Economical and evidence-based procedure to diagnose gestational diabetes mellitus in the community

Gestational diabetes mellitus (GDM) is associated with a significant incidence of diabetes in the later life of the mother and an increase in the fetal, neonatal morbidity, and future development of obesity and diabetes in the offspring. Studies conducted in different populations and with different methodologies consistently reported an increase in GDM in all ethnic groups, suggesting that there is an increase in GDM prevalence.[1] A true increase in the prevalence of GDM aside from its adverse consequences for the infant in the newborn period might reflect or contribute to the ongoing pattern of increasing diabetes and obesity.[1] The existing diagnostic criteria except World Health Organization (WHO) are country specific, e.g., American Diabetes Association, Canadian Diabetes in Pregnancy Study Group (CanDIPS), National Diabetes Data Group (NDDG) criteria, Australasian criteria, Japan Diabetes Association, German Diabetes Association, and Diabetes UK. These diagnostic criteria require the pregnant woman to visit the prenatal clinic twice, (1) for screening and (2) then to undergo diagnostic oral glucose tolerance test (OGTT). The pregnant woman resents undergoing the present diagnostic procedure, as she has to allot 2 days to attend the prenatal clinic and in addition, the numbers of blood samples drawn are too many. These observations emphasize the need for an appropriate tool to diagnose GDM and to incorporate them into the local health service strategies.

Diagnostic Criteria

American Diabetes Association (Carpenter and Coustan) criteria: The diagnostic criteria for GDM suggested by O'Sullivan and Mahan were based on whole blood glucose values. Carpenter and Coustan by applying conversion formula switched from whole blood glucose to venous plasma glucose values and suggested that normal glucose level during pregnancy with 100 g OGTT as fasting plasma glucose (FPG) ≤ 95 mg/dL, 1 h PG ≤ 180 mg/dL, 2 h PG ≤ 155 mg/dL, and 3 h ≤ 140 mg/dL, respectively. Any two values meet or exceed the above figures is diagnosed as GDM. These values were recommended based on the predictive value of the subsequent risk of diabetes in the mother and not specifically on the fetal outcome. NDDG also has the same deficiency. To clarify the associations of levels of maternal glucose lower than those diagnostic of diabetes with perinatal outcome, Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study was initiated. The objective was accomplished by performing a 75 g OGTT directly without screening in diverse cohort of 23,316 women in third trimester of gestation.

WHO criteria and validation: GDM is diagnosed by WHO criteria, if 2 h PG is ≥140 mg/dL, with 75 g OGTT similar to that of impaired glucose tolerance (IGT), outside pregnancy.[2] WHO procedure for diagnosing GDM was not developed specifically for use during pregnancy, nor are threshold set for detection of either maternal or fetal complications.[2] However, studies have shown that WHO criteria of 2 h PPG ≥140 mg/dL identifying a large number of cases may have a greater potential for prevention of diabetes.[3,4] To ascertain, the utility of WHO criteria, a community-based study "Diabetes in Pregnancy, Awareness and Prevention" (DIPAP) was performed in the state of Tamil Nadu, India. This was the largest follow-up study outside HAPO involving a cohort of 12,056 pregnant women living in urban, semi-urban, and rural areas in whom WHO criteria were used to diagnose GDM. Among them, the prevalence of GDM was 17.8%, 13.8%, and 9.9% in the urban, semi-urban, and rural area, respectively. The overall prevalence of GDM was 13.9%. Further, to elucidate the consistency of WHO criteria in diagnosing GDM, after determining the desired sample size with the required statistical power, a total of 1246 pregnant women underwent 75 g OGTT. Among them, 13.2% were detected to have GDM with 2 h PG ≥ 140 mg/dL. These findings substantiate and validate the previous prevalence data, as well as the WHO criteria.

IADPSG recommendation

The existing Carpenter and Coustan criteria are

Correspondence to: **Dr V. Seshiah**, Chairman, Dr V. Seshiah Diabetes Research Institute, India. E-mail: vseshiah@gmail.com

diagnostic when any two values with 75 g OGTT meet or exceed FPG > 95 mg/dL, 1 h PG > 180 mg/dL, and 2 h PG > 155 mg. 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.[5] 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, 1 h, 2h, or any two values for diagnosis. This flexibility will compromise the uniformity and likely to pose difficulty in comparing outcome data. IADPSG recommendation is acceptable; however, it requires multiple blood samples such as Carpenter and Coustan criteria. Thus, it is difficult to carry out IADPSG procedure in different levels of community health care delivery systems in the country except in medical college hospitals, corporate hospitals, and private clinics. The advantage of IADPSG recommended procedure is the use of 75 g oral glucose load for an OGTT in all clinical settings in or outside of pregnancy. No screening test is needed.

A random blood sugar ≥200 mg/dL is likely to be overt diabetes and confirmed by FPG of ≥7.0 mmol/L (126 mg/dL) or A1C ≥ 6.5%. In early pregnancy, FPG ≥ 5.1 mmol/L (92 mg/dL) also is classified as GDM and if found normal, the test has to be repeated between 24 and 28 weeks of gestation.

Short-term and long-term implications of GDM

Short term: 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 newborn. In the HAPO study, though the composite outcomes (which includes both primary and secondary outcomes) occur from 2 h PG ≥ 153 mg/dL, the primary outcome appears to manifest gradually from 2 h PG 126 mg/dL (7.0 mmol/L) and is discernible from 2 h PG 140 mg/dL (7.8 mmol/L).[6] In the DIPAP study, the prevalence of macrosomia was 8% with maternal glucose of 2 h ≥ 120 mg/dL, which increased to 15% from maternal glucose of 2 h PG > 140 mg/dL. A sub-study of DIPAP project also observed that the occurrence of macrosomia was a continuum, as the 2 h PG with 75 g OGTT increased above 120 mg/dL.[7]

Long term: 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/dL.[8]

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

A single-step procedure with a single-glucose value

Attending the first prenatal visit in the fasting state is impractical in many settings[5] and the dropout rate is very high when a pregnant woman is asked to come again for the glucose tolerance test.[9,10] In addition, in all GDM the FPG values do not reflect the postprandial hyperglycemia. Oral glucose tolerance testing is more sensitive in detecting diabetes than is measurement of fasting glucose levels.[11] Hence at the first visit itself, 75 g oral glucose load has to be administered irrespective of whether the pregnant woman had anything to eat or not, and 2 h venous blood is drawn for the estimation of plasma glucose and GDM is diagnosed, if 2 h PG ≥ 140 mg/ dL.[12] This "single-step procedure with a single-glucose value" is able to correctly identify subjects with GDM, as well as woman with normal glucose tolerance (NGT).[13] Plasma glucose value with a glucose challenge test (GCT) was unaffected by the time after a meal or time of the day in NGT subjects but expected to change in subjects with glucose intolerance.[14] The advantages of this procedure are (a) causes least disturbance in a pregnant woman's routine activities, (b) serves as both screening and diagnostic procedure, and (c) ideal for countries with low resources but requiring universal screening.

Conclusion

IADPSG recommendation represents the opinions of individual members of the IADPSG consensus panel and does not necessarily reflect the position of the organizations they represent.[5] The report is expected

to be considered by diabetes, obstetric, and other organizations and will serve as a basis for internationally endorsed criteria for the diagnosis and classification of diabetes in pregnancy.[5] HAPO study was a basic epidemiological investigation on which IADPSG recommendations are based.[5] It was not a clinical trial.[5]

IADPSG suggests simpler and more cost-effective strategies that do not require performing an OGTT on most pregnant women for future consideration.[5] Our responsibilities to our patients and their offspring demand that all women should be offered a definitive single-step glucose test in every pregnancy.[15] "A single-step procedure with a single-glucose value" of WHO 2 h PG of ≥140 mg/ dL with 75 g oral glucose load,[16,17] which has been validated and is being followed in much of the world, including India can be continued for diagnosing GDM till global guidelines are framed.

References

1. Ferrara A. Increasing prevalence of Gestational Diabetes Mellitus - A Public Health Perspective. Diabetes Care 2007;30:S141-6.
2. Alberti K, Zimmett P. Definition, diagnosis and classification of diabetes mellitus and its complications, Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53.
3. Schmidt MI, Duncan BB, Reichelt AJ, Branchtein L, Matos MC, Costa e Forti A, *et al*. For the Brazilian Gestational Diabetes Study Group. Gestational diabetes mellitus diagnosed with a 2-h 75-g oral glucose tolerance test and adverse pregnancy outcomes. Diabetes Care 2001;24:1151-5.
4. Meltzer SJ, Snyder J, Morin L, Nudi M. Validation of Normative Data for 75g Oral Glucose Tolerance Test (OGTT) in a Montreal Pregnant Population Considering Ethnicity. Abstract book of the 64th Scientific Sessions of the American Diabetes Association; Florida: 2004. p. A19.
5. International Association of Diabetes and Pregnancy Study Groups (IADPSG) Recommendations on the diagnosis and classification of Hyperglycemia in pregnancy. IADPSG consensus panel. Diabetes care 2010;33:676-82.
6. The HAPO study Cooperative Research Group, Hyperglycemia and Adverse pregnancy Outcomes, N Engl J Med 2008;358: 1991-2002.
7. Balaji V, Balaji MS, Seshiah V, Mukundan S, Datta M. Maternal glycemia and neonates birth weight in Asian Indian Women. Diabetes Res Clin Pract 2006;73:223-4.
8. Franks PW, Looker HC, Kobes S, Touger L, Tataranni PA, Hanson RL, *et al*. Gestational glucose tolerance and risk of type 2 diabetes in young Pima Indian offspring. Diabetes 2006;55:460-5.
9. de Aguiar LG, de Matos HJ, de Brito Gomes M. Could fasting plasma glucose be used for screening high-risk outpatients for gestational diabetes mellitus? Diabetes Care 2001;24:954-5.
10. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational Diabetes Mellitus in India. J Assoc Physicians India 2004;52:707-11.
11. Kousta E, Lawrence NJ, Penny A, Mallure BA, Robinson S, Dornhost A, *et al*. Implications of diagnostic criteria for abnormal glucose homeostasis in women with previous gestational diabetes. Diabetes Care 1998;22:993-37.
12. Pettitt DJ, Bennett PH, Saad MF, Charles MA, Nelson RG, Knowler WC. Abnormal glucose tolerance during pregnancy in Pima Indian women. Long-term effects on offspring. Diabetes 1991;40:126-30.
13. Anjalakshi C, Balaji V, Balaji MS, Ashalatha S, Suganthi S, Arthi T, *et al*. A Single test procedure to diagnose gestational diabetes mellitus. Acta Diabetol 2009;46:51-4.
14. Philips LS, Ziemer DC, Kolm P, Weintraub WS, Vaccarino V, Rhee MK, *et al*. Glucose challenge test screening for prediabetes and undiagnosed diabetes. Diabetologia 2009;52:1798-807.
15. Moses RG, Cheung NW. Point: Universal Screening for Gestational Diabetes Mellitus. Diabetes Care 2009;32:1349-51.
16. Seshiah V, Sahay BK, Das AK, Shah S, Banerjee S, Rao PV, *et al*. Gestational Diabetes Mellitus- Indian guidelines. J Indian Med Assoc 2009;107:799-806.
17. Seshiah V. DIPSI Guidelines - Kolkata Declaration. Fifth national conference of diabetes in pregnancy study group, India. J Assoc Physicians India 2010;58:329-30.

V. Seshiah
Chairman, Dr. V. Seshiah Diabetes Research Institute and Dr. Balaji Diabetes Care Centre, President, Diabetes Pregnancy Study Group, India. Advisor, Gestational Diabetes Mellitus Project, Government of Tamil Nadu, Member, Expert Review Committee – Global Guidelines on Diabetes and Pregnancy, International Diabetes Federation

DOI: 10.4103/0973-3930.70855