes mellitus during pregnancy is associated with significantly increased risks of adverse perinatal outcomes. Whereas some data suggest that current diagnostic criteria for GDM^[3] are too restrictive and that lesser degrees of hyperglycemias also increase risk,^[8-13] however risks associated with hyperglycemia that is less severe than that diagnostic of overt diabetes mellitus are uncertain for a number of reasons. First, till now there are no

consensus international standards for diagnosis of GDM.^[4] In addition, the extent to which adverse outcomes associated with GDM may be explained by confounders (including but not limited to obesity, associated maternal medical conditions, advanced maternal age, etc) is unclear.^[14-16] Caregiver bias in apprehension of adverse outcomes due to GDM may increase the likelihood of disorders or problems due to increased intervention.^[17]

The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study^[18] was a large multinational epidemiologic study, involving 25,505 pregnant women at 15 centers in nine countries. It demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously increased as a function of maternal glycemia at 24-28 weeks, even within ranges previously considered normal for pregnancy. For most complications, there was no threshold for risk. The HAPO study tried to clarify the risks of adverse outcomes associated with various degrees of maternal glucose intolerance less severe than that in overt diabetes mellitus. These results have led to careful reconsideration of the diagnostic criteria for GDM.

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) was formed in 1998 as an umbrella organization to facilitate collaboration between the various regional and national groups that have a primary or significant focus on diabetes and pregnancy. The principal objectives of IADPSG are to foster an international approach to enhancing the quality of care, facilitating research, and advancing education in the field of diabetes in pregnancy. IADPSG is an international consensus group with representatives from multiple obstetrical and diabetes organizations. IADPSG's affiliated organizations include the Diabetes in Pregnancy Study Group India (DIPSI), the Diabetic Pregnancy Study Group of the European Association for the Study of Diabetes, the Japanese Association of Diabetes and Pregnancy, the Australasian Diabetes in Pregnancy Society, the West Coast USA Diabetic Pregnancy Study Group of North America, and the Canadian Special Interest Group for Diabetes and Pregnancy. Associated organizations include the European Association of Perinatal Medicine, the Society for Maternal Fetal Medicine of the USA, the Pregnancy and Reproductive Health Interest Group of the American Diabetes Association (ADA), and the Saredia International Association.^[19] After deliberations in 2008-2009, starting with an IADPSG sponsored International Workshop Conference on Gestational Diabetes Diagnosis and Classification in Pasadena, California, it developed revised recommendations for diagnosing GDM which were published in March 2010^[20] and these were endorsed in the ADA position statement in Jan 2011.^[21]

WHO SHOULD BE SCREENED?

There is continuing debate about whether all pregnant women should be tested, or whether testing should be done only if risk factors are present. However, there is a general agreement about the major risk factors for GDM. These include but are not limited to increasing maternal age and weight, previous GDM or a macrosomic infant, family history of diabetes, being from an ethnic background with a moderate to high prevalence of diabetes, and polycystic ovary syndrome. While there is no doubt that women with some or all of these risk factors are more likely to develop GDM, the reality is that any woman can develop this problem.

The American Diabetes Association has proposed that women at low risk for GDM—that is, women who have all of the following characteristics: less than 25 years of age, normal body weight, no first-degree relative with diabetes mellitus, not a member of an ethnic group at increased risk for type 2 diabetes mellitus, no history of abnormal glucose metabolism, and no history of poor obstetric outcome—need not be screened.^[22] Griffin *et al.*,^[23] found that risk-based screening missed about half the women with GDM than what were diagnosed using universal screenings. In their study, risk-based screening found an incidence of 1.45%, whereas universal screening reported an incidence of GDM as 2.7% in the same population. Moses^[24] concluded that excluding the low-risk group of women would still require 80% of the women to be tested and would miss 10% of all cases of GDM. A retrospective study by Williams and co-workers^[25] reported that testing according to risk factors would still require 90% of the population to be tested. Coustan reported in the *Green Journal (Obstetrics and Gynecology)*^[26] that testing women according to the older age based on American College of Obstetricians and Gynecologists (ACOG) criteria would miss almost one third of cases of GDM. The limited evidence so far indicates that a sorting system cannot be conducted in an efficient manner,^[27] and that women with GDM without risk factors appear to be no different from women with GDM and risk factors.

In light of the above, it seems that sufficient evidence is not available to arrive to a definitive opinion on the advantages of selective testing. More so, in the Indian context with the *Asian Indian Phenotype* in background it is strongly felt by the author that a universal screening must be done for all pregnant women. It is felt that first, identification of women with GDM, followed by appropriate treatment and monitoring, will reduce adverse perinatal outcomes. Second, given the high likelihood that women who manifest

GDM will develop type 2 diabetes mellitus, identification of these patients will permit interventions after delivery that might delay or prevent the onset of type 2 diabetes mellitus. Similar feelings advocating universal screening of GDM have been echoed by Gabbe and Graves in their writings on the subject^[28] and also in recent IADPSG review on the subject.^[20]

WHEN TO SCREEN?

The timing of glucose tolerance testing during pregnancy is critical, because delayed diagnosis increases the duration of deranged maternal metabolism and accelerated fetal growth. However, because the prevalence of GDM increases with advancing gestation due to rising insulin resistance mediated by placental hormones, testing too early can overlook some patients who will develop disease later. Traditionally, risk factor assessment for GDM is performed at the first prenatal visit of all pregnant women. Patients with any of these risk factors undergo screening as soon as feasible, and if results are negative, tests are to be repeated at 24 to 28 weeks' gestation. This time window is selected because the insulin resistance that causes hyperglycemia increases as the third trimester progresses, early testing may miss some patients who later become glucose-intolerant. Performing the test too late in the third trimester limits the time in which metabolic intervention can take place. For this reason, it has been recommended that glucose tolerance testing be performed in all patients at 24 to 28 weeks' gestation.

The International Workshop Conferences on GDM have till recently all defined the condition as “any degree of glucose intolerance with onset or first recognition during pregnancy.”^[6,29] Therefore, for all these years, GDM has been defined as such. Although most cases resolve with delivery, the definition applied whether or not the condition persisted after pregnancy and did not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy. This definition facilitated a uniform strategy for detection and classification of GDM (interestingly, in a topic maze with controversies, definition was amazingly non-controversial), but its limitations were recognized for many years. As ongoing epidemics of obesity and diabetes resulted in more type 2 diabetes in young women, the numbers which were undiagnosed before pregnancy started increasing.^[30,31] The need to identify these women and address perinatal risks that may be particular to their greater degree of hyperglycemia also became more important. After deliberations in 2008–2009, IADPSG recommended that women found to have diabetes at their initial prenatal visit, receive a diagnosis of overt, not gestational, diabetes.

A direct effect of this was a desire fuelled by scientific evidence (all agree that overt diabetes mellitus during pregnancy is associated with significantly increased risks of adverse perinatal outcomes, affecting right from period of embryogenesis) to detect overt diabetes in pregnancy as early as possible to provide an opportunity to optimize pregnancy outcome. Insulin is detectable in the fetal pancreas as early as 9 weeks after conception.^[32] An increase in pancreatic beta-cell mass and insulin secretion in the fetus occurs by the 16 weeks of gestation, in response to maternal hyperglycemia.^[33,34] This early effect on the fetal beta cells may account for the persistence of fetal hyperinsulinemia throughout pregnancy and its associated effects,^[35] even when the pregnant lady becomes normoglycemic in later pregnancy.^[36] Because of variation in time of enrolment for prenatal care, no limit is placed on the timing of initial assessment for detection of overt diabetes in pregnancy; however, it is emphasized that screening should be done in early pregnancy and at the first opportunity. However, if enrolment is at 24 weeks gestation or later and overt diabetes is not found, the initial test should be followed by a 75-g OGTT.

The present recommendation given by IADPSG, and recently endorsed by ADA for screening and diagnosis of diabetes mellitus in pregnancy has two discrete phases. The first is detection of women with overt diabetes not previously diagnosed or treated outside of pregnancy. Universal early testing in populations (with a high prevalence of type 2 diabetes) is recommended at the first prenatal visit. The second phase is a 75-g OGTT at 24–28 weeks gestation in all women not previously found to have overt diabetes or GDM.

It is strongly recommended that screening should be offered at the first prenatal visit and if not diagnosed previously with overt diabetes or GDM, repeat testing be done at 24–28 weeks' gestation.

HOW TO SCREEN AND DIAGNOSE GESTATIONAL DIABETES MELLITUS?

At present, there is a lack of international consistency with regard to the diagnosis of GDM. While a glucose tolerance test (GTT) is commonly employed, glucose challenge dosages vary and diagnostic thresholds are myriad. The 75-g glucose challenge is widely used throughout the world for diagnostic testing in the non-pregnant state. At the Third International Workshop Conference on GDM in 1990^[37] a series of recommendations were made that included universal employment of the 75-g glucose challenge during pregnancy. Some sets of diagnostic criteria, such as those

proposed by the World Health Organization (WHO), were simply based on criteria used in non-pregnant individuals, and did not take into account changes in carbohydrate metabolism brought about by the pregnant state. Others, like the O'Sullivan criteria^[5] were based on data from pregnant women, but were mathematically derived as being 2 SD above the mean, and were validated for their predictive value for future diabetes in the mother and were not correlated to pregnancy outcomes. The lack of uniform criteria for diagnosis and the reliance on observational data drawing on historic controls has limited the accurate determination of the relationship between mild degrees of hyperglycemia and perinatal outcomes.^[38]

Currently, a two-stage diagnostic procedure is conducted in some parts of the world, including a greater part of India. A two-stage procedure involves a non-fasting glucose challenge test (GCT) with a 50 g glucose load irrespective of fasting status; followed by a formal OGTT for women who have a positive result. In this setting, the sensitivity of the GDM testing regimen depends on the threshold value used for the 50-g GCT. Recommendations from the ADA^[39] and ACOG^[40] elucidate that using a threshold value of 140 mg/dL results in approximately 80% detection of GDM, whereas using a threshold of 130 mg/dL results in 90% detection. A potential disadvantage of using the lower value of 130 mg/dL is an approximate doubling in the number of OGTTs performed. Few experts recommend that using a threshold plasma glucose value of 130 mg/dL in practices with a significant proportion of higher risk gravidas. Dooley *et al.*,^[41] reported that among non-white women, the risk of GDM with a 1 h glucose value equaling or greater than 200 mg/dL is greater than 90%. Bobrowski and co-workers^[42] reported a 100% risk in patients with a screening result above 216 mg/dL. Based on such results, most experts omit an OGTT test for patients with GCT results of 200 mg/dL or greater and manage the patient as a case of gestational diabetes.

The GCT will inevitably miss some women with GDM. In addition, there has been little systematic examination of certain important facets of two step testing like how many women who are positive on a GCT fail to return for the definitive OGTT and whether a two-stage procedure delays the diagnosis and treatment of GDM, and what the effect of such a possible delay might be.

For the reasons mentioned, it was thought that a one-stage definitive procedure may be preferable. But still, a two stage procedure will continue to suit many healthcare arrangements, especially for economic reasons. The current one-step option involves direct administration of the 3-h, 100-g glucose OGTT. Direct, one-step administration

of the 3-h, 100-g OGTT test was considered by few experts in women with prior GDM, especially those with additional risk factors. However, it was also a contemporary thinking that adoption of a lower glucose load (75 g) and a shorter duration of the testing procedure may lead to reconsideration about the need for a two-stage procedure.

As noted above, in setting of a two-step testing, an abnormal screening test necessitates a 100-g oral GTT, performed after an overnight fast but with the patient consuming her usual unrestricted daily diet in the days preceding the test. A fasting plasma level is first drawn, followed by blood samples at 1, 2, and 3 h. If two or more values are met or exceeded, the diagnosis of GDM is established. Most capillary glucose meters lack the precision needed for screening and hence if a meter is being used, its precision should be known, and the relationship between simultaneously drawn venous blood samples and capillary blood samples must be determined.^[40] Meters, however, should never be used to *diagnose* GDM.^[43] Two sets of cut-off values for diagnosis of GDM are currently used: those put forth by the National Diabetes Data Group in 1979 (NDDG values)^[44] and a modification of these values by Carpenter and Coustan in 1982 (Carpenter and Coustan values).^[45] The Carpenter and Coustan criteria have been endorsed by the ADA.^[22] Use of later criteria with lower values increased the diagnosis of GDM from approximately 3% to 5%.^[46] But a big unsolved question was that what should be done with patients who have a single abnormal value? Although some did recommend these patients be treated as though they had GDM, it was also considered reasonable to repeat the oral GTT in 4 weeks and decide thereafter.

The HAPO study^[18] provided an opportunity to revise diagnostic criteria for GDM. The proposed criteria for the 75 g, 2 h OGTT are that any of the following thresholds be met or exceeded:

- Fasting plasma glucose 92 mg/dL (5.1 mmol/L).
- One-hour plasma glucose 180 mg/dL (10 mmol/L).
- Two-hour plasma glucose 153 mg/dL (8.5 mmol/L).

These proposed diagnostic criteria are based on their predictive value for adverse pregnancy outcomes, are based on multinational data and international consensus, and allow the diagnosis to be made with a single elevated value. Treatment has been demonstrated to be efficacious at similar glucose levels. IADPSG has endorsed these criteria. The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), a large, randomized trial of treatment for GDM, concluded that treatment reduces serious perinatal complications and may also improve

health-related quality of life.^[47] Maternal–Fetal Medicine Units Network conducted a randomized clinical trial for the treatment of mild gestational diabetes,^[48] results of which provided further compelling evidence that among women who have GDM and normal fasting glucose levels, treatment that includes dietary intervention and insulin therapy, as necessary, reduces rates of adverse pregnancy outcomes including perinatal mortality, neonatal hypoglycemia, neonatal hyperbilirubinemia, elevated cord blood C-peptide level, and birth trauma.

These new criteria will significantly increase the prevalence of GDM, primarily because only one abnormal value, not two, is sufficient to make the diagnosis. The diabetic associations around the globe recognize the anticipated significant increase in the incidence of GDM to be diagnosed by these criteria and are sensitive to concerns about the “medicalization” of pregnancies previously categorized as normal. Moses in an editorial^[49] accompanying the IADPSG recommendations^[20] brought out that the new criteria shall be diagnosing around 18% of pregnant women with GDM. However, these diagnostic criteria changes are being made in the context of worrisome worldwide increases in obesity and diabetes rates, with the intent of optimizing gestational outcomes for women and their babies; and recent studies have brought out evidence in this context as discussed previously. Admittedly, there are few data from randomized clinical trials regarding therapeutic interventions in women who will now be diagnosed with GDM based on only one blood glucose value above the specified cutpoints (in contrast to the older criteria that stipulated at least two abnormal values). Expected benefits to their pregnancies and offspring is inferred from intervention trials that focused on women with more mild hyperglycemia than identified using older GDM diagnostic criteria and that found modest benefits.^[47,48] The frequency of their follow-up and blood glucose monitoring is not yet clear but likely to be less intensive than women diagnosed by the older criteria.

It is pertinent to emphasize that additional well-designed clinical studies are needed to determine the optimal intensity of monitoring and treatment of women with GDM diagnosed by the new criteria who would not have been diagnosed as per the prior definition of GDM. It is also important to note that only 20% of treated Australian Carbohydrate Intolerance Study trial subjects and 8% of Maternal-Fetal Medicine Units Network subjects required insulin, implying that lifestyle intervention and dietary intervention will be effective 80-90% of women with GDM.

DIABETES IN PREGNANCY STUDY GROUP INDIA: ROLE AND RELEVANCE

Diabetes in Pregnancy Study Group India (DIPSI) formally came into existence on 12 December 2004 as an organization consisting of Endocrinologists, Physicians, Obstetricians, and other stake holders with interest in GDM. Through a highly successful series of conferences and publications, DIPSI has been able to bring GDM to a centre stage in India. It helped fuel interest in potential complications of GDM as well as in its screening and management. In August 2006, it recommended that as a pregnant woman walks into the antenatal clinic in the *fasting state*, she should be given a 75 g oral glucose load and at 2 h a venous blood sample be collected for estimating plasma glucose.^[50] DIPSI recommended this one-step procedure of challenging women with 75 g glucose and diagnosing GDM as simple, economical, and feasible. Recently, after its fifth national conference, DIPSI in their Kolkata Declaration amended the previous recommendations, which were published in May 2010.^[51] It stated that to diagnose GDM in the community, in the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination to be given a 75 g oral glucose load, *irrespective of whether she is in the fasting or non fasting state*, without regard to the time of the last meal. A venous blood sample is to be collected at 2 h for estimating plasma glucose. GDM is diagnosed if 2 hour plasma glucose is ≥ 140 mg/dL. This seems to be based on the observations of the Diabetes in Pregnancy and Awareness Project (DIPAP).^[52] However, the cut offs have not been put to test to find their correlation with adverse perinatal outcomes.

WOULD A SINGLE GLUCOSE VALUE DIAGNOSIS SERVE AS STANDARD OF CARE?

Indeed, it would have simplified matters if a single glucose determination, such as fasting plasma glucose, or any other one value would have been sufficient for the diagnosis, so as to preclude the need for a full OGTT. Therefore, the relative independent contributions of the fasting, 1-hour and 2-hour glucose values were considered by IADPSG keeping in background the HAPO trial. Each of the three samples contributed at least partially independently as a predictor of adverse pregnancy outcome, and therefore IADPSG has recommended the full 2-h, 75 g OGTT. However, the possibility that a particular professional organization might opt to eliminate one or more of the three tests has been left open; which although will reduce the sensitivity of the process but also shall decrease the cost and inconvenience.

To prove the point, the mean glucose value at each of the three time points was chosen as the reference value, against which proposed thresholds were compared. Thresholds that yielded odds ratios (OR) of 1.5, 1.75, and 2.0 times the likelihood of adverse outcomes at mean glucose levels were considered. Setting thresholds at an OR of 1.5 identifies around 25% of the cohort with more than one glucose value that met or exceeded the threshold. Using an OR of 1.75 rather than 2.0 increased the yield of cases with similar risks of adverse outcome by 83%, and identified 16.1% of the population of the HAPO cohort as having GDM. At ORs of 2.0, frequencies of birth weight, cord serum C-peptide, or percent infant body fat greater than 90th percentile in those meeting threshold were modestly higher than those for OR 1.75, but the number of participants meeting threshold decreased from 16.1% to 8.8%, meaning that the higher thresholds would fail to identify many cases with nearly comparable risk of adverse outcomes. The thresholds recommended represent ORs of 1.75, and are fasting plasma glucose 92 mg/dL, 1 h after the 75-g challenge 180 mg/dL, and 2 h after the 75-g challenge 153 mg/dL. At the proposed threshold of 92 mg/dL for fasting plasma glucose, 8.3% of the HAPO study population was identified and 19.5% of the babies were LGA. Adding the 1-hour threshold of 180 mg/dL identified an additional 5.7% of the population who did not have an elevated fasting value and a total of 16.5% of identified pregnancies delivered babies with LGA. Adding the 2-hour threshold of 153 mg/dL identified an additional 2.1% of the population, and a cumulative total of 16.2% with LGA. The proportion with LGA babies decreased with the addition of patients identified by only the 1-h and/or 2-h thresholds because the positive predictive value of these thresholds was slightly lower than that of the fasting, which did not preclude values for 1-h and/or 2-h also above threshold.

Among the HAPO cohort, 11.1% had only one elevated result, 3.9% had two elevated results, and 1.1% had elevation of all three results. Therefore, by the preceding discussion it is clear that although diagnosing GDM by a single glucose value may be acceptable and the only feasible alternative in a resource challenged community setting; however it comes at a cost of decreased sensitivity, which will exclude many women with GDM from being diagnosed and deny them the benefit of treatment.

WHAT TO DO FINALLY?

In this Google age flooded with information, knowledge needs to be extracted and perfected.

In the last couple of years, a few scientific studies, which

have been discussed extensively in this review, have paved the way for evidence-based knowledge to be put in practice to care for pregnant women whose pregnancies are complicated with diabetes, either overt or GDM. The first and the most vital step in good clinical practice is correct diagnosis. All of us would remember from our medical school days the scholarly professors emphasizing the importance of a correct diagnosis. Treatment comes next, because it comes only if a disease is diagnosed. In light of the HAPO study results and the recommendations by IADPSG the following is recommended as standard of care in screening and diagnosis of pregnancy, with the present day knowledge and evidence.

On the first prenatal visit, measure fasting plasma glucose, HbA1C or random plasma glucose on all women. If results indicate overt diabetes, i.e. fasting plasma glucose equals or is more than 126 mg/dl, HbA1C 6.5%, random plasma glucose equaling or more than 200 mg/dl (followed by confirmation by FPG or Hb A1C) then start treatment and follow-up as for preexisting diabetes. If results not diagnostic of overt diabetes and fasting plasma glucose equals or is more than 92 mg/dl but less than 126 mg/dl, diagnose as GDM. If fasting plasma glucose is less than 92 mg/dl at the first prenatal visit, then again test for GDM from 24 to 28 weeks' period of gestation with a 75-g OGTT. However, if first visit is at or after 24 weeks gestation and overt diabetes is not found, the initial test should be followed by a 75-g OGTT.

At 24–28 weeks gestation perform a 2-h 75-g OGTT after overnight fast on all women not previously found to have overt diabetes or GDM during testing earlier in this pregnancy. At this period of gestation also, if fasting plasma glucose equals to or is more than 126 mg/dL, then she is given a diagnosis of overt diabetes. She should be diagnosed as having GDM if one or more values equals or exceeds the threshold which is for FPG 92 mg/dL, for 1-h plasma glucose 180 mg/dL and for 2-h plasma glucose 153 mg/dL. And normal if all values on OGTT less than thresholds. One must remember to conduct a postpartum glucose testing on all women diagnosed with overt diabetes during pregnancy or GDM.

These criteria of diagnosing GDM will definitely bring up the incidence of diabetes in pregnant women. It must be remembered that GDM bears a similarity to “prediabetes,” which has been defined as impaired fasting glucose (fasting plasma glucose 100-125 mg/dL) or impaired glucose tolerance (2 h, 75-g OGTT plasma glucose value 140-199 mg/dL), short of the diagnostic criteria for diabetes. The incidence and prevalence of prediabetes is much greater than that of diabetes. Consequently, it should not be a

great surprise that a greater population of the pregnant population might have GDM, and the new diagnostic criteria when brought into standard clinical practice will not only benefit this generation by affording them an opportunity to manage their illness but also help future generations as seeds of type 2 diabetes mellitus are many a times sown in the womb.

However, in the resource challenged areas which include a greater part of South East Asia, if it is not feasible to carry out the above mentioned screening program, then the DIPSI recommended one-step single glucose value testing will prove very valuable. It causes least disturbance in a pregnant woman's routine activities and serves as both a screening and diagnostic procedure.

CONCLUSION

Any diagnostic or therapeutic modality claiming to treat or prevent health issues must withstand the rigor of scientific studies of efficacy and safety, and has to prove its worth fullness in this era of evidence based medicine. Treatment of GDM has been subjected to this requirement and has passed this test. Therefore, whatsoever methods are adopted, it is an obligation on all clinicians in general, and the physicians caring for the pregnant women in particular, to screen and treat them for diabetes. As brought out initially, our nation has earned the dubious distinction of “*the diabetes capital of the world*,”. Now if we do a good job of screening and managing GDM, we can lay claim to be the “*diabetes care capital of world*.”^[53] Our genes may have been responsible for the former and we may not have any fault in earning the dubious distinction, however we can take pride in our medicare system if we are able to achieve the latter. We can't eradicate diabetes but we can definitely prevent its ill effects by managing it efficiently. Let's all join hands in doing so, and in one way it will help in decreasing the incidence of type 2 diabetes mellitus in generations to come, again something which will be like a primary prevention of the disease for next generation. This is the least we owe to our next generations.

REFERENCES

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27:1047-53.
2. Sicree R, Shaw J, Zimmet P. The Global Burden: Diabetes and impaired glucose tolerance. *Diabetes Atlas International Diabetes Federation*. 4th ed. Belgium: International Diabetes Federation; 2009. p. 1-105.
3. American Diabetes Association. Clinical practice recommendations 2001: Gestational Diabetes Mellitus. *Diabetes Care* 2001;24 Suppl 1:S77-9.

4. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. *Diabetes Care* 1998;21 Suppl 2:B161-7.
5. O'Sullivan JB, Mahan CM. Criteria for oral glucose tolerance test in pregnancy. *Diabetes* 1964;13:278-85.
6. Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, *et al.* Summary and recommendations of the Fifth International Workshop- Conference on Gestational Diabetes Mellitus. *Diabetes Care* 2007;30 Suppl 2:S251-60.
7. WHO Expert Committee on Diabetes Mellitus: second report. *World Health Organ Tech Rep Ser* 1980;646:1-80
8. Jensen DM, Damm P, Sorensen B, Mølsted-Pedersen L, Westergaard JG, Klebe J, *et al.* Clinical impact of mild carbohydrate intolerance in pregnancy: A study of 2904 nondiabetic Danish women with risk factors for gestational diabetes. *Am J Obstet Gynecol* 2001;185: 413-9.
9. Yang X, Hsu-Hage B, Zhang H, Zhang C, Zhang Y, Zhang C. Women with impaired glucose tolerance during pregnancy have significantly poor pregnancy outcomes. *Diabetes Care* 2002;25:1619-24.
10. Vambergue A, Nuttens MC, Verier-Mine O, Dognin C, Cappoen JP, Fontaine P. Is mild gestational hyperglycemia associated with maternal and neonatal complications? The Diagest Study. *Diabet Med* 2000;17:203-8.
11. Langer O, Brustman L, Anyaegbunam A, Mazze R. The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. *Am J Obstet Gynecol* 1987;157:758-63.
12. Sacks DA, Greenspoon JS, Abu-Fadil S, Henry HM, Wolde-Tsadik G, Yao JF. Toward universal criteria for gestational diabetes: The 75-gram glucose tolerance test in pregnancy. *Am J Obstet Gynecol* 1995;172:607-14.
13. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, *et al.* Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. *Am J Obstet Gynecol* 1995;173:146-56.
14. Jarrett RJ. Reflections on gestational diabetes mellitus. *Lancet* 1981;2:1220-1.
15. Hunter DJ, Keirse MJ. Gestational diabetes. In: Chalmers I, Enkin M, Kierse M, editors. *Effective care in pregnancy and childbirth*. Oxford, England: Oxford University Press; 1989. p. 403-10.
16. Spellacy WN, Miller S, Winegar A, Peterson PQ. Macrosomia: Maternal characteristics and infant complications. *Obstet Gynecol* 1985;66:158-61.
17. Coustan DR. Management of gestational diabetes mellitus: A self-fulfilling prophecy? *JAMA* 1996;275:1199-200.
18. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, *et al.* Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991-2002.
19. Available from: <http://www.joomla.iadpsg.org> [Last accessed on 2011 Jun 19].
20. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, *et al.* International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676-82.
21. Position Statement: American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2011;34:S62-9.
22. American Diabetes Association. Gestational diabetes mellitus. *Diabetes Care* 2003;26(Suppl 1):S103-5.
23. Griffin ME, Coffey M, Johnson H, Scanlon P, Foley M, Stronge J, *et al.* Universal vs. risk factor-based screening for gestational diabetes mellitus: detection rates, gestation at diagnosis and outcome. *Diabet Med* 2000;17:26-32.
24. Moses RG, Griffiths R, Davis W. Gestational diabetes. Do all women need to be tested? *Aust NZ J Obstet Gynaecol* 1995;35:387-9.
25. Williams CB, Iqbal S, Zawacki CM, Yu D, Brown MB, Herman WH, *et al.* Effect of selective screening for gestational diabetes. *Diabetes Care* 1999;22:418-21.
26. Coustan DR, Nelson C, Carpenter MW, Carr SR, Rotondo L, Widness JA. Maternal age and screening for gestational diabetes: A population-based study. *Obstet Gynecol* 1989;73:557-61.
27. Simmons D, Devers MC, Wolmarans L, Johnson E. Difficulties in the use of risk factors to screen for gestational diabetes mellitus (letter). *Diabetes Care* 2009;32:e8.
28. Gabbe SG, Graves CR. Management of diabetes mellitus complicating pregnancy. *Obstet Gynecol* 2003;102:857-68.
29. American Diabetes Association. Diagnosis and classification of diabetes mellitus (Position Statement). *Diabetes Care* 2009; 32(Suppl 1):S62-7.
30. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of pre-existing diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. *Diabetes Care* 2008;31:899-904.
31. Feig DS, Razzaq A, Sykora K, Hux JE, Anderson GM. Trends in deliveries, prenatal care, and obstetrical complications in women with pregestational diabetes: A population based study in Ontario, Canada, 1996-2001. *Diabetes Care* 2006;29:232-5.
32. Girling J, Dornhorst A. *Pregnancy and Diabetes Mellitus* In: Pickup JC, Williams G (eds) *Textbook of diabetes*, 3rd edn. Blackwell publishing company, Oxford, pp 65-66.
33. Reiher H, Fuhrmann K, Noack S, Woltanski KP, Jutzi E, Hahn von Dorsche H, *et al.* Age-dependent insulin secretion of the endocrine pancreas *in vitro* from fetuses of diabetic and non-diabetic patients. *Diabetes Care* 1983;6:446-51.
34. Nahum GG, Wilson SB, Stanislaw H. Early-pregnancy glucose screening for gestational diabetes mellitus. *J Reprod Med* 2002;47:656-62.
35. Carpenter MW, Canick JA, Hogan JW, Shellum C, Somers M, Star JA. Amniotic fluid insulin at 14-20 weeks' gestation: Association with later maternal glucose intolerance and birth macrosomia. *Diabetes Care* 2001;24:1259-63.
36. Schwartz R, Gruppuso PA, Petzold K, Brambilla D, Hiilesmaa V, Teramo KA. Hyperinsulinemia and macrosomia in the fetus of the diabetic mother. *Diabetes Care* 1994;17:640-8.
37. Metzger BE; and the Organizing Committee. Summary and recommendations of the third international workshop-conference on gestational diabetes mellitus. *Diabetes* 1991;40 Suppl 2:197-20 1.
38. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, *et al.* Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-Hospital Gestational Diabetes Project. *Am J Obstet Gynecol* 1995;173:146-56.
39. American Diabetes Association. Standards of Medical Care in Diabetes - 2007. *Diabetes Care* 2007;30 (suppl 1):S4-41.
40. American College of Obstetricians and Gynecologists (ACOG): Committee on Practice Bulletins--Obstetrics. ACOG practice bulletin. Clinical management guidelines for Obstetrician-Gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994). Gestational diabetes. *Obstet Gynecol* 2001;98:525-38.
41. Dooley SL, Metzger BE, Cho NH, Liu K. The influence of demographic and phenotypic heterogeneity on the prevalence of gestational diabetes mellitus. *Int J Gynaecol Obstet* 1991;35:13-8.

42. Bobrowski RA, Bottoms SF, Micallef JA, Dombrowski MP. Is the 50-gram glucose screening test ever diagnostic?. *J Matern Fetal Med* 1996;5:317-20.
43. Sacks DB, Bruno DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2002;48:436-72.
44. Eastman RC, Vinicor F, The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997;20:1183-97 .
45. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol* 1982;144:768-73.
46. Ferrara A, Hedderston MM, Quesenberry CP, Selby JV. Prevalence of gestational diabetes mellitus detected by the national diabetes data group or the carpenter and coustan plasma glucose thresholds. *Diabetes Care* 2002;25:1625-30.
47. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, *et al*. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005;352:2477-86.
48. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, *et al*. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009;361:1339-48.
49. Moses RG. Editorial: New consensus criteria for GDM. *Diabetes Care* 2010;33:690.
50. Seshiah V, Das AK, Balaji V, Joshi SR, Parikh MN, Gupta S, *et al*. Gestational Diabetes Mellitus – Guidelines. *J Assoc Physicians India* 2006;54:622-8. Available from: <http://www.dipsi.in>; [Last accessed on 2011 Jul 23].
51. Seshiah V. Fifth National Conference of Diabetes in Pregnancy Study Group, India. *J Assoc Physicians India* 2010;58:329-30. Available from: <http://www.dipsi.in>; [Last accessed on 2011 Jul 23].
52. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Kapur A. Pregnancy and diabetes scenario around the world: India. *Int J Gynaecol Obstet* 2009;104 Suppl 1:S35- 8.
53. Kalra S. Capacity building in diabetes care in South Asia. *Int J Clin Cases Investig* 2011. Available from: http://www.ijcci.info/index.php?option=com_content&view=article&id=102%3Acapacity-buiding-in-diabetes-care-in-south-asia&catid=57%3Apresentation&Itemid=1 [Last accessed on 2011 Jun 20].

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