

# Screening and Diagnosis of Gestational Diabetes Mellitus: from Controversy to Consensus



Pikee Saxena<sup>1\*</sup>, Sakshi Miglani<sup>1</sup> and Aruna Nigam<sup>2</sup>

<sup>1</sup>Department of Obstetrics & Gynaecology, Lady Hardinge Medical College, India

<sup>2</sup>Department of Obstetrics & Gynaecology, Hamdard Institute of Medical Sciences & Research, India

**Submission:** July 4, 2017; **Published:** June 19, 2017

**\*Corresponding author:** Pikee Saxena, Department of Obstetrics & Gynaecology, Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital, India, Email: pikesaxena@hotmail.com

## Abstract

Hyperglycemia in pregnancy is associated with adverse fetal and maternal outcomes. Even lower values of glucose intolerance have been shown to be detrimental and adverse effects are proportionate to the plasma glucose levels. However, defining glucose intolerance in pregnancy has been an issue of considerable debate, and has led to different recommendations by various authorities worldwide over the last three decades. Multitude of procedures have been described and glucose cut offs proposed for the diagnosis of glucose intolerance in pregnancy have led to considerable confusion. There are a number of controversies regarding significance of screening for gestational diabetes mellitus (GDM), universal/selective screening, when to screen and how to screen-using single or double step, how much should be the glucose load, how many samples to be taken, fasting or non fasting test to be used. No single test is superior to the other and the most appropriate test may be used as per the need and feasibility. These issues will be discussed in the article.

**Abbreviations:** GDM: Gestational Diabetes Mellitus; ACOG: American College of Obstetricians and Gynecologists; ADA: American Diabetic Association; WHO: World Health Organization; FIGO: Federation of Gynecology and Obstetrics; IADPSG: International Association of Diabetes and Pregnancy Study Group

## Introduction

Increasing prevalence of diabetes and hence, the ever increasing ratio of diabetes in pregnancy has led different authorities worldwide, to suggest various methods for screening of gestational diabetes mellitus which have been changed several times over last few decades. According to the principles of screening, the test should have a high sensitivity, cost effectiveness and be agreeable to the population under consideration. Traditionally, gestational diabetes mellitus (GDM) has been defined as an onset or first recognition of abnormal glucose tolerance during pregnancy [1]. The American College of Obstetricians and Gynecologists (ACOG) still uses this terminology [2]. The disadvantage of this terminology is that it fails to differentiate between the women who develop insulin resistance during pregnancy from those who already have pre-existing diabetes. Recently, the International Association of Diabetes and Pregnancy Study Group (IADPSG), the American Diabetic Association (ADA), the World Health Organization (W.H.O.) and the International Federation of Gynecology and Obstetrics (FIGO) have attempted to recognize those women who already have pre-existing diabetes [3-6]. Hence, the following terms have been coined:

A. Diabetes in pregnancy or pre-gestational diabetes or overt diabetes: It is diabetes diagnosed during the early pregnancy or before conception by non-pregnant criteria.

B. Gestational Diabetes Mellitus: Hyperglycemia recognized in second half of pregnancy and not meeting the criteria for diabetes in pregnancy. Although GDM shows milder degree of hyperglycemia, it is associated with adverse maternal and fetal outcome, not only during pregnancy but is associated with greater chances of developing type 2 diabetes, hypertension and cardiovascular disease in both mother and the child later in their lives.

## Significance of screening

The world prevalence of GDM is 1-28% [7,8]. Several adverse outcomes to the mother and the fetus have been associated with diabetes in pregnancy (Table 1). These adverse outcomes increase as the maternal plasma glucose level increase in a continuous manner. Maternal hyperglycemia also affects the intrauterine environment increasing the probability of the fetus to develop obesity, hypertension and type 2 diabetes mellitus later in life besides the fetal and neonatal complications.

Approximately, 50% of the women who have GDM develop type 2 diabetes mellitus within 20-28 years of delivery. Early screening and diagnosis GDM not only gives an opportunity to treat the mother in current pregnancy to avoid maternal and fetal adverse outcomes, but also to start various strategies to prevent diabetes in later life.

**Table 1:** Maternal and fetal complications due to hyperglycemia in pregnancy.

Maternal	Fetal
Spontaneous miscarriage	Congenital malformations
Pre-eclampsia	Macrosomia
Polyhydramnios	Fetal growth restriction
Infections	Intra-uterine death
Operative delivery	Still births
Post partum hemorrhage	Neonatal hypoglycemia
End organ damage	Neonatal hyperbilirubinemia
Cardiovascular disease	Neonatal respiratory distress

### Whom to screen?

There are two schools of thought regarding screening of diabetes

**High risk or selective screening:** ACOG [2] and NICE (2015) [9] support this by assessing the risk factors at the first visit and recommend selective screening for high risk pregnant women. High risk factors are-

- BMI > 30kg/m<sup>2</sup>
- Previous macrosomic baby weighing 4.5 kg or above
- Previous still birth or anomalous baby
- Previous gestational diabetes
- Family history of diabetes (first degree relative)
- High risk ethnic population for DM- African, Asians and Non-Caucasians
- History of polycystic ovarian syndrome (PCOS)

**Universal screening:** screening of the entire population or sub group irrespective of the risk factors is advocated by ADA, IADPSG, W.H.O. and Diabetes In Pregnancy Study group India (DIPSI) [4-6,8]. Every country should decide whether to follow selective or universal screening depending upon its incidence, feasibility and cost-benefit ratio. In India, universal screening is needed, as Indian women have 11 fold increased risk of developing glucose intolerance in pregnancy as compared to Caucasian women [8].

### When to screen?

Data from human and animal studies have co-related the existence of chronic diseases such as obesity, diabetes mellitus and cardio vascular diseases to the perinatal nutrition [10], a process known as early metabolic imprinting. It has been observed that fetal beta cells respond to maternal hyperglycemia

as early as 16 weeks and undergo permanent epigenetic changes. Hence, screening in the first trimester helps to identify those women who already have pre-existing diabetes to control the sugar levels and avert the complications by modifying the nutrition and lifestyle at an early gestation.

- ADA and IADPSG: Recommend screening at first ANC visit and then at 24-32 weeks in previously undiagnosed GDM
- DIPSI: Recommends screening at first visit, if normal then at 24-28 weeks and again at 30-32 weeks
- NICE: Recommends screening at 24-28 weeks in high risk population
- ACOG: Recommends screening at 24-28 weeks, except in women with high risk factors who are screened at first visit [2].

### How to screen and diagnose?

A universal guideline for the ideal screening and diagnostic method is lacking. A number of methods have been suggested on the basis of population risks, cost effectiveness but there is a lack of consensus for the most appropriate universal screening and diagnostic criteria.

#### ACOG

Two step procedure:

- Step 1 Glucose Challenge Test (GCT)/ Glucose Loading Test (GLT):** Patient is given 50 gram oral glucose load irrespective of last meal. If one hour venous plasma glucose >140mg/dl, second step with fasting OGTT is done. If one hour venous plasma glucose is ≥ 200mg/dl, then a diagnosis of diabetes in pregnancy is made. GCT has a sensitivity of 70-88% and specificity of 69-89%.
- Step 2 Glucose Tolerance Test (GTT):** After an overnight fast of 8-10 hours and three days of unrestricted diet, fasting plasma glucose is measured following which a glucose load of 100 grams is given orally and blood is then drawn 3 times at hourly intervals. If patient has any two or more than two deranged values, gestational diabetes mellitus is diagnosed. Blood sugar value cut offs for ACOG are given below in Table 2. ACOG criteria is based on the risk of development of overt diabetes mellitus and not on the fetal and maternal outcome. Both Carpenter and Coustan and NDDG criteria are considered in ACOG. Advantage of 2 step screening is that not all women have to undergo intensive 3hr OGTT, where 5 blood samples are drawn. Disadvantage is that patient has to come for a second visit in a fasting state and therefore may be lost to follow up especially in developing countries, where 50-60% women receive antenatal care and about one third are lost to follow up [13]. It is costly and time consuming as five samples are required.

**Table 2:** ACOG Criteria for diagnosis of GDM.

Time	Carpenter & Coustan [2,11]	NDDG [12]
Fasting	95mg/dl	105mg/dl
One Hour	180mg/dl	190mg/dl
Two Hour	155mg/dl	165mg/dl
Three Hour	140mg/dl	145mg/dl

**NICE**

A woman has gestational diabetes mellitus if she has either fasting plasma glucose  $\geq 5.6$ mmol/l or 100mg/dl or 2 hour plasma glucose  $\geq 7.8$ mmol/l or 140mg/dl after 75g of glucose intake [9]. Although it is a one step screening test, disadvantage is that the patient has to come for a second visit in a fasting state and may be lost to follow up.

**ADA and IADPSG**

Based on the Hyperglycemia and Adverse Pregnancy Outcomes study (HAPO) [14], cut off levels for diagnosis of GDM were lowered to give an odd's ratio of 1.75 times the likelihood of adverse outcomes at mean glucose levels of HAPO study. As shown by HAPO study, adverse pregnancy outcomes, that is fetal macrosomia, pre-eclampsia, primary caesarean delivery, neonatal adiposity and cord blood c-peptide levels were noted even below the threshold of diagnostic criteria of GDM ( $< 95$ mg/dl) [4]. ADA and IADPSG recommend the screening during the first antenatal visit by fasting plasma glucose or random plasma glucose or HbA1c. If fasting glucose value is 92-125mg/dl, the woman is diagnosed as having GDM. If fasting glucose  $\geq 126$ mg/dl or HbA1c  $\geq 6.5\%$  or random plasma glucose  $\geq 200$ mg/dl, then the woman is diagnosed as having diabetes in pregnancy [4].

This is followed by repeat screening at 24-28 weeks. Fasting plasma glucose is measured followed by 75 gram oral glucose load and plasma glucose is estimated at one and two hours after glucose load. If any one or more values are deranged, diagnosis of GDM is made (Table 3). If fasting glucose  $\geq 126$ mg/dl or any value  $> 200$ mg/dl, diabetes in pregnancy is diagnosed. Lowering the thresholds for diagnosis of GDM would result in increasing the prevalence and hence, the cost of care [2]. Prevalence has increased from 4-7% to 18% by using screening method of IADPSG. Seshiah et al [8] studied the Indian population and

**Table 5:** Summary of tests for diagnosis of GDM.

Organization	Year	Screening mode	Approach	Glucose load	Diagnostic criteria (mg/dl) F 1hr 2hr 3hr				Remarks
					95	180	155	140	
ACOG	2013	Universal	Two step	100gm	105	190	165	145	Carpenter & Coustan; $\geq 2$ value abnormal
					95	180	155	140	NDDG; $\geq 2$ value abnormal
NICE	2015	Selective	One step	75gm	100	-	140	-	$\geq 1$ value abnormal
WHO	2013	Universal	One step	75gm	92-125	180	153-199	-	$\geq 1$ value abnormal
ADA & IADPSG	2010	Universal	One step	75gm	92	180	153	-	$\geq 1$ value abnormal
DIPSI	2006	Universal	One step	75gm	-	-	140	-	$\geq 140$ : GDM

debated that IADPSG had a few disadvantages. The Asians have higher insulin resistance in pregnancy and hence increased blood glucose levels, unlike Caucasians on whom HAPO study was conducted. Most, pregnant women do not come fasting to the hospital and if asked to come back in a fasting state, the dropout rate is very high, especially in developing countries. Blood has to be drawn 3 times during the second visit and is cumbersome and time consuming. HbA1c is an expensive test and is not possible in low resource setting.

**Table 3:** IADPSG/ADA criteria for diagnosis of GDM.

Time	Plasma Glucose (mg/dl)
Fasting	$\geq 92$
1 Hour	$\geq 180$
2 Hour	$\geq 153$

**DIPSI**

DIPSI recommends universal screening of all pregnant women in India due to high prevalence of diabetes. A one step screening and diagnostic procedure with 75gm of oral glucose is advocated during the first ANC visit, irrespective of the last meal. Venous sample is drawn at 2 hours. The criterion for diagnosis of GDM is shown in Table 4. This single step procedure is convenient, highly specific and economical [8,15]. Patient need not be fasting and there is no issue of loss to follow up as patient is screened at the first visit.

**Table 4:** DIPSI criteria for diagnosing GDM.

Plasma Glucose level (mg/dl)	Diagnosis in Pregnancy	Diagnosis Outside Pregnancy
$< 120$	Normal	
120-139	Gestational Glucose Intolerance	
$\geq 140-200$	Gestational Diabetes Mellitus	Impaired Glucose Tolerance
$\geq 200$	Pre- existing Diabetes	Diabetes Mellitus

**W.H.O.**

Hyperglycaemia first detected at any time during pregnancy should be classified as either 'Diabetes mellitus in pregnancy' or 'gestational diabetes mellitus'. In 2013, W.H.O. adopted the IADPSG criteria described above [5] (Table 5).

### Conclusion

Diabetes in pregnancy whether gestational diabetes or diabetes in pregnancy have increased in prevalence, may be due to an altered dietary habits, advanced maternal age of conception and increased incidence of obesity. It has been seen that an early management helps to avert these harmful effects. Hence, the need for screening for diabetes and early diagnosis is of paramount significance. There is a lack of uniform consensus on the methods of screening and diagnosis of diabetes in pregnancy. Therefore, physician should choose a method which is based on the prevalence of diabetes in their population, it's cost effectiveness and patient compliance. For low and middle income countries with high prevalence of diabetes, universal, early screening with a single step, DIPSI criteria seems to be convenient and highly cost effective.

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DOI: [10.19080/CRDOJ.2017.2.555600](https://doi.org/10.19080/CRDOJ.2017.2.555600)

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