

# A comparative study on the efficacy of single step 75 g oral glucose tolerance test with Carpenter–Coustan criteria to diagnose gestational diabetes mellitus

Sri Revathy Sadasivam<sup>1</sup>, D. Asha Devi<sup>2</sup>, D. Vimala<sup>3</sup>, Philips Abraham<sup>4</sup>

<sup>1</sup>Post-graduate Student, <sup>2</sup>Senior Resident, <sup>3</sup>Professor, Department of Obstetrics and Gynaecology, <sup>4</sup>Associate Professor, Department of Biochemistry, Vinayaka Missions Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu, India

## ABSTRACT

**Introduction:** Prevalence of gestational diabetes mellitus (GDM) is simultaneously increasing with the global rise of diabetes. In the Indian context, screening is essential for all pregnant women as the Indian women have 11-fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women. Because 80-90% of women with GDM can be managed with lifestyle therapy alone, universal screening for GDM is increasingly considered justified. Various agencies which conduct studies on diabetes recommends two step procedure to identify GDM including oral glucose tolerance test (OGTT) which is not practical in the Indian scenario, where 70% of the population lives in rural area. In this framework, a simple one step procedure recommended by Diabetes in Pregnancy Study Group in India (DIPSI) is found to be relevant and sensible in screening and identifying the GDM cases. So, a study had been designed to identify the validity of using single step 75 g OGTT as a diagnostic tool for identifying GDM in pregnant women with no known risk factors. **Materials and Methods:** 150 pregnant women (24-28 weeks of gestation) attending the antenatal clinic of Vinayaka Missions Medical College were randomly selected. Both DIPSI and Carpenter–Coustan recommended OGTT was conducted in these groups in an interval of 1-week time. Kappa agreement was used to examine the reliability of the values. **Results and Discussion:** The incidence of GDM by 75 g single step OGTT was found to be 16.7%, whereas the incidence of GDM by Carpenter–Coustan method using 100 g OGTT was found to be 13.3%. This high pick up rate by 75 g OGTT may help to control the incidence of diabetes mellitus and related complications. On correlation in predicting GDM, single step 75 g OGTT was found to be 75% sensitivity and 92.3% specificity. **Conclusion:** Besides being economical, high sensitivity and specificity of the single step method have affirmed the fact that it can be used as a reliable diagnostic procedure for GDM.

**Key words:** Diabetes in Pregnancy Study Group in India, Gestational diabetes mellitus, Single step oral glucose tolerant test

## INTRODUCTION

The prevalence of diabetes is increasing globally and the causes attributed are the aging population, urbanization, obesity epidemic, physical inactivity, and stressful modern life. It is not surprising that the incidence of gestational diabetes mellitus (GDM) is also increasing in parallel to the overall rise in obesity and Type-2 diabetes.<sup>[1,2]</sup>

GDM is defined as any degree of glucose intolerance occurring first time during pregnancy. GDM

commonly develops, when maternal glucose metabolism is unable to compensate for the progressive development of insulin resistance, arising primarily from the consistently rising diabetogenic placental hormones. It classically develops during the second or third trimester.<sup>[3]</sup>

*In-utero* exposure to hyperglycemia has been shown to be associated with increased occurrence of impaired glucose tolerance (IGT) and defective insulin secretory response in later stages of life, independent of genetic

### Address for Correspondence:

Dr. D. Asha Devi, Department of Obstetrics and Gynaecology, Vinayaka Missions Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu, India. E-mail: drasha1979@gmail.com

predisposition to Type 2 diabetes mellitus.<sup>[4,5]</sup> In addition, children exposed to maternal diabetes *in-utero* and are known to have a higher risk (around eight-fold) of obesity and diabetes compared to their unexposed siblings, suggesting non-genetic factors for the increased risk among exposed offsprings.<sup>[6,7]</sup>

In light of the fact that 80-90% of women with GDM can be managed with lifestyle therapy alone, universal screening for GDM is increasingly considered justified.<sup>[8]</sup> Various national agencies which conduct studies on diabetes such as American Diabetes Association, Canadian Diabetes Association, and Diabetes UK54, recommends two step procedures to identify GDM patients, namely, (1) Screening based on risk factors and (2) Diagnosis of diabetes in selective population by oral glucose tolerance test (OGTT).<sup>[9]</sup> In the Indian context, screening is essential for all pregnant women as the Indian women have an 11-fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women. Compared with selective screening, universal screening for GDM detects more cases and improves maternal and offspring prognosis.<sup>[10]</sup>

GDM diagnosis is overlooked in about 1/3<sup>rd</sup> of the women where selective rather than universal screening is performed, and when this is applied to the 20 million reproductive age women in India, chances of missing a lot of women with glucose intolerance will be significantly high.<sup>[11]</sup> In this context, a simple one step procedure recommended by Diabetes in Pregnancy Study Group in India (DIPSI) is found to be theoretically relevant in identifying the GDM cases.<sup>[12,13]</sup>

So, a study has been designed to compare the efficacy of DIPSI recommended one step procedure to identify GDM cases with established Carpenter–Coustan method and to analyze the validity of this simple one step procedure a screening and diagnostic tool.

## MATERIALS AND METHODS

150 pregnant ladies from 24 to 28 weeks of gestation attending the antenatal clinic of Vinayaka Mission's Kirupananda Variyar Medical College and Hospital were selected randomly for the study. Pregnant ladies with multiple pregnancy, body mass index  $\geq 35$  kg/m<sup>2</sup>, age  $\geq 35$  years, history of diabetes in first-degree relatives, recurrent abortions, previous history of macrosomia, stillbirth or congenital anomaly, polycystic ovarian disease, persistent glycosuria, and diagnosed with diabetes mellitus were excluded

from the study. The study protocol was approved by the Ethics Committee of Vinayaka Missions Medical College and Hospitals. Written informed consent was obtained from the study subjects. Details of family history of diabetes, history of previous pregnancies, and the socio-economic status were obtained, and the blood pressure measurements were recorded.

Study subjects were given 75 g oral glucose load irrespective of their last meal timings, and venous blood was drawn after 2 h. They all were requested to come after a week on an empty stomach for 100 g OGTT as recommended by Carpenter–Coustan. Venous blood was drawn in the fasting state, 1 h, 2 h, and 3 h after the glucose load. The plasma glucose (PG) level was estimated by glucose oxidase-peroxidase method using commercially available standard kits (Agappe Diagnostics). The results were analyzed taking into consideration of DIPSI recommendation and was compared with an age old gold standard test of Carpenter–Coustan criteria (Table 1). According to DIPSI criterion (Table 2), pregnant women with 2 h PG  $\geq 7.8$  mmol/L (140 mg/dL) were diagnosed as GDM and PG between 120 and 139 mg/dL were considered as gestational glucose intolerance (GGI).

Pregnant ladies with two or more of the venous plasma concentrations more than the above values were diagnosed as GDM.

Results of both tests were analyzed. Specificity, sensitivity, percentage of false positive, percentage of false negative, positive predictor value (PPV), and negative predictor value (NPV) of single step OGTT, when compared to reference method, were determined.

## RESULTS

The average age group in this study was 25.62  $\pm$  4.21 years (range 18-35). The study group has the

**Table 1: Carpenter–Coustan criteria**

Time	100 g OGTT
Fasting	95 mg/dl (5.3 mmol/L)
1 h	180 mg/dl (10 mmol/L)
2 h	155 mg/dl (8.6 mmol/L)
3 h	140 mg/dl (7.8 mmol)

OGTT: Oral glucose tolerance test

**Table 2: DIPSI criteria**

Condition	PG (mg/dL) 2 h after glucose load
GGI	120-139
GDM	140-199
Diabetes	>200

PG: Plasma glucose, GGI: Gestational glucose intolerance, GDM: Gestational diabetes mellitus, DIPSI: Diabetes in Pregnancy Study Group in India

highest percentage of pregnant women from the age group of 21 to 25 years (38%), and there were 33% seen in the age group 26-30 years. Out of 150, 84 subjects (56%) were primigravida and the rest (44%) were multigravida (Table 3).

According to DIPSI guideline, from one step OGTT study, 99 pregnant women (66%) were identified as normal glucose tolerant. PG level of 25 subjects (16.6%) was between 120 and 139 mg/dL and was considered as GGI group. 25 women (16.6%) whose value was between 140 and 199 were identified as GDM and 1 patient was diagnosed for the first time as true diabetes mellitus (Table 4). Based on Carpenter–Coustan method, 20 patients (13.3%) were diagnosed to have GDM, and 86.7% patients ( $n = 130$ ) were found to be normal (Table 5). Sensitivity and specificity of the single step OGTT were found to be 100% and 96%. Percentage of false positive and false negative was found to be 3.85 % and 0%. PPV and NPV of the single step OGTT, when compared to the reference method, were found to be 80% and 100%.

## DISCUSSION

The prevalence of diabetes is increasing globally, and these numbers include women with GDM. GDM is considered as a transient abnormality of glucose intolerance during pregnancy.<sup>[14]</sup> Women with GDM are at increased risk of diabetes in future as are their children and the following subsequent generations.<sup>[15]</sup> GDM is associated with increased risk of maternal and

perinatal short- and long-term complications.<sup>[16]</sup> These facts point toward the necessity to have an efficient method to screen this segment of population especially in developing countries.

75 g 2 h OGTT with a cut off PG level of 140 mg/dL at 2 h is considered as a standard method to assess IGT in human subjects. Carpenter–Coustan criteria, a modified version of O’Sullivan and Mahan method, recommended a 3 h 100 g OGTT to identify GDM (Criteria being any two values should meet or exceed fasting PG >95 mg/dL, 1 h PG >180 mg/dL, 2 h PG >155 mg/dL, and 3 h PG >140 mg/dL.) This raised glucose load of 100 g was based on the concept that pregnant ladies have an increased frequency of dietary intake than the normal subjects. These criteria were validated against the future risk of women developing diabetes mellitus and not on fetal outcome. Retrospective studies have shown that the diagnosis of GDM with these criteria did not make any differences in the perinatal outcome which emphasize the need of changing the inclusion criteria. So, now Carpenter himself accepted a standard 75 g 2 h OGTT with decreased threshold PG level (more inclusive diagnostic criteria) of 140 mg/dL at 2 h to diagnose GDM. So, to improve the perinatal outcome and considering the fact that pregnant ladies have an increased frequency of dietary intake, DIPSI have recommended a 75 g non-fasting OGTT with threshold of 140 mg/dL PG level.<sup>[17]</sup>

During the study period, 150 patients underwent OGTT 75 g between 24 and 28 weeks of gestation. All of them irrespective of the results also underwent 100 g OGTT within a week’s time of the previous test. Mean age distribution in this study was  $25.62 \pm 4.21$  years. In this study, age group between 26 and 30 years has relatively high number of GDM (45.5%) when compared to other age groups. 56% of the study population were primigravida and 64% were multigravida. In our study, among primigravida, 11% were diagnosed to have GDM and 14% as GGI. In multigravida, 15.5% GDM and 10% GGI were seen. No significant difference in the incidence of GDM or GGI was observed among groups with different parity, which underlines the fact that risk of glucose intolerance does not vary with parity.

The incidence of GDM by 75 g single step OGTT was found to be 16.7%, whereas the incidence of GDM by Carpenter–Coustan method using 100 g OGTT was 13.3%, which goes in favor of high pick up rate in 75 g single step OGTT. On comparison with 100 g GTT, the sensitivity of single step 75 g OGTT was found to be 100% and specificity is 96%.

**Table 3: Parity distribution of patients studied**

Parity	Number of patients	%
Primi	84	56
Multi	66	44
Total	150	100

**Table 4: Incidence of GDM by OGTT75**

GDM by OGTT75	Number of patients	%
Normal	99	66
GDM	25	16.7
GGI	25	16.7

GDM: Gestational diabetes mellitus, GTT: Glucose tolerance test, OGTT: Oral glucose tolerance test

**Table 5: Incidence of GDM by GTT 100**

GDM by GTT	Number of patients	%
Normal	129	86.7
GDM	20	13.3
Total	150	100

GDM: Gestational diabetes mellitus, GTT: Glucose tolerance test

There was no fetal, perinatal mortality, and morbidity noted in our study group.

A study by Seshiah *et al.* had also found a sensitivity of 79.8% for this method. Any screening test with the sensitivity more than 60% and specificity more than 90% can be used in a community for analysis and results of our study strongly favor and recommend the use of this one step procedure for the diagnosis of GDM.<sup>[13,18-20]</sup>

Percentage of false negative results and NPV of the single step procedure was found to be 0% and 100%, which means in our study, this procedure recognized all the GDM positive cases identified by C&C Method. Percentage of false positive and PPV of this method was found to be 3.85% and 80%. This clearly states that single step method has a high pick up rate than the reference method. This high pick up rate by 75 g OGTT helps to eliminate any chance of occurrence of false negative results and thus facilitates in the fight to control the incidence of diabetes mellitus in later life.<sup>[21,22]</sup> A study by Aruna *et al.* had also reported 3 times high pick up rate for this method when compared to ADA criteria.<sup>[21]</sup> In the single step OGTT, women were given 75 g glucose load irrespective of their last meal timings. A normal glucose tolerant woman would be able to maintain euglycemia despite glucose challenge due to brisk and adequate insulin response. Whereas for a woman who has an impaired insulin secretion, the glycemic level will be high with a normal meal and with an added glucose challenge, the glycemic excursion exaggerates further.<sup>[23]</sup> This cascading effect might be the reason for high pick up rate and is advantageous as this would not result in a false negative diagnosis of GDM.<sup>[19,20]</sup>

This overdiagnosis helps to identify the patients at risk so that they can be counseled early in their life for some alteration in their life pattern. Through single step procedure, pregnant ladies who had a PG level between 120 and 139 mg/dL were grouped as GGI. These patients were advised to undergo lifestyle modification, nutritional modification, and to carry out exercise. Thus, the test was able to make people aware of their glucose intolerance at the very early stages, and advice on the importance of healthy eating habits and exercise patterns for maintaining ideal body weight can be given at the beginning stage.<sup>[19]</sup> Thus, it can drastically bring down the incidence and can make a remarkable effect on the incidence of diabetes by this very early intervention.

Moreover, the single step DIPSI criterion requires estimation of PG in one blood sample to diagnose GDM. As it is a cost-effective and evidence-based

procedure, it can be suggested to every pregnant woman belonging to any socio-economic status.<sup>[19,24,25]</sup> Another advantage is that it can be performed according to the availability of patients, as the timing of last meal or time of visit to the hospital is insignificant in this procedure.<sup>[25,26]</sup> In conclusion, single step OGTT can be considered as a patient-friendly test and cause the least disturbance in the pregnant woman's routine activities.

## CONCLUSION

Besides being economical, high sensitivity and specificity of the single step method have affirmed the fact that it can be used as a reliable diagnostic procedure for GDM.

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