Original Research Article

Early Screening for Gestational Diabetes Mellitus with Oral Glucose Challenge Test and the Comparative Study of the Pregnancy Outcome in Women with Normal and Abnormal OGCT Values

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Abstract: The objective of the study was to evaluate the applicability of 50gms. OGCT as a screening test for GDM and to compare the pregnancy outcome between GDM, false positive OGCT (following OGTT results) and women with normal screening test. It was a prospective study carried out on 200 pregnant women at 12- 20 weeks and at 24 -28 weeks of gestation and a comparative study was conducted on the pregnancy outcome in women with normal and abnormal screening results (OGCT values). Pregnant women were selected randomly considering the inclusion and exclusion criteria and the results were analysed. The results were divided into 4 groups and the pregnancy outcome were compared between those four groups. 7 cases of GDM were diagnosed in early screening and 28% of the study population falls under false positive OGCT cases with sensitivity of 100% and specificity of 62.50% with positive predictive value of 18.82%.
Keywords: GDM – gestational diabetes mellitus, OGCT – oral glucose challenge test, OGTT – oral glucose tolerance test.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as 'carbohydrate intolerance of variable severity with the onset and first recognition during the present pregnancy."The definition applies irrespective of whether or not insulin is used for the treatment or the condition persists after pregnancy [1].

Prevalence of NIDDM in adult population of India is high. India falls under moderately high-risk group .Virtually all new cases of diabetic pregnancies are a transient form of type 2 Diabetes. A small portion of cases of de novo diabetes are found to persist after pregnancy. As per the recent WHO reports 177 million people in the world are diabetic, 20% of them are hailing from India. The rising prevalence of diabetes mellitus—21 million people (7% of the population) have some form of diagnosed diabetes[2] ; another 6 million people may be undiagnosed[3] —particularly type 2 among women of childbearing age in the United States, has resulted in increasing numbers of pregnant women with pre existing diabetes.

Carbohydrate metabolism

The body's energy requirements depend on continuous supply of glucose from the circulation. Regulation of blood glucose is by insulin.

Post - absorptive phase

Several hours after meal, glucose concentration returns to normal and insulin production reduces. Insulin promotes glucogenesis and suppresses gluconeogenesis and lipolysis. In fed state, insulin serves as an anabolic and anti- catabolic factor.

Fasting state

- Two changes occur in maternal intermediary metabolism;
- Decrease in plasma glucose concentration
- Increase in fat metabolism
- Relative absence of insulin allows endogenous glucose production and muscle and fat catabolism.

Fuel metabolism in early pregnancy

Pregnancy is a diabetogenic state. Hormones like Human placental lactogen have strong anti-insulin

and lipolytic effects. The combination of increased mobilization of glucose and decreased insulin sensitivity places the women at risk of developing GDM. However not all women do. Estrogen and progesterone leads to Beta cell hyperplasia – hyperinsulinemia and lipogenesis.

Fuel metabolism in second half of pregnancy

Reduction of insulin sensitivity observed due to hormones of maternal and placental sources – HPL, Placental growth hormone variant, Cortisol, Estrogen, Progesterone, Prolactin. Increase body weight and caloric intake are other contributing factors. There is an accelerated switch from carbohydrate to fat metabolism and utilisation facilitated by peripheral insulin resistance and high blood levels of lipolytic hormones.

GDM occurs when the woman's beta cell function is not able to overcome the antagonism created by the anti-insulin hormones of pregnancy and the increased fuel consumption required to provide for the growing feto maternal unit. - Dr Alberto de Leiva [4].

Maternal-Fetal Metabolism in Diabetes
Inadequate maternal pancreatic insulin results in maternal and fetal hyperglycemia. This manifests as recurrent postprandial hyperglycemic episodes causing fetal hyperinsulinemia which results in macrosomia.

Conversion of excess glucose into fat results in foetal hypoxia which stimulates adrenal catecholamines resulting in hypertension, cardiac hypertrophy, stimulation of erythropoietin, red cell hyperplasia, and increased Haematocrit, poor circulation, and postnatal hyperbilirubinemia.

Women with a history of GDM are at increased risk of future diabetes, predominately type 2 diabetes, as are their children. GDM is associated with risks to the fetus and newborn, including shoulder dystocia, birth injuries, hyperbilirubinemia and it has also been shown to pose maternal risks, including preeclampsia, caesarean delivery and an increased risk of developing type 2 diabetes later in life.Beard and Hoet concluded that GDM is a clinical entity associated with increased fetal and maternal morbidity [5].

ACOG reports that GDM, which already complicates about 7% of all pregnancies in the United States, is on the rise, likely because of increasing rates of obesity and overweight.

Established risk factors were found more frequently in GDM group, but women without risk factors also developed GDM. Hence, there is a need for universal screening. It's been demonstrated that perinatal and maternal morbidity among GDM can be reduced with application of a systematic approach to the

identification and management of the disease. Early screening ensures identification of previously undiagnosed diabetic women and women with early onset diabetes. This would help in appropriate counseling, diagnostic procedures and treatment.

In 2001, ACOG recommends a "2-step" approach for screening and diagnosing for the disease. The recommendations are as follows: "All pregnant women should be screened for GDM by patient history, clinical risk factors, or a 50-g, 1-hour loading test to determine blood glucose levels."

"The diagnosis of GDM can be made based on the result of the 100-g, 3-hour oral glucose tolerance test. Either the plasma or serum glucose level using Carpenter and Coustan or the National Diabetes Data Group is appropriate to use. Replacing NDDG criteria with Carpenter and Costa's criteria would increase by 54% the diagnosis of GDM women who otherwise would be misdiagnosed.

OGCT is used as a screening test and those women with high OGCT values are subjected for 100gm OGTT as a diagnostic test. Women with high OGTT values are considered as GDM cases, while women with normal OGTT values are considered as false positive cases. Many studies have not been done regarding pregnancy outcome in false positive OGCT cases. Hence we have proposed a comparative study of pregnancy outcome in GDM, false positive OGCT (with OGTT as diagnostic test) and normal cases.

MATERIALS AND METHODS:
This is a prospective comparative study conducted in the Department of OBG (KIMS Bangalore) for 1 year. All pregnant women attending antenatal OPD, who subsequently delivered at KIMS Hospital, were included in the study.

Inclusion Criteria
- All pregnant women attending antenatal OPD on the first visit (12-20 weeks) who subsequently deliver in the same hospital.

Exclusion Criteria
- Women with overt diabetes
- Women with previous history of renal disease, hypertension, heart disease, Bleeding Disorders.
- Multiple gestations.

Data collected in a predesigned proforma which included detailed patient history and examination which was followed by a two-step biochemical approach,

STEP 1 - THE ORAL GLUCOSE CHALLENGE TEST (OGCT)

At the first antenatal visit (12-20 wks), the pregnant women were given 50 grams of glucose powder in 150 to 200 ml of water orally irrespective of the last meal and the time of day. A venous blood sample was drawn 1 hr after the ingestion of glucose and was sent to the laboratory for plasma glucose estimation by the glucose oxidase method.

STEP 2 - THE ORAL GLUCOSE TOLERANCE TEST with 100gms Glucose (OGTT) as per O' Sullivan – Mahan criteria as modified by carpenter and Coustan.

Table 1: Interpretation

Time	mg/dl	mmol/l
Fasting	95	5.3
1 hr	180	10.0
2 hr	155	8.6
3 hr	140	7.8

Interpretation (OGCT)
- **Normal**: Value <130 mg/dl
- **Abnormal**: Value > than 130mg/dl

Women with abnormal OGCT1 value underwent OGTT1. Those with 2or more abnormal values of GTT were considered as GDM. The test was repeated at 24 –28 wks in women with normal OGCT1. OGTT2 was done in women with abnormal OGCT2 (24 -28wks.).

Based on the GTT2, they were divided into following groups.
False positive OGCT: OGCT positive, GTT was normal
Impaired Glucose Tolerance (IGT) : If one value of GTT was abnormal.

Gestational Diabetes Mellitus (GDM): If 2 or more abnormal value of GTT

Routine investigations for pregnancy and investigations for monitoring maternal and fetal condition as required were done. The outcome of pregnancy (maternal, neonatal, and fetal) was recorded.

Statistical Methods:

Chi-square and Fisher exact test have been used to test the significant correlation of OGCT and GTT. The statistical software namely SPSS 11.0 and Syst at 8.0 were used for the analysis of the data.

RESULTS OF THE SCREENING TEST

Table-2 showing results of GCT 1(12-20wks)

GCT	Number of cases
≤ 130	193
131-140	0
>140	7
Total	200

Among 7 cases of the study population were GCT positive.

Table-3: showing the Correlation of OGCT 1 & GTT1

GCT	GTT Negative	Positive	
≤ 130	193	-	193 (96.5%)
>130	-	7	7 (3.5%)
Total	193	7	200
Inference – OGCT is significantly correlated with the outcome of GTT1			

Table-4: Showing the results of OGCT 2 (24 -28wks)

GCT	Number of cases
≤ 130	117
131-140	13
>140	63
Total	193

Table-5 Showing the Correlation of OGCT2 with GTT2

GCT2	GTT2		
	Negative	Positive	
≤ 130	117	-	117
>130	54	22	76
Total	171	22	193
Inference – OGCT2 is significantly correlated with the outcome of GTT2			

Diagnostic outcome - 200 cases were screened for diabetes and the results of the study are listed below.28% of the study population falls under false positive OGCT cases. Incidence of GDM in the study population is 8%.13 (6.7%) of the study population had OGCT values more than 130. If the OGCT cutoff values were taken as 140, then these cases would be undiagnosed. Out of the 13 cases with OGCT values between 131 –140. 12 cases were false positive OGCT cases and 1 belongs to IGT group.
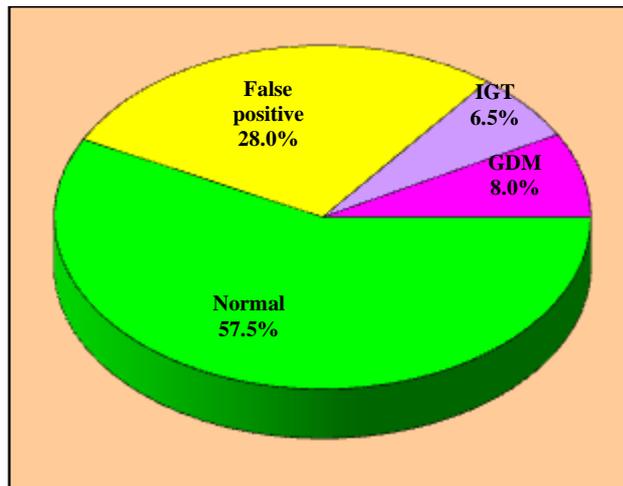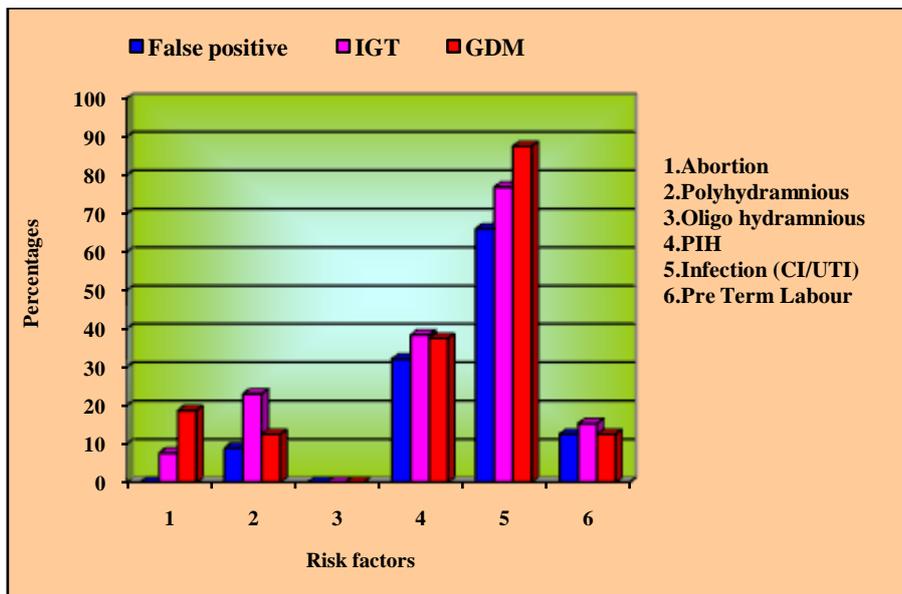

Fig-1: Diagnostic outcome of OGCT and GTT

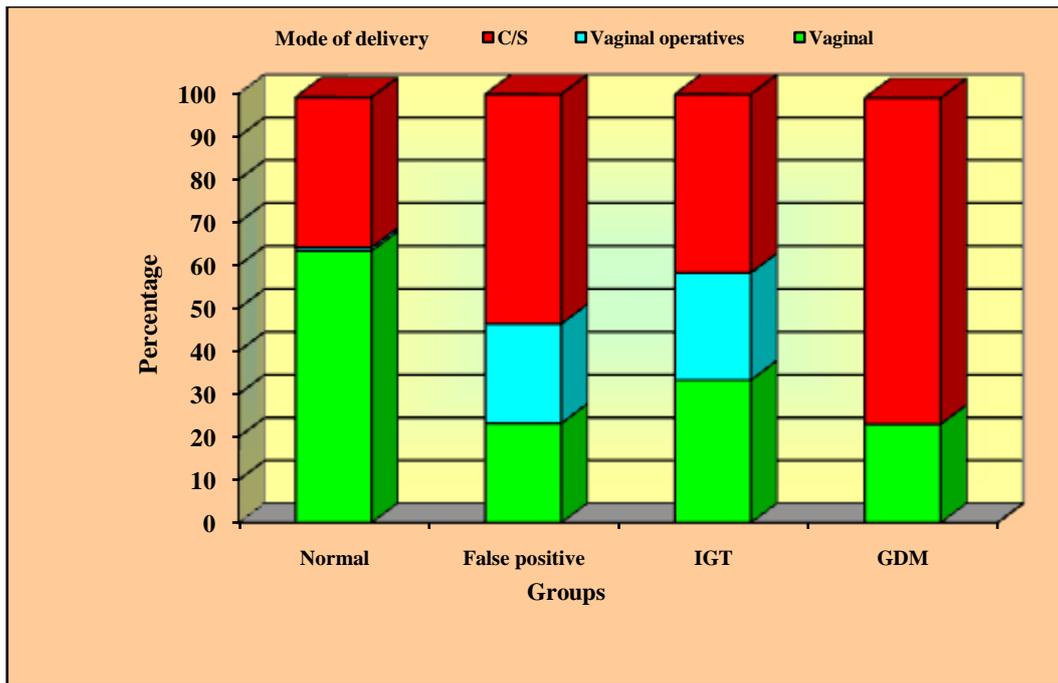**Fig-2: Pregnancy complications with outcome**

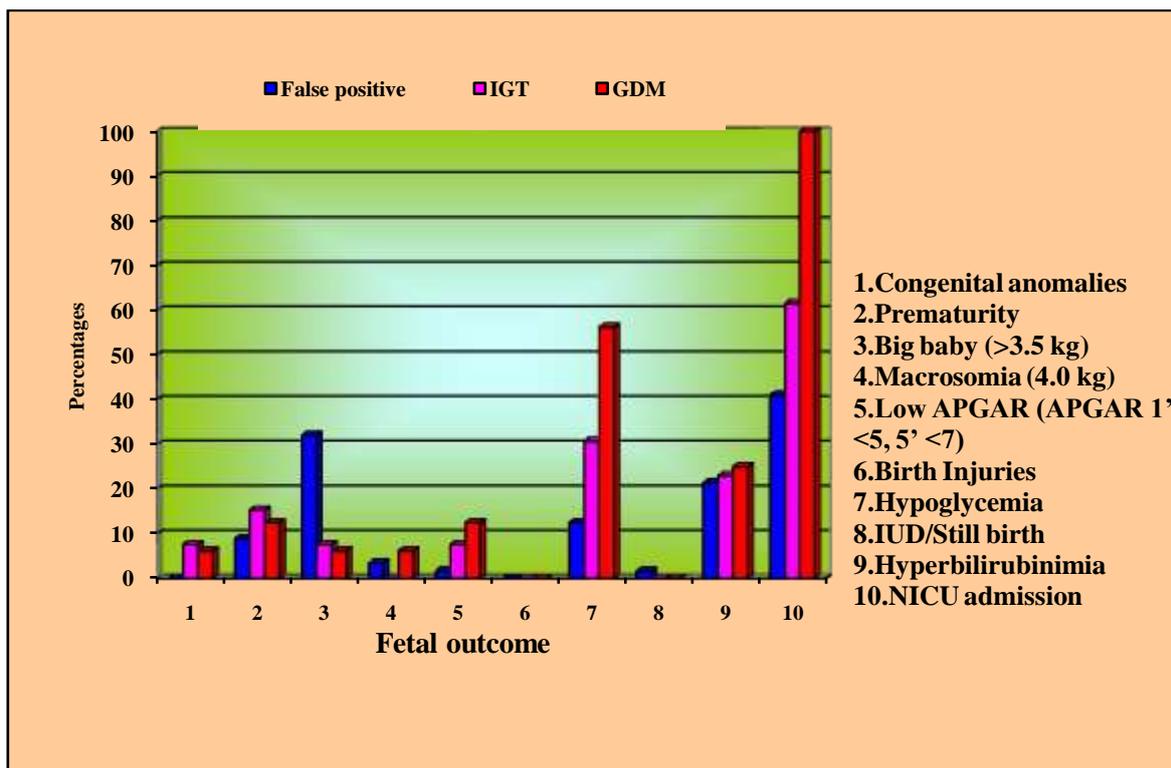**Fig-3: Showing the Mode of delivery compared in all the four groups**

Fig-4: Showing the Association of Foetal outcome in all three groups (abnormal OGCT and GTT values)

DISCUSSION

Prevalence of NIDDM in adult population of India is high. Adult females who are genetically predisposed would be at risk of developing GDM during pregnancy. 7% of all pregnancies are complicated by GDM with a greater frequency in high-risk racial population (Indians). In a random survey performed in various cities in India in 2002-2003, an overall GDM prevalence of 16.55 per cent was observed [6].

The diagnosis of GDM is made by the 75-g or 100-g oral glucose tolerance test (OGTT). A screen followed by the diagnostic OGTT (in screen positive

patients) is called the two-step approach, while OGTT directly without screen is called the one-step approach.

August 24, 2011 — The American College of Obstetricians (ACOG) is standing by its recommendation for a 2-step approach to screening and diagnosis for gestational diabetes mellitus (GDM) in the continued absence of an international consensus on whether the benefits of some screening approaches outweigh the costs, according to a published in the September issue of Obstetrics &Gynecology [7].

In 2010, IADPSG recommended universal screening of all pregnant women with the 75-g oral glucose tolerance test (OGTT) [8]. International Diabetes Federation guidelines currently have accepted the current WHO 2013/IADPSG criteria [9].

In India, A single step is recommended by measuring plasma glucose 2 h after ingestion of 75-g glucose irrespective of the last meal. This test is called the DIPSI Test. However, other countries like Thailand mostly use the two-step approach (the diagnostic criteria of the NDDG or C and C) or WHO 1999 criteria (75-g OGTT) [10]. Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, which found an increased risk for adverse pregnancy and neonatal outcomes even at mild levels of maternal hyperglycemia.

If having false positive GCT as an independent risk factor for adverse pregnancy outcome, then such women could be benefited by additional therapies such as intensive fetal monitoring, nutritional counselling. With this in mind, we conducted a study to determine whether patients with positive GCT and negative GTT viz. false positive OGCT, are at increased risk for adverse pregnancy outcome.

Among 200 cases studied, 115 (57%) were normal cases, 56 (28%) were false positive OGCT cases, 13 (6.5%) were impaired GTT and16 (8%) were GDM cases.

Results of screening test

Table-6: Prevalence of gestational diabetes mellitus in different studies

Study	Incidence
Rural Haryana 2014 [11]	9.7%
Gestational diabetes in rural women of Jammu [12]	6.7%.
Study by Seshiah et al.; [13]	13.8%
Present Study	8%

Comparison of Validity of the test: OGCT (cut off 130mg/dl)

NEW YORK (Reuters Health) Feb 03 - The 50-g glucose challenge test is an "acceptable" screening test for GDM, but it can't replace OGTT, clinicians from the Netherlands in a report online January 20 in the British Journal of Obstetrics and Gynecology (BJOG) [14].

Table 7: Comparison of Validity of the test: OGCT

	Navid Alam et al [14]	BJOG [15]	Present study
Specificity	89.6%	77%	62.50%
Sensitivity	76.92%	78%	100%
Positive predictive Value	52.6%	4%	18.82%

Table-8: Showing the results of maternal and foetal outcome in different studies In Abnormal glucose values

Pregnancy outcome	Priyanka Kalra, et al.; [16]	Pikee Saxena et al.; [17]	Present Study
Polyhydramnios	NE	20%	10%
Caesarean delivery	79%	42%	45%
PIH	27%	40%	38%
Vaginal candidiasis /UTI	24.2%	NE	31.5%
Prematurity	NE	12%	8.5%
Macrosomia	18%	28%	7.95%
Hypoglycemia	9.09%	14%	10 %
Hyperbilirubinemia	12.12%	34%	32%
NICU admission	27.2%	10%	25%
Congenital anomaly	NE	10%	1%

Pregnancy outcome was compared between four groups. In our study we had 2 babies with congenital anomalies. One baby was born to mother diagnosed to have impaired glucose tolerance. Anomalies detected were skeletal dysplasia with polydactyly in all four limbs. Deformed and narrow thorax with? Meningo myelocele over upper cervical region. Another baby born had microcephaly, depressed nasal bridge, low set ears, generalized anasarca, and imperforate anus. Both mothers had polyhydramnios.

Majority of the cases with abnormal glucose values were induced, and indications for induction were term GDM and impaired glucose tolerance. Out of the 47 induced group most of them had vaginal deliveries. Majority of the false positive women had vaginal operative deliveries. The section rate in the abnormal glucose group were high 28% of the total study population were diagnosed as false positive OGCT cases.

CONCLUSION
- Incidence of GDM in the study population was 8%
- 7 cases of GDM were diagnosed in early screening, which suggests that early screening is better than the routine screening 24-28 weeks.
- 28% of the study population falls under false positive OGCT cases with sensitivity of 100% and specificity of 62.50% with positive predictive value of 18.82%. Thus, taking OGCT value cut off as 130 mg/dl increases the sensitivity rate at the cost of specificity.
- On an average, the pregnant woman in the false positive groups was older, higher parity, high BMI and is associated with one or two risk factors. Pregnancy outcome suggests that they have higher prevalence infections, PIH, preterm labour, increased operative deliveries and fetal outcome like macrosomia; big babies (BW > 3.5 kg) hypoglycaemia, hyperbilirubinemia and most babies required intensive fetal monitoring.

Until the more reliable diagnostic test for GDM is developed, patients in this group might benefit from intensive prenatal care, such as nutritional counseling and antenatal fetal assessment and require more antenatal follow up than the normal group and they must be managed like GDM group.

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