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A Minireview on Diagnostic Criteria Of Gestational Diabetes Mellitus (GDM)

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Abstract

Gestational diabetes mellitus represents glycaemic dysregulation and an aggravating factor for the risk of future diabetes in both the mother and child. Diagnosis of GDM has always been with problems related to differing diagnostic criteria with conflicting evidence regarding the maternal and fetal outcomes. Pregnant women belonging to a high risk ethnic population like Indians require Universal Screening. Out of a wide variety of national and international guidelines the pioneering Diabetes in Pregnancy Study Group India (DIPSI) guideline for the screening and diagnosis of GDM has set new standards for quality diabetes care in India and around the world. DIPSI criterion requires estimation of plasma glucose in one blood sample to diagnose GDM. This cost-effective and evidence-based procedure meets our responsibility of offering "a single-step definitive glucose test" to every pregnant woman belonging to any socio-economic status.

Key words: ADA, DIPSI, GDM, WHO

INTRODUCTION

Indian scenario: Indian population is a diverse group of varying genetic and demographic profiles making Indian women more predisposed to develop insulin resistance or diabetes during pregnancy. The incidence of diabetes in general and GDM in particular is on the rising tide due to changing lifestyles, making them potential public health catastrophes without timely intervention.**(1)** Currently, there are a number of country-specific guidelines on diagnosis and treatment of GDM. Existing guidelines do not address the clinical questions about the considerations related to diabetes management, maternal and fetal outcome during pregnancy in India specifically. In light of the 11-fold increased risk of developing glucose intolerance during pregnancy in Asian women compared to Caucasian women, universal screening is preferable in India**.(2)** Compared with selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis**.(3)** For this we need a simple procedure which is economical and feasible. Thus, the current recommendations have been formulated with the framework of the pioneering DIPSI (diabetes in pregnancy study group in India) guideline to comprehensively diagnose and manage GDM in India. **(1)** The Diabetes in Pregnancy Study group India (DIPSI) is reporting practice guidelines for GDM in the Indian environment **(3)** and it can be used as a single-step definitive, screening and diagnostic test. Our study is a simple attempt to focus on available guidelines and to update the advantages of DIPSI over other criteria.

Definitions of GDM (4)

1. According to WHO 1999 criteria, diagnosis was based on a 2-h VPG value of ≥140 mg/dl (7.8 mmol/l) done in the fasting state.
2. According to the IADPSG criteria, diagnosis of GDM was based on any one of the following criteria, i.e. fasting ≥92 mg/dl (5.1 mmol/l), 1 h ≥ 180 mg/dl (10 mmol/l) and 2 h ≥ 153 mg/dl (8.5 mmol/l).
3. According to the DIPSI criteria, diagnosis of GDM was based on a 2-h VPG ≥140 mg/dl (7.8 mmol/l) in the non-fasting OGTT.

Necessity of universal screening

In India more than 70% of population live in rural settings and facilities for diagnosing diabetes itself is limited. (3) The importance of GDM is that two generations are at risk of developing diabetes in the future. Women with a history of GDM are at increased risk of future diabetes, predominately type 2 diabetes, as are their children. (2,3) The recent data on the prevalence of GDM in our country was 16.55% by WHO criteria of 2 hr PG -140 mg/dl.5 As such Universal screening during pregnancy has become important in our country As per a prospective study done by Seshiah et al. in 2008 GDM was detected in 17.8% women in urban, 13.8% in semi urban and 9.9% in rural areas (1,5) GDM manifests in all trimesters of pregnancy, with an Indian study showing that 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.(1,6)

Various guidelines diagnostic criteria

There are a number of country-specific guidelines on diagnosis and treatment of GDM. These include American Diabetes Association (ADA) guidelines, American College of Obstetricians and Gynecologists (ACOG) guidelines and National Institute of Health and Clinical Excellence (NI CE)guidelines and IADPSG guidelines(1). The controversy

and confusion still exists because of various guidelines for diagnosis of GDM**.**

a) American Diabetes Association (ADA) (Carpenter and Couston)
Recommends two step 3 hour 100 gm OGTT procedures. GDM is diagnosed if any 2values meet or exceed FPG > 95 mg/dl, 1 hr PG > 180mg/dl, 2 hr PG > 155 mg/dl and 3 hr PG > 140 mg/dl. Carpenter later recommends a 2hour OGTT with 75 gm glucose in order to standardize with a non-pregnant (2). [Table 1]

Table 1 ADA Criteria

	100 gr OGTT	**75 gr OGTT**
Fasting	95 mg/dl (5.3 mmol/l)	95mg/dl
1hr	180 mg/dl (10 mmol/l)	180 mg/dl
2hr	155 mg/dl (8.6 mmol/l)	155 mg/dl
3hr	140 mg/dl (7.8 mmol/l)	

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

Table 2: With 75 gm OGTT (WHO criteria)

Criteria	**In Pregnancy**	**Outside Pregnancy**
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

C) International Association of Diabetes and Pregnancy Study Groups (IADPSG)
In 2010, based on the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed a new set of criteria which has since been adopted in many countries recently, the WHO has also adopted the IADPSG criteria (4, 7).This criterion requires three samples i.e., fasting, 1 h, and 2 h after 75 g glucose. The IADPSG recommends that 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. The IADPSG also 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. Fasting > 5.1 mmol/L and < 7.0 mmol/L is diagnosed as GDM. (8)

d) DIPSI (a modified version of WHO).
"A one step procedure with a single glycemic value", to diagnose GDM in the community. In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination is 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 collected at 2 hours for estimating plasma glucose by the GOD- POD method. GDM is diagnosed if 2- hour plasma glucose is ≥ 140 mg/ dl. **(3, 9) [**Table 3]

Table 3: DIPSI guideline for diagnosis of GDM

Criteria	**In Pregnancy**	**Outside Pregnancy**
2 hr. ≥ 200 mg/dL	Diabetes	Diabetes
2 hr. ≥ 140 mg/dL	GDM	IGT
2 hr. ≥ 120 mg/dL	DGGT	—

GDM: Gestational diabetes mellitus; DGGT: Decreased gestational glucose tolerance;
IGT: Impaired glucose tolerance
Advantages of the DIPSI procedure are:
- Pregnant women need not be fasting18
- Causes least disturbance in a pregnant woman's routine activities
- Serves as both screening and diagnostic procedure and in management.

This single-step procedure has been approved by Ministry of Health, Government of India and also recommended by WHO. (8, 10, 11).

The following table showing the comparison of various criteria [table 4]

Table 4: Comparison of different diagnostic criterias

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	100gm	> 95	> 180	> 155	>140
WHO	F, 2hr	Fasting	75 gm	>126	-	>140	-
IADPSG	F,1hr,2hr	Fasting	75gm	>92	> 180	>153	-
DIPSI	2hr	Irrespective of time and meals	75 gm	-	-	>140	-

DISCUSSION

A universal approved screening test is essential to diagnose GDM which adds to the burden of the society. Curtailing the confusion and disadvantages of different diagnostic criteria DIPSI emerged out as a single simple test that overcomes all the short comings of other so far followed criteria. ADA is meant to screen and diagnose diabetes in selective high risk population (9), originally validated against the future risk of those women developing diabetes and not on the fetal outcome. WHO diagnostic criteria is followed in most of the world because it is a simple two-step procedure but not designed to diagnose GDM(4,9). More over the thresholds are not set for detection of either maternal or fetal complications. It appears an anomaly that in the WHO criteria, the fasting cut-off had been set at 126 mg/dl which is diagnostic of diabetes in non-pregnant adults, whereas the 2-h cut-off was set at 140 mg/dl, which is the diagnostic cut-point for IGT in non-pregnant adults(7) .This inherent contradiction in the fasting values of WHO criteria are not particularly useful to diagnose GDM 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 in a study done by Sivagnanam Nallaperumal etal. (2, 3, 7)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 DIPSI modified WHO can pick up cases of GDM and improve quality of life.

In HAPO study, population from India, China, South Asian countries (except city of Bangkok, Hong Kong), Middle East and Sub Saharan countries were not included. This is particularly designed for Caucasian population. (7, 10) Asian Indians have high insulin resistance and as a consequence, their 2-hour PG is higher compared to Caucasians. Disadvantages of the IADPSG suggestions are whenever fasting is adviced to a pregnant women it is impractical in many settings ,they will not turn up because of commutation and belief not to fast for long hours and dropout rate is very high .

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. (7) If a pregnant woman has a FPG ≥ 126 mg/dl, it is considered overt diabetes and not as GDM by the IADPSG criteria. Too many women would get diagnosed as GDM because of the low FPG cut-off in the IADPSG criteria .It is thus possible that by reducing the FPG cut-point to 92 mg/dl, we could be over-diagnosing GDM in normal pregnant women. This could lead to overloading of the health systems (8). Insulin resistance during pregnancy escalates further and hence FPG is not an appropriate option to diagnose GDM in Asia Indian women (1). In this population by following FPG > 5.1 mmol/L as cut-off value, 76% of pregnant women would have missed the diagnosis of GDM made by WHO

If we consider the sensitivity of the 2-h, value is much higher than the fasting plasma glucose among non-pregnant Indian adults. Thus, it is reasonable to assume that since the IADPSG has raised the 2-hr value in the IADPSG to 153 mg/dl, many cases of GDM could be missed. (HAPO) study demonstrates that maternal hyperglycemia, even at a level below diagnostic of diabetes, is associated with a strong and continuous trend of increased birth weight and increased cord-blood serum C-peptide levels.(1)

The DIPSI is reporting practice guidelines for GDM in the Indian environment. Due to high prevalence, screening is essential for all Indian pregnant women. DIPSI recommends one step procedure of challenging women with 75 gm glucose and diagnosing GDM is simple, economical and feasible.(9) Serves as both screening and diagnostic procedure. Causes least disturbance in a pregnant woman's routine activities

After a meal, a normal glucose tolerant woman would be able to maintain euglycemia despite glucose challenge due to brisk and adequate insulin response. Whereas, a woman with GDM who has impaired insulin secretion, her glycemic level increases with a meal and with glucose challenge, the glycemic excursion exaggerates further.(1,3,) This cascading effect is advantageous as this would not result in false positive diagnosis of GDM.(1)

A single WHO cut-point of 2 h > 140 mg/dl appears to be suitable for large-scale screening for GDM in India and other developing countries. This procedure assumes clinical relevance as WHO criteria based on glucose level > 140 mg/ dl at 2 hours was able to correctly identify subjects with GDM, as well as woman with normal glucose tolerance(7).

Furthermore, the DIPSI criterion avoids the use of FPG for screening as recommended by the IADPSG guideline, which would have led to only one- third of South Asian subjects with diabetes being diagnosed. (3, 12,) 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, **(10)** decreased macrosomia rate, reduced risk of pregnancy outcome. Wahi et al. observed in their randomized controlled study, the advantage of adhering to a cut-off level of 2-hour PG ≥ 7.8 mmol/L in diagnosis and management of GDM for a significantly positive effect on pregnancy outcomes both in relation to mother as well the child. Perucchini et al. also suggest one-step diagnostic procedure (2-hour PG ≥ 7.8 mmol/L) to diagnose GDM.. Franks et al. documented that when maternal 2-hour PG was ≥ 7.8 mmol/L, the cumulative risk of offspring developing type 2 DM was 30% at the age 24 years.(13,14,15)

Gestational Weeks for Screening

By following the usual recommendation of screening between 24 and 28 weeks of gestation, the type 2 diabetes that existed prior to this index pregnancy is likely to be missed. Hence the recent concept is to screen for glucose intolerance in the first trimester itself as the fetal beta cell recognizes and responds to maternal glycemic level as early as 12th week of gestation. (2) If found negative at this time, the screening test is to be performed again around 24th –

28th week and finally around 32nd – 34thweek. If the 2-hour PG is > 200 mg/dL in the early weeks of pregnancy, she may be a pre-GDM and A_{1C} of ≥ 6.5 is confirmatory. (10)

Target Blood Glucose Levels

In normal pregnancy, the mean plasma glucose for fasting is 89 mg/ dl, and 2- hour is 122 mg/dl Thus, maintenance of MPG level ~ 105 to 110 mg/ dl is desirable for a good fetal outcome.(9) This is possible if FPG and peak postprandial glucose levels are maintained ~ 90 (80- 90) mg/ dl and ~ 120 (110 - 129) mg/ dl respectively

CONCLUSION

Out of many diagnostic criteria DIPSI emerged as a Simple, Single step procedure, non-fasting, cost effective, feasible that meets Indian standards and criteria. It was found to diagnose and screen large scale GDM cases with a good perinatal and neonatal outcome

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