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ADA, WHO, DIPSI or IADPSG: Which Diagnostic Criteria for GDM to Prefer?

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Abstract

Gestational diabetes mellitus is diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation. This is also helpful for diagnosing unrecognized pre-existing diabetes. Gestational diabetes mellitus is an aggravating factor for the risk of future diabetes in both the mother and child and represents glycaemic dysregulation. In order to prevent an adverse event in the course of pregnancy and post-partum, it is important to screen, diagnose and treat hyperglycemia in pregnancy. Over the years, different diagnosing criteria with regards to maternal and fetal outcomes for the diagnosis of GDM have always been a problem. Universal Screening is recommended always for pregnant women belonging to a high risk ethnic population like Indians. According to DIPSI, a single step 75g of glucose non-fasting Oral Glucose Tolerance Test (OGTT) with a cut-off of ≥ 140 mg/dl after 2-hours is diagnostic of GDM, whereas a fasting OGTT after 75g glucose with a cut-off plasma glucose of ≥ 140 mg/dl after 2-hour is recommended by WHO. For screening of women at risk of diabetes, the ADA/IADPSG criteria recommends, for diagnosis of GDM in the first and subsequent trimester at 24-28 weeks by 75 g OGTT and fasting 92 mg/dl, 1 hour 180 mg/dl, 2 hour 153 mg/dl by universal glucose tolerance testing. There is an air of controversy regarding over diagnosis of GDM and unnecessary interventions. The ACOG still prefer a 2 step procedure, GCT with 50g glucose non-fasting if value > 140 mg/dl followed by 3-hour OGTT for confirmation of diagnosis. In conclusion, based on Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, as mild degree of dysglycemia are associated with adverse outcome and high prevalence of Type 2 DM in later life, the IADPSG criteria is recommended. The only outcome based criteria is the IADPSG criteria as it has the ability to diagnose and treat GDM earlier, thereby reducing the fetal and maternal complications associated with GDM. It is simple in execution, more patient friendly, diagnostically accurate, single step procedure and close to international consensus. Due to the diversity and variability of Indian population, application of single international criteria may not be conclusive. This warrants further comparative studies on different diagnostic criteria in relation to adverse pregnancy outcomes.

Keywords: ADA; WHO; DIPSI; IADPSG; GDM; Pregnancy; Diabetes

Abbreviations: OGTT: Oral Glucose Tolerance Test; HAPO: Hyperglycemia and Adverse Pregnancy Outcome; GDM: Gestational Diabetes Mellitus; ADA: American Diabetes Association; HAPO: Hyperglycemia and Adverse Pregnancy Outcome; IADPSG: International Association of Diabetes and Pregnancy Study Group; ACOG : American College of Obstetricians and Gynecologists; NICE: National Institute of Health and Clinical Excellence; WHO: World Health Organization; PG: Plasma Glucose; FPG: Fasting Plasma Glucose.

Introduction

For many years, Gestational Diabetes Mellitus (GDM) was defined as any degree of glucose intolerance that was first recognized during pregnancy [1]. Regardless of the degree of hyperglycemia. This definition facilitated a uniform strategy for detection and classification of GDM, but this definition has serious limitations like not excluding pre-existing diabetes [2]. So the current recommendation by American Diabetes Association (ADA) for gestational diabetes mellitus is diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation [3]. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [4]. a large-scale multinational cohort study completed by more than 23,000 pregnant women, demonstrated that risk of adverse maternal, fetal and neonatal outcomes increased considerably as a function of maternal hyperglycemia at 24–28 weeks of gestation, even for values previously considered normal for pregnancy. There was no threshold of glycaemia for risk for most of the complications.

The adverse complications associated with GDM for the mother include hydramnios, hypertension, increased operative intervention, preeclampsia, urinary tract infection and future diabetes mellitus. Complications such as macrosomia, congenital anomalies, metabolic abnormalities, RDS and subsequent childhood and adolescent obesity are associated with foetus and neonates [5]. Therefore, early diagnosis and prompt treatment are very vital to prevent complications. When it comes to its screening, diagnosis and its cost-effectiveness, GDM has always been a topic of considerable controversy. Over three decades, the precise level of glucose intolerance characterizing GDM has always been controversial.

In India, 10-14.3% of all pregnant females report to have GDM which is much higher than the west. In next 10 years, it is expected that there will be a rise of 20%. In India more than 70% of population live in rural settings and facilities for diagnosing diabetes itself is limited [6]. As per a prospective field study done by Seshiah et al. in 2008 in Tamil Nadu under the “Diabetes in Pregnancy” – Awareness and Prevention project, of the 4151, 3960 and 3945 pregnant women screened in urban, semi urban and rural areas respectively, the prevalence of GDM was 17.8% in the urban, 13.8% in the semi urban and 9.9% in the rural areas [7,8]. An Indian study showed that GDM manifests in all trimesters of pregnancy and out of all women diagnosed for GDM, 16.3% were diagnosed at ≤ 16 weeks of gestation while 22.4% were diagnosed between 17-23 weeks and 61.3% were diagnosed after 23 weeks of gestation [7,9].

There have been no definite guidelines by the previous reviews on whether to do universal screening or risk based screening. According to the American Diabetes Association (ADA) in low risk women, i.e, those with no previous history of abnormal glucose tolerance or adverse obstetrics outcome, those with age less than 25 years, who are not a member of ethnic group, with BMI 25kg/m2 or less and no known history of diabetes in first degree relatives, there is no need to screen and they are less likely to benefit from any screening [10]. The incidence of GDM was found to be 1.45% in risk based screening of women as against universal screening which showed 2.7% in the same population. This showed that risk based screening has missed half of the GDM [11]. Based on these facts there is a need for universal screening especially in South East Asians countries more so in Indian women as they have high prevalence of Type 2 DM and genetic predisposition.

When to Screen

It is seen that the insulin resistance increases during the second trimester. Thus, the glucose levels rise in women who do not have the ability to produce enough insulin to adopt this resistance. As the pregnancy advances, there is more of insulin resistance mediated by the placental hormones thus increasing GDM, so testing too early may not be helpful in some patients. Similarly, performing tests too late in third trimester limits the time in which metabolic interventions can take place. Due to the above reasons, it is advised to perform the tests at 24-28 weeks of gestation. The Government of India and American Diabetes Association (ADA) follow the recommendations given by International Association of Diabetes and Pregnancy Study Group (IADPSG) based on Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, which endorses to do fasting plasma glucose, HbA1C or random plasma glucose in all women on the first prenatal visit. If overt DM is not diagnosed and fasting plasma glucose ≥ 92 mg/dl, then diagnosis of GDM is made. If fasting glucose is < 92mg/dl at the first antenatal visit a 2-hour 75g OGTT should be repeated at 24-28 weeks [12].

Screening and Diagnostic Criteria

There are a number of guidelines on diagnosis and treatment

of GDM which vary from country to country. These include American Diabetes Association (ADA) guidelines, American College of Obstetricians and Gynecologists (ACOG) guidelines and National Institute of Health and Clinical Excellence (NICE) guidelines and IADPSG guidelines. Risk factors for GDM include obese women, BMI above 30 kg/m^2, previous macrosomic baby weighting 4.5 kg or above, previous GDM, family history of DM (first degree relative with DM), ethnic family origin with a high prevalence of DM, clinical conditions associated with insulin resistance like PCOD, acanthosis nigricans, history of hypertension or hypercholesterolemia. However universal screening is a must especially in Indian pregnant women.

American Diabetes Association (ADA) 2020 [13]

The diagnosis of GDM can be achieved with either of two methods:

1. The "one-step" 75-g OGTT derived from the IADPSG criteria or
2. The older "two-step" approach with a 50-g (non-fasting) screen followed by a 100-g OGTT for those who screen positive, based on the work of Carpenter and Coustan's interpretation of the older O'Sullivan criteria. (Table 1)

Criteria	100g OGTT	75g OGTT
Fasting	95 mg/dl	92 mg/dl
1hr	180 mg/dl	180 mg/dl
2hr	155 mg/dl	153 mg/dl
3hr	140 mg/dl	-

Table 1: ADA Criteria.

WHO Criteria [14]

In 1999, the World Health Organization (WHO) in order to standardize the diagnosis of GDM, proposed using a 2 hour OGTT, 75 gm anhydrous glucose in 250–300 ml water after overnight fasting (8–14 hours) [1, 2]. Both fasting and 2 hours after meal plasma glucose was measured. The cut-off venous plasma glucose concentration of ≥ 140 mg/dl (7.8 mmol/l) at 2 hours, similar to that of IGT outside pregnancy is diagnosed as GDM. The WHO diagnostic criterion considers 2 hr plasma glucose (PG) of 140 mg/dL. (Table 2)[15].

Criteria	100g OGTT	75g OGTT
2 hr. ≥ 200 mg/dL	Diabetes	Diabetes
2 hr. ≥ 140-199 mg/dL	GDM	IGT
2 hr. ≥ 120-139 mg/dL	DGGT	-
2 hr. - 120 mg/dL	Normal	Normal

Table 2: WHO Criteria.

International Association of Diabetes and Pregnancy Study Groups (IADPSG) [16]

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) based on the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study in 2010 proposed a new set of criteria which has been welcomed by many countries. According to this criterion, three samples are required i.e., fasting, 1 h, and 2 h after 75 g glucose. According to the IADPSG guidelines, the 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. Regarding overt diabetes, it 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. For GDM Fasting > 5.1 mmol/L and < 7.0 mmol/L is diagnostic.

DIPSI (Diabetes in Pregnancy Study Group India) [17]

The DIPSI guideline is very innovative and patient friendly. "It's a single step procedure having only one diagnostic glycemic value", to diagnose GDM in the community. In the antenatal clinic, irrespective of whether a pregnant woman is in the fasting or non-fasting state, she is given a 75 g oral glucose load without regard to the time of the last meal. After 2 hours, using GOD-POD method plasma glucose is estimated from her venous sample. A 2- hour plasma glucose of ≥ 140 mg/ dl is diagnostic of GDM (Table 3).

Criteria	100g OGTT	75g OGTT
2 hr. ≥ 200 mg/dL	Diabetes	Diabetes
2 hr. ≥ 140 mg/dL	GDM	IGT
2 hr. ≥ 120 mg/dL	DGGT	-

Table 3: DIPSI Criteria.

Advantages of The DIPSI Procedure

- Pregnant women need not be fasting.
- There is least disturbance in the pregnant woman's routine activities.
- Can be used both as screening and diagnostic procedure and in management.
- It has been approved by Ministry of Health, Government of India and also recommended by WHO as a single step procedure for GDM detection.

Criteria	Sample	Fasting / Non Fasting	Glucose Load	Fasting mg/dl	1hr mg/dl	2hr mg/dl	3hr mg/dl
ADA	F,1hr,2hr,3hr	Fasting	100 gm	> 95	> 180	> 155	> 140
WHO	F,2hr	Fasting	75 gm	> 126	-	> 140	-
IADPSG	F,1hr,2h	Fasting	75 gm	> 92	> 180	> 153	-
DIPSI	2hr	Non Fasting	75 gm	-	-	> 140	-

Table 4: The following table showing the comparison of various criteria.

Discussion

GDM which carries risk for both mother and foetus needs to be dealt seriously and a universally approved screening test is utmost essential for the same. To overcome all the short comings of other so far followed criteria, DIPSI emerged out as a single simple test, best suited for the Asian population who are in the high risk category. The ADA guideline is validated against the future risk of those women developing diabetes and not on the foetal outcome and is meant to screen and diagnose diabetes in selective high risk population [18]. The most commonly followed criteria is that of WHO because it is a simple two- step procedure but not designed to diagnose GDM [18,19]. According to the WHO criteria, the fasting cut-off is 126 mg/dl which is same as diabetes in non-pregnant adults, whereas the 2-h cut-off is 140 mg/dl, which is again same as cut-point for IGT in non-pregnant adults. This is an anomaly as glycaemic targets in GDM should be lesser than normal individuals [20]. In a study done by Sivagnanam Nallaperumal et al, this inherent contradiction in the fasting values of WHO criteria have been picked up and this might explain why the DIPSI (WHO 2-h) value alone picked up over 98% of all cases diagnosed by both fasting and 2-h WHO criteria [6,17,20].

Still some studies show the 2-h cut-off value of > 140 mg/dl for diagnosis of GDM was found to reduce serious perinatal morbidity and also improved the woman's health-related quality of life. Thus the DIPSI guidelines which have been accepted by WHO can help pick up missed or hidden cases of GDM and also improve the quality of life. The IADPSG criteria which is predominantly based on HAPO study was particularly designed for Caucasian population and patients from India and South Asian countries were not included [20,21]. Asian Indians have high insulin resistance and higher 2-hour PG as compared to Caucasians. Due to their difficulty in commutation and belief not too fast for long hours, the drop-out rate is very high which a major disadvantage of the IADPSG is.

In all GDM cases diagnosed by IADPSG, FPG values do not reflect the 2-hour post glucose with 75 g oral glucose which is the hallmark of GDM [20]. Low FPG cut- off in the IADPSG criteria would result in too many women getting diagnosed as GDM. This could lead to medicalization of pregnancy and overloading on the health systems [22]. In Asian population, FPG is not an appropriate option to diagnose GDM as insulin resistance escalates as pregnancy progresses [23]. By following the WHO criteria, in Asian population, with FPG > 5.1 mmol/L (92 mg/dL) as cut-off value, 76% of pregnant women would have missed the diagnosis of GDM. If we consider among non-pregnant Indian adults, the sensitivity of the 2-h value is much higher than the fasting plasma glucose. Thus, it can also be assumed that by raising the 2-hr value in the IADPSG to 153 mg/dl, many cases of GDM can also be missed. In the HAPO study, it was demonstrated that even at a level below diagnostic of diabetes, maternal hyperglycaemia is associated with a strong and continuous trend of increased cord-blood serum C-peptide levels and increased birth weight [23,24].

In the Indian environment, the DIPSI guidelines for GDM are

more feasible. Due to high prevalence and high risk category, screening is essential for all Indian pregnant women. DIPSI recommends one step procedure of challenging women with 75 gm glucose irrespective of timing of food intake and thus diagnosing GDM is simple, economical and feasible [18]. It serves as both screening and diagnostic procedure. Due to its flexibility, it causes least disturbance in a pregnant woman's routine activities.

Even if the test is to be repeated in each trimester, the cost in performing the procedure is estimated to be 66% less than the cost of performing IADPSG recommended procedure. An Evidence-based study performed by Crowther et al. found that treatment of GDM diagnosed by modified WHO criterion reduces serious perinatal morbidity and may also improve the women's health-related quality of life resulting in decreased macrosomia rate and reduced risk of pregnancy outcome [21]. In a randomized controlled study done by Wahi et al, it was observed that there is significant positive effect on pregnancy outcomes both in relation to mother as well the child by adhering to a cut-off level of 2- hour PG ≥ 140mg/dL in diagnosis and management of GDM. The one-step diagnostic procedure (2-hour PG ≥ 140mg/dL) to diagnose GDM was also suggested by Perucchini et al. In a study, it was observed that the cumulative risk of offspring developing type 2 DM was 30% at the age 24 years when maternal 2-hour PG was ≥ 140mg/dL which was documented by Franks et al [25-27].

Conclusion

GDM is not only associated with adverse maternal and perinatal outcome but also increases the risk of future diabetes in both mother and child, which can be prevented by early screening and proper diagnosis. Being in the high risk category, universal screening is a must for Southeast Asians countries, irrespective of the method used. In order to avoid the cumbersome OGTT method, more effective and simpler strategies should be developed in future clinical practice. In HAPO study, when fasting plasma glucose was ≤ 4.4mmol/l (80mg/ dl), the risk of adverse outcomes was very low. But before recommending FPG as a screening method, further evaluation is required which may potentially identify pregnancies with very low risk of GDM. After reviewing all the related articles on GDM, one important aspect which comes to mind is that the Indian population is diverse and variable, hence judging international criteria on Indian population may not be conclusive. So more rigorous and diverse comparative studies are required on different diagnostic criteria in relation to pregnancy outcomes in GDM. But in our opinion, both the ADA and DIPSI criteria can be used concurrently according to the patient profile and both are equally effective to diagnose GDM.

Conflict of Interest

None

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