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## Research Article

# WHO 75 gram OGTT-A single step procedure for screening and diagnosis of gestational diabetes mellitus

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## ABSTRACT

**Background:** Indian women have an eleven fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women. Universal screening for GDM is essential in India. This study was undertaken to find out a single step procedure which serves both as a screening and a diagnostic tool.

**Methods:** This study was carried out in a tertiary care teaching institute in Karnataka. 839 pregnant women with gestational age between 24-28 weeks were subjected to 50 gram OGCT and venous blood was drawn after 1 hour. These patients were requested to come after 72 hours on empty stomach for WHO-75 gram OGTT. Fasting and 2 hour blood samples after 75 gram of glucose were drawn.

**Results:** Amongst the 839 pregnant women who underwent 50 gram OGCT, 136 (16.2%) women had one hour plasma glucose >140 mg/dl. Subsequent 75 gram OGTT revealed that only 43 (31.62%) of screen positive patients were diabetic. 93 women who tested positive by 50 gram OGCT were false positive cases (10.58%). Prevalence of GDM in study population was 6.3 % (53/839). Screening OGCT missed 10 (15.87%) of gestational diabetes mellitus cases which were picked up by 75 gram WHO OGTT only.

**Conclusions:** The diagnosis of Gestational Diabetes Mellitus by OGTT based on initial OGCT screening leaves 15.87% undiagnosed. The two step method of screening OGCT and diagnosing GDM with subsequent OGTT is tedious and not economical. Instead a single step WHO 75 gram fasting OGTT with 2 hour PPG  $\geq$  140 mg/dl is simple and precise.

**Keywords:** GDM, OGCT, OGTT

## INTRODUCTION

India is being recognized as “The Diabetes Capital of the World”. Diabetes is a major health problem in India with prevalence rates between 4.6% and 14% in urban areas, and 1.7% and 13.2% in rural areas respectively. India has an estimated 62 million people with Type 2 Diabetes mellitus; this number is expected to go up to 79.4 million by 2025.<sup>1</sup> In parallel with increased diabetes prevalence,

there is a rise in the prevalence of gestational diabetes mellitus.

Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with recognition or onset during pregnancy, irrespective of the treatment with insulin.<sup>2</sup>

The prevalence of Gestational diabetes mellitus has been reported to range from 3.8% in Kashmir<sup>3</sup> to 41% in Lucknow.<sup>4</sup>

### Impact of GDM

Women with a history of GDM are at increased risk of future diabetes.<sup>5</sup>

Children born to mothers with uncontrolled diabetes, either pre-gestational or gestational in origin are four to eight times more likely to develop diabetes in later life as compared to their siblings born to the same parents in a non-GDM pregnancy.<sup>6</sup>

Increasing maternal carbohydrate intolerance in pregnant women without GDM is associated with a graded increase in adverse maternal & foetal outcomes.<sup>7</sup>

### Need for screening

Universal screening is essential in Indian women, as they have an eleven fold increased risk of developing glucose intolerance during pregnancy.<sup>8</sup>

ADA recommends two step methods for screening and diagnosis of gestational diabetes in selective population. Compared to Selective screening, Universal screening for GDM detects more cases and improves maternal and foetal prognosis.<sup>9</sup>

Treatment of Gestational diabetes mellitus, as defined by WHO criteria has reduced serious perinatal morbidity and improved the woman's health related quality of life.<sup>10,11</sup>

This study was undertaken to devise a simplified, economical; single screening and diagnostic test for Gestational diabetes mellitus acceptable in the Indian context.

## METHODS

This study was carried out in a tertiary care teaching institute in Karnataka from November 2007 to October 2009. Pregnant women with gestational age between 24-28 weeks were enrolled in this study. All women were informed about the nature of the study and informed consent taken.

A total of 839 pregnant women underwent detailed clinical examination, irrespective of presence or absence of risk factors. Details of family history of diabetes, history of previous pregnancies, and the socio-economic status were obtained. Blood pressure measurement and the body mass index were recorded.

Initially, pregnant women were subjected to 50 gram OGCT. Fifty gram of glucose was dissolved in 200 ml of water and the patient was asked to drink it over a five minute period, irrespective of time of the day and her last

meal. After 1 hour of time of ingestion of glucose, venous blood was drawn. If blood sugar was  $\geq 140$  mg/dl, the screening was considered as positive. The plasma glucose was estimated by glucose oxidation and per-oxidation (GOD-POD) method by Eco-Pak glucose kit.

All 839 women were requested to have their regular diet for three days and return after observing overnight fast of 8-12 hours for the 75 gram oral glucose tolerance test (OGTT) recommended by WHO. Blood sample was drawn in the fasting state and 2 hours after ingestion of 75 gram glucose. A pregnant woman was diagnosed with Gestational Diabetes Mellitus if the Fasting plasma glucose  $\geq 126$  mg/dl, and/or 2 hours plasma glucose  $> 140$  mg/dl.

### Statistical analysis

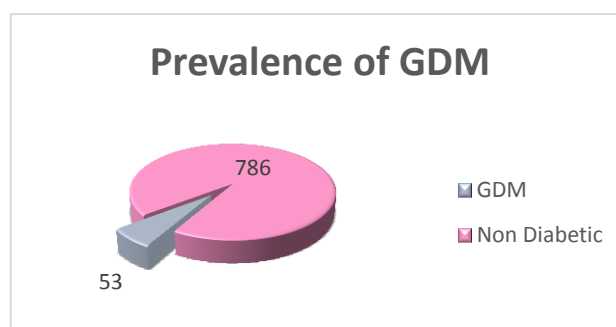
Descriptive and inferential statistical analysis has been carried out in the present study.

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

## RESULTS

Eight hundred and thirty nine pregnant women were enrolled in our study at a tertiary care teaching institute in Karnataka.

Prevalence of GDM in Study population was 6.3% (53/839) as shown in Figure 1.



**Figure 1: Prevalence of GDM**

Table 1 shows that 16.2% (136/839) of study population had positive screening for 50 gram OGCT. Rest 703 patients were screen negative.

31.62% (43/136) of OGCT screen positive patients were diagnosed with gestational diabetes mellitus.

93 cases were diagnosed false positive (10.58%) by 50 gram oral glucose challenge test.

**Table 1: Results of 50 gram OGCT**

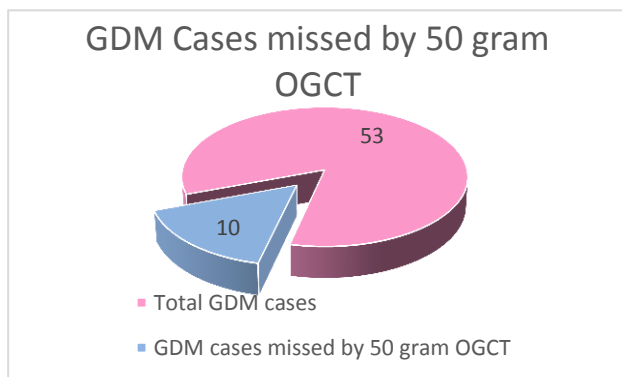
Results of 50 gram OGCT		
Blood sugar (mg/dl)	No. of patients	%
<140	703	83.8
≥140	136	16.2
<b>Total</b>	<b>839</b>	<b>100.0</b>

Table 2 and Figure 2 shows that 10 out of 53 Gestational Diabetes cases were diagnosed by 75 gram WHO OGTT method only, which was missed by 50 gram OGCT screening.

**Table 2: Comparison between 50 gram OGCT and 75 gram WHO OGTT**

Comparison between 50 gram OGCT and 75 gram WHO OGTT			
OGCT 50 Gram	WHO 75gram OGTT		Total
	GDM Present	GDM Absent	
<b>Positive</b>	43	93	136
<b>Negative</b>	10	693	703
<b>Total</b>	<b>53</b>	<b>786</b>	<b>839</b>

WHO: World Health Organisation; OGTT: Oral Glucose Tolerance Test; OGCT-Oral Glucose Challenge Test

**Figure 2: GDM cases missed by 50 gram OGCT**

OGCT-50 gram had a sensitivity of 84.12%. The false negative rate of 50 gram OGCT was 15.87%. The predictive value of a positive test was 36.30% only as shown in Table 3.

## DISCUSSION

GDM not only influences immediate maternal (Preeclampsia, Stillbirths, Macrosomia, PPH, Shoulder dystocia, Caesarean section) and neonatal outcomes

(Hypoglycaemia, Hyperbilirubinemia, respiratory distress), but also increases the risk of future Type 2 diabetes in mother as well as her offspring.

**Table 3: Parameters of 50 gram OGCT**

Parameters of 50gram OGCT		Percentage
<b>1</b>	Sensitivity	<b>84.12%</b>
<b>2</b>	Specificity	<b>89.41%</b>
<b>3</b>	Predictive value of a Positive test	<b>36.30%</b>
<b>4</b>	Predictive value of a Negative test	<b>98.74%</b>
<b>5</b>	Percentage of false negatives	<b>15.87%</b>
<b>6</b>	Percentage of false positives	<b>10.58%</b>

It is essential to screen & diagnose GDM so as to prevent both the short term and long term implications on the mother and her offspring.

Universal screening is essential in Indian women, as they have an eleven fold increased risk of developing glucose intolerance during pregnancy.<sup>8</sup> The Asian Indian Phenotype refers to unique clinical & biochemical abnormalities in Indians which includes increased insulin resistance, greater abdominal adiposity, and a higher waist circumference. This phenotype makes Indians more prone to diabetes.<sup>12</sup>

Apart from ethnicity, high prevalence rate of GDM in Indian population is due to trending towards older maternal age, decrease in physical activity, adoption of modern lifestyle, and increasing prevalence of obesity and diabetes.<sup>13</sup>

## OGCT

Pregnant women with gestational age between 24-28 weeks enrolled in our study were subjected to both 50 gram OGCT and WHO 75 gram OGTT.

The timing of glucose tolerance testing during pregnancy is critical, because delayed diagnosis increases the duration of deranged maternal metabolism and accelerated foetal growth.<sup>12</sup>

Insulin is detectable in the foetal pancreas as early as 9 weeks after conception.<sup>14</sup> The recent concept is to screen for GDM in the first trimester itself as the foetal beta cells recognizes and responds to maternal hyperglycaemia.<sup>15</sup> If results are negative, tests are to be repeated at 24 to 28 weeks of gestation. This time window is selected because insulin resistance increases as third trimester progresses and early testing may miss some patients who later develop carbohydrate intolerance.<sup>12</sup>

In our study, Screening OGCT had a sensitivity of 84% and specificity of 89.41%; and missed 15.87% of the GDM cases which is comparable to results of Huynh J et al.

Huynh J et al<sup>16</sup> found that Screening OGCT has a sensitivity of 83%, specificity of 75% and would miss 17% of the cases and concluded that OGTT alone is the best procedure without prior GCT.

The false positive rate of OGCT was as high as 10.58% in our study. This imposed extra testing burden and raised undue concern in these patients. This is comparable to 14.5% false positive rate of OGCT in study by Das et al.<sup>17</sup>

Predictive value of a Positive and Negative OGCT was 36.30% and 98.74% respectively in our study, which is comparable to 24.5% and 90.1% respectively in study by Seshiah et al.<sup>18</sup>

The most important observation of the study was the identification of 10(15.87%) potential GDM women who were negative as per OGCT criteria and were not even required to go in for the subsequent OGTT confirmation.

**Table 4: Comparison of various criteria for diagnosis of GDM**

Definition of GDM by different criteria					
Criteria	Method	Fast-ing (mg/dl)	1 hr (mg/dl)	2 hr (mg/dl)	3hr (mg/dl)
WHO	Fasting 75 g OGTT	≥126	-	≥140	-
IADPSG	Fasting 75 g OGTT	≥92	≥180	≥153	-
DIPSI	Non fasting 75 g OGTT	-	-	≥140	-
ADA	Fasting 100 g OGTT	95	180	155	140

GDM: Gestational Diabetes Mellitus; WHO: World Health Organisation; ADA: American Diabetes Association; IADPSG: International Association of Diabetes and Pregnancy Study Groups; DIPSI: Diabetes In Pregnancy Study Group in India; OGTT: Oral Glucose Tolerance Test

Mohan V et al concluded in their study that, current DIPSI guidelines of a single non-fasting OGTT using 2 hr cut-off point of 140mg/dl would miss 72.3% of women with GDM diagnosed by WHO criteria.<sup>19</sup>

Brazilian Gestational Diabetes Study Group evaluated the ADA & WHO diagnostic criteria against pregnancy outcomes in an observational study of nearly 5000 women and found that WHO criteria identified more cases of GDM compared to ADA(7.2% vs 2.4%).<sup>20</sup>

Schmidt et al found that the diagnostic pick up rate in their study on GDM was three times more with the WHO criteria than ADA criteria. They also detected increased rate of morbidity in women diagnosed as GDM by WHO criteria. They documented an important observation that the subjects with GDM by WHO criteria delivered macrosomic infants.<sup>20</sup>

ADA criteria were originally validated against the future risk of maternal diabetes and not based on adverse perinatal outcome<sup>21</sup>. WHO testing for glucose tolerance during pregnancy was abnormal in the greater percentage of women with adverse outcome than the cumbersome two step ADA test in a study by Pettitt DJ et al.<sup>22</sup>

Fasting glucose tends to have low sensitivity in South Asians. Hence 2 hour Postprandial Glucose is more sensitive than Fasting glucose in diagnosing GDM in Indians.<sup>23, 24</sup>

Further, assuming that the effective treatment is available, WHO criteria of 2 hour Postprandial Glucose ≥ 140mg/dl identifying a large number of case may have a greater potential for prevention which has been confirmed by Meltzer et al.<sup>25</sup>

Treatment of Gestational diabetes mellitus as defined by WHO criteria has reduced serious perinatal morbidity and improved the woman's health related quality of life.<sup>10, 11</sup>

The two step procedure of screening with 50 g GCT and then diagnosing GDM based on the cut off values with 100 g or 75 g OGTT is not practical as the pregnant women have to visit the antenatal clinic at least twice and the number of blood samples drawn varies from 3 to 5 which women resent.<sup>21</sup>

The recent IADPSG criteria, although adopted recently by a WHO expert group, may be difficult to adopt in developing countries due to shortage of trained phlebotomists, extra costs and the lack of laboratory.<sup>19</sup>

Studies from the Western countries state that the use of IADPSG criteria would lead to inflated rates of GDM.<sup>26-28</sup>

It is reasonable to assume that since the IADPSG has raised the 2-h value to 153 mg/dl, many cases of GDM could be missed.

WHO criteria of >140 mg/dl alone appears to be sufficient to diagnose GDM, as it picks up the majority of GDM cases diagnosed by both the whole WHO criteria as well as the same number of cases as the three sample IADPSG criteria.<sup>29</sup>

#### **Prevalence of GDM:**

Prevalence rates are found to be higher in black Hispanic, Latino, Native American and Asian women compared to



Caucasians. Yue et al, in an Australian study, reported a higher relative risk in Indian women (17%) as compared to 3%, 10% and 15% in Anglo-Celtic, Aboriginal and Chinese inhabitants respectively.<sup>30</sup>

Increasing trend in prevalence rates has been documented in different regions of the country. The prevalence of Gestational diabetes mellitus in our study was 6.3%. This is comparable to 6.0%, 6.6% and 6.7% prevalence rates of study of Nilofer AR et al<sup>31</sup>, Kalra P et al<sup>32</sup> and Verma et al<sup>33</sup> respectively.

## CONCLUSIONS

For universal screening, we suggest a single fasting OGTT with a 75 gram of oral glucose load and diagnosing women with 2 hour PPG  $\geq 140$  mg/dl as GDM. This method, recommended by WHO serves both as a one-step screening and diagnostic procedure and is easy to perform besides being economical.

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