

# Is Non Fasting Glucose Challenge test Sensitive Enough to Diagnose Gestational Diabetes Mellitus?

ORIGINAL

## Abstract

**Background:** There is a no consensus over the most sensitive and practical approach to diagnose Gestational Diabetes Mellitus (GDM). The standard 75 grams glucose tolerance test (GTT) is widely practiced to diagnose GDM. However, non-fasting 75-gram Glucose Challenge Test (GCT) with the 2-hour cutoff value of  $\geq 140$ mg/dL is also recommended by some professional bodies. The aim of this study was to investigate the sensitivity and specificity of GCT when compared to GTT for diagnosing GDM.

**Methods:** Pregnant women in period of gestation between 24-28 weeks were recruited by simple random sampling method. Non fasting 75g GCTs were performed in all followed by fasting 75g GTTs within a week time. International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria of GTT were used as the reference test to diagnose GDM and 2-hour value of GCT was compared.

**Findings:** According to IADPSG criteria, 21.5% (59/274) of pregnant women had GDM, in compared to 13.1% (36/274) detected by GCT. Sensitivity and specificity of GCT were 40.6% and 94.4% respectively. The area under the ROC curve for the ability of 2-hour value of GCT to predict GDM detected by GTT was 0.758 (SE 0.039). According to GTT values, FBS  $\geq 92$  mg/dL alone recognized 11.7% (32/274) of study sample as having GDM. Additional 9.1% (25/274) and 0.7% (2/274) of GDM cases were detected with 1-hour value  $\geq 180$  mg/dL and 2-hour hour value  $\geq 153$  respectively.

**Conclusion:** GCT with 2-hour cutoff value  $\geq 140$ mg/dL is not sensitive enough to diagnose GDM recognized by GTT.

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## Keywords

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## Background

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy and it is associated with increased risk of several adverse perinatal and maternal outcomes [1, 2]. Adverse perinatal outcomes include neonatal hypoglycemia, macrosomia which resulting in an increased risk for shoulder dystocia, and the need for neonatal intensive care [3]. Maternal complications of GDM include increased risk of caesarean delivery and pre-eclampsia. Furthermore, women with GDM have up to 60% risk of developing type 2 diabetes mellitus (T2DM) within 5-15 years of delivery, and it has been suggested that children prenatally exposed to a diabetic milieu have an increased risk for the development of T2DM later in life [3, 4]. There are several studies showing a significant reduction of those adverse outcomes, if prompt & proper interventions were taken for early diagnosis and to maintain satisfactory control of hyperglycaemia in pregnancy [1, 3]. The landmark study of Hyperglycemia and Adverse Pregnancy Outcome (HAPO) as well as many other studies including the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial had shown maternal hyperglycemia less severe than that used to define overt diabetes was related to clinically important perinatal disorders or problems and that their effects can be reduced by means of treatment [5] [6]. Therefore, the methods used in the diagnosis of GDM should have higher sensitivity to detect even milder cases of GDM.

There is a lack of international consistency with regard to the most sensitive and practical approach to diagnose GDM. While a 75-gram glucose tolerance test (GTT) is commonly employed, glucose challenge test (GCT) with different cutoff values is also widely used throughout the world.

Based on the result of HAPO study, a one-step approach using a 75-g 2-h GTT with new diagnostic criteria has been recommended by International Association of the Diabetes and Pregnancy Study

Groups (IADPSG) [6] and these new criteria have been adopted by several societies, including the American Diabetes Association and the Endocrine Societies [3, 7]. Other methods used in GDM diagnosis include two step method with combination of GCT and GTT. In this method, GCT is performed in all pregnant women and GTT only for those with positive GCT. Even though this method is widely accepted as the best method, complexity of the procedure is a limiting factor. An alternative method has been proposed by the World Health Organization (WHO) using a 2-h 75 g GTT, with a threshold plasma glucose concentration of greater than 140mg/dL or 7.8 mmol/L at 120 min [7]. A number of studies have documented that the treatment of gestational diabetes as defined by WHO criterion reduced serious perinatal morbidity and also improved the woman's health-related quality of life [8]. Diabetes in Pregnancy Study Group India (DIPSI) diagnostic criterion of 2-h PG  $\geq 7.8$ mmol/L with 75 g oral glucose load is a modified version of WHO, in that the WHO procedure requires women to be in the fasting state, whereas DIPSI procedure is performed in the fasting/non-fasting state irrespective of the last meal timing. Several studies conducted in India have shown it to be effective [8, 9].

Sri Lankan College of Obstetricians & Gynecologists (SCOG) recommendation on GDM screening and diagnosis is similar to DIPSI and include 75-gram GCT with cutoff value of 140mg/dL irrespective of fasting state [10]. Even though there are advantages such as simplicity and easy to perform as it doesn't require pregnant women to be in fasting, this method has not been validated with gold standard for local population. Hence, this prospective study was undertaken to ascertain the validity of GCT with cutoff value of 7.8 mmol/L (140 mg/dL) to diagnose GDM in pregnant women in Sri Lanka.

## Method

### Study design

This study was conducted as a clinic based cross sectional study in a Tertiary Hospital, in Sri Lanka. The study was commenced after the approval of the institutional ethics committee, Faculty of Medicine, Galle, Sri Lanka. The minimum sample size required for the study was 139 pregnant women and was calculated based on the estimated prevalence of GDM in Sri Lanka as 10 % with an absolute precision of 5% in an infinite population. However, the prevalence of GDM is reported to be as high as 22% with the new diagnostic criteria in a previous single center study in Sri Lanka [11]. Therefore, 296 pregnant women in 24 to 28 weeks of gestation were recruited by simple random sampling method.

All women who consented for the study were subjected to non-fasting 75-gram GCT on the day of recruitment. All of them were invited for the standard 75-gram oral glucose tolerance test (GTT) within a week of recruitment. GTTs were performed after an overnight fast of at least 8 hours and not exceeding 14 hours, and following at least 3 days of unrestricted carbohydrates (>150g per day) and exercise as per WHO guidelines. Two medically qualified investigators collected data using an interviewer administered questionnaire. The details including age, height, weight, history of diabetes in the family, history of GDM in previous pregnancy, history of previous delivery of large babies, socio-economic status were obtained using this questionnaire. Participant provided data were confirmed using pregnancy records, previous medical records and hospital records. The body mass index (BMI) of the subjects was calculated using the height and weight. Blood pressures of all the women were recorded. Collection of blood sample was carried out by qualified medical laboratory technicians using standard protocols. All laboratory tests were quality controlled and abnormal results were repeated and confirmed. Plasma glucose measurements were

carried out with an automated analyser using the glucose oxidase enzymatic calorimetric assay.

GDM was diagnosed according to standard IADPSG (international Association of the Diabetes and Pregnancy Study Groups) criteria and the diagnosis is made when any of the following three 75g 2 hour OGTT thresholds are met or exceeded: Fasting 92mg/dL, one hour  $\geq$  180 mg/dL, two hours  $\geq$  153 mg/dL.

### Statistical analysis

To compare the mean values between the groups independent t-test was used and for proportions, Chi-square test was employed. A receiver operating characteristics (ROC) curve was constructed to test the ability of the 2-hour value of GCT to identify patients with a diagnosis of GDM and to determine the best cutoff value in predicting a GDM diagnosis in our population. P-value < 0.05 was considered statistically significant. Data analysis was done using statistical package for social science (SPSS) version 20.

### Ethical considerations

Ethical clearance was obtained from ethical review committee of Faculty of Medicine, University of Ruhuna. A written consent was obtained from all pregnant women after detailed written and verbal explanation about the study. Pregnant women found to have GDM were referred to antenatal clinic for treatment and follow up.

## Results

Of the total of 296 women recruited, 15 didn't come for GTT and 07 could not complete the test due to nausea and vomiting. **Table 1** shows the baseline characteristics of the 274 women who completed the study. On average, pregnant women were relatively old with mean age of  $31.4 \pm 6.7$  years and of average pre-conception BMI ( $21.7 \pm 4.6$  kg/m<sup>2</sup>). The differences of the baseline characteristics between

**Table 1.** Baseline characteristics between subjects with and without GDM.

		GCT $\geq$ 140	GCT<140	with GDM*	without GDM*
Age in years	<20	2	11	2	11
	20-30	9	77	8	78
	>30	24	151	49	126
Parity	1	11	72	12	71
	2	8	69	18	59
	$\geq$ 3	16	98	29	85
POG <sup>1</sup>		26.8 $\pm$ 3.9	25.9 $\pm$ 4.7	25.5 $\pm$ 4.7	26.1 $\pm$ 4.4
BMI	<18	4	47	8	43
	18-24.9	20	149	35	134
	25-29.9	10	35	15	30
	>30	1	8	1	8
Past history of GDM		3	6	4	5
Family history of GDM		17	66	23	60
Past history of macrosomia		6	28	8	26

<sup>1</sup>Data are means  $\pm$ SD, \*based on IADPSG criteria, GCT $\geq$ 140mg/dL or  $\geq$  7.8 mmol/L, GCT<140 mg/dL or <7.8mmol/L. POG-period of gestation, BMI-body mass index, GDM-gestational diabetes mellitus, GCT -Glucose Challenge Test.

subjects with and without GDM (based on IADPSG criteria) and GCT  $\geq$  140 and <140 were shown in **table 1**.

Being overweight according to pre-conception BMI (39.3%) and age over 35 years (39.6%) were the two most frequently detected risk factors for GDM among the participants in this study. Past history of GDM was reported in 3.3% and 30.5% had a first degree relative with diabetes mellitus. Prevalence of the risk factors for GDM within the study population is shown in **Table 2**.

According to IADPSG criteria of the 75-gram GTT, 21.5% (59/274) subjects in the sample were diagnosed to have GDM; however, only 13.1% (36/274) were detected to have GDM with GCT using 2-hour cutoff value  $\geq$  140 mg/dl. Out of the 36 cases detected by 2-hour value  $\geq$ 140 mg/dl, 12 women were found to have normal GTT (false positive). Thus, only 24 cases of GDM were diagnosed by GCT with 2-hour value of  $\geq$  140 mg/dL, giving the sensitivity of 40.6% and specificity of 94.4%. Close to 60% (35/59) of patients with true GDM were missed with GCT.

**Table 2.** Prevalence of risk factors in the study population.

Risk factor	N	%
Past history of GDM	09	3.3
Maternal age $\geq$ 35 years	108	39.6
Pre conception BMI $\geq$ 23 kg/m <sup>2</sup>	105	39.3
Bad obstetric history- miscarriages, still births, IUD etc.)	65	23.8
Delivering large babies (>3.45kg)	34	12.4
History of T2DM/GDM among first degree relatives	83	30.5

GDM -Gestational Diabetes Mellitus, BMI- Body Mass Index, IUD- Intra Uterine Death, T2DM-type 2 diabetes mellitus.

When the non-fasting 2-hour cutoff value of GCT is increased to  $\geq$  152 mg/dL (the cutoff value used in IADPSG criteria), the detection rate of GDM dropped to 5.8% (16/274). Furthermore, out of three glucose test of GTT, 1-hour value has the highest sensitivity in detecting GDM followed by FBS (**Table 3 & figure 1**). FBS  $\geq$  92 mg/dL recognized 11.6% (32/274) of study sample as having GDM. Additional of 9.1% (25/274) and 0.7% (2/274) of GDM cases

**Table 3.** Comparison of GCT with GTT using IADPSG criteria in diagnosing GDM.

GCT $\geq$ 140 mg/dL	GTT using IADPSG criteria as gold standard		Total
	Positive	Negative	
Positive	24	12	36
Negative	35	203	238
Total	59	215	274

GTT-Glucose tolerance test, GCT -Glucose Challenge Test, GDM -Gestational Diabetes Mellitus, IADPSG- International Association of the Diabetes and Pregnancy Study Groups.

**Table 4.** Number of patients with GDM diagnosed by FBS, 1<sup>st</sup> hour value and 2<sup>nd</sup> hour value of GTT.

	GDM	No GDM	sensitivity
FBS*	32	242	11.6%
1st hour value*	37	237	13.5%
2nd hour value*	16	258	5.8%
With all 03*	59	215	21.5%

\*Based on IADPSG (International Association of the Diabetes and Pregnancy Study Groups) criteria.

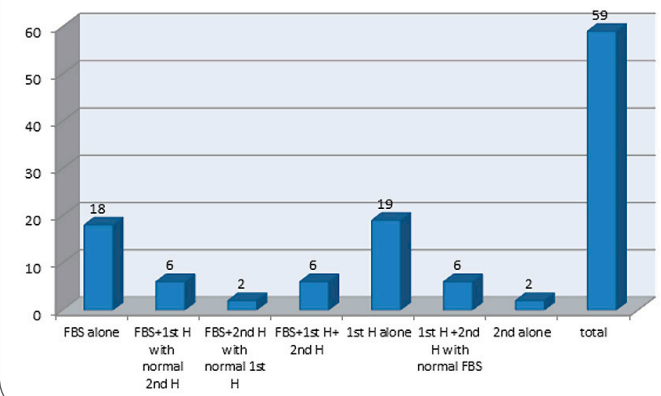
were detected with 1-hour value  $\geq$  180 mg/dL and 2-hour hour value  $\geq$  153 respectively.

The area under the ROC curve for the ability of 2-hour value of GCT to predict altered FBS and 1st-hour value of GTT was 0.758 (SE 0.039) (Fig. 2). The best cutoff point of 2-hour value to predict abnormal FBS and 1st-hour values occurred at 120 mg/dL (sensitivity of 64.9%, the specificity 76.5%) (Fig. 2). If the cutoff 2-hour value of GCT is increased to 140mg/dL, sensitivity dropped 37% and specificity increased to 96% and this is a clear indication that GCT with cutoff 2-hour value of 140 is not sensitive enough to diagnose GDM in compared to gold standard GTT (Fig 2).

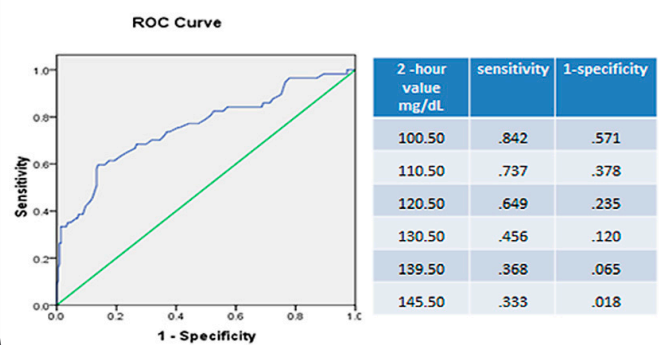
The distribution of 2-hour glucose of GCT in women with GDM (n = 59) and without GDM (n = 215) is shown in Figure 3. Of note, there was considerable overlap in the distribution of 2-hour value between these two patient populations. This probably indicates that there was no clear thresh-

old level of 2-hour glucose that can be used to identify GDM.

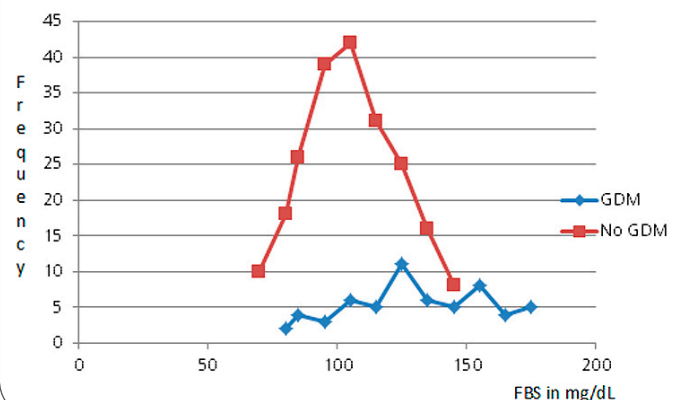
**Figure 1:** Number of patients with GDM diagnosed by FBS (fasting blood glucose), 1<sup>st</sup> H (1<sup>st</sup> hour value of GTT, 2<sup>nd</sup> H (2<sup>nd</sup> hour value of GTT) based on IADPSG criteria.



**Figure 2:** ROC curve of 2-hour value to predict abnormal FBS and 1-hour value.



**Figure 3:** Histogram showing the distribution of 2-hour glucose level of GCT in women with GDM and without GDM.





## Discussion

Number of studies have shown the value of fasting Glucose Challenge Test (GCT) with a cutoff value of 140 mg/dl in diagnosing GDM [1, 8, 12, 13]. Professional organizations including Diabetes in Pregnancy Study Group of India (DIPSI) and Sri Lankan College of Obstetricians & Gynecologists (SCOG) have recommended non fasting GCT to diagnose GDM based studies carried out in India [9, 10, 14]. However, in these studies GCT was not compared with standard GTT and the cutoff value was justified on the basis of equal prevalence macrosomia in GDM group and non GDM group. Equal prevalence is thought to be due to appropriate recognition and treatment of GDM cases in these studies. However, prevalence of macrosomia as the surrogate marker to diagnose GDM is not accurate as many factors including success of the treatment can confound the prevalence of macrosomia. There are other studies showing poor sensitivity of GCT in diagnosing GDM [15, 16]. In a recent study done in Indian ethnicity had shown very low sensitivity of non- fasting GCT when compared to IADPSG criteria (sensitivity 22.6 %, specificity 97.8 %) [17]. Other studies done in South Asian ethnicity as well as in Caucasians too had revealed poor sensitivity of 50-gram and 75-gram GCT [15, 18, 19].

Results of our study clearly indicated that the non-fasting GCT had a poor sensitivity (40.6%) when compared to GTT with IADPSG criteria. Even though sensitivity of GCT in our study is slightly better when compared to the study conducted by Mohan V et al, the sensitivity of 40% is far below the acceptable limit to use as a screening tool. GCT would not only miss around 60% of cases, but it would falsely diagnose 33% cases as having GDM (false positive rate of 33%, 12/36). All this 33% of cases detected as GDM will unnecessarily undergo more investigations and intervention including dietary modification. Magnitude of recommending and using wrong test can be un-

derstood if we look at the prevalence of GDM. A previous study conducted in a tertiary care center showed alarmingly high prevalence of GDM (22%) among pregnant women in Sri Lanka. If GCT is used in a Tertiary care Hospital which has delivery rate of 1000/per month it would miss around 132 GDM cases per month.

The main reason for recommending GCT over GTT is the simplicity of non-fasting GCT. Advocators of non-fasting GCT believe that GTT is too complex to perform in the antenatal clinic setting and also would result in significant low turnover as it require pregnant women to be overnight fast. However our study as well as previous studies had shown that pregnant women had good compliance with GTT when motivated [17].

Our study has clearly shown 1-hour value of GTT was better target than the 2 hour value. Similar finding was observed in the HAPO study and shown that when adjusted for confounders, the 1-hour plasma glucose level remained a better predictor of primary outcome. In HAPO study FBS  $\geq$  92 mg/dl alone recognized 8.3% of the HAPO population as having GDM. 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 adding the 2 hour threshold of 153 mg/dl identified an additional 2.1% of the population [20]. The finding of HAPO study had indicated that targeting 2-hour value after glucose load was not the best option. Our findings were also similar to the finding of HAPO study. In our study FBS  $\geq$  92 mg/dL recognized 11.6% (32/274) of study sample as having GDM. Additional of 9.1% (25/274) and 0.7% (2/274) of GDM cases were detected with 1-hour value  $\geq$  180 mg/dL and 2-hour hour value  $\geq$ 153 respectively.

## Conclusions

The fasting GCT with cutoff value of  $\geq$  140mg/dL lacks adequate sensitivity to diagnose GDM. We

recommend fasting GTT to diagnose GDM in all pregnant women even though it needs fasting state and three blood tests. If performing full GTT is practically difficult, FBS together with 1-hour plasma glucose after 75 gram glucose load is a good alternative.

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## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

MH designed the study, supervised and performed the study, analyzed data and wrote the article, TPW analyzed data and critically reviewed the manuscript, DU collected the data and reviewed the manuscript.

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