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100-g Oral Glucose Tolerance Test as a Single Step Screening Test in First Trimester at High Risk Pregnancies: An Alternate Screening Modality

Fadiloglu E*, Ozten G, Unal C, Tanacan A and Beksac MS

Division of Perinatology, Department of Obstetrics and Gynecology, Hacettepe University, Ankara, Turkey

***Corresponding author:** Fadiloglu E, Division of Perinatology, Department of Obstetrics and Gynecology, Hacettepe University, Ankara, Turkey, Tel: +90 5464750175, E-mail: erdemfadiloglu@hacettepe.edu.tr

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Abstract

Aim: To show the utility of the 100-g Oral Glucose Tolerance Test (OGTT) in first trimester screening of high risk patients as an alternate screening modality.

Methods: This retrospective study consisted of 125 pregnancies screened with 100-g OGTT in the first trimester due to increased risk of impaired glucose metabolism. Screening criteria of the American Diabetes Association and American Congress of Obstetrics and Gynecology were used for determination of the high-risk group.

Results: Eleven patients (8.8%) were diagnosed with DM according to first trimester screening results. Five of 11 (45.4%) patients were followed-up with carbohydrate restricted diet, while six (54.6%) patients required insulin administration throughout the pregnancy. Only one newborn was macrosomic despite overt DM in mothers (9.1%). Eight patients (6.4%) were diagnosed as impaired glucose tolerance according to first trimester screening results. The second trimester screening test also defined two patients with impaired glucose tolerance and Gestational Diabetes Mellitus, which were followed-up with diet and insulin regimens, respectively. One hundred six patients (84.8%) were evaluated as glucose tolerant. Second trimester screening results detected impaired glucose tolerance and Gestational Diabetes Mellitus in 7 and 2 cases, respectively.

Conclusion: 100-g OGTT as a single step screening test may be an alternate approach for GDM and overt DM screening with favorable perinatal and maternal outcomes in high risk patients.

Keywords: Pregnancy; Diabetes Mellitus; 100 g Oral Glucose Tolerance Test

Introduction

Gestational Diabetes Mellitus (GDM) and Diabetes Mellitus (DM) are critical conditions requiring close follow-up during pregnancy to prevent neonatal and maternal morbidities such as increased rates of fetal macrosomia, respiratory distress syndrome, hypoglycemia, increased rates of cesarean section and operative delivery [1]. Screening of these impaired glucose metabolism disorders is a key point for preventing complications and has been shown to improve perinatal and maternal outcomes [2]. Prevalence of GDM and preexisting DM among live births is reported to be around 6.6% and 0.9% in the USA [3] while these rates are reported to be around 11.1% for GDM in Turkey [4,5]. Worldwide prevalance of hyperglycemia in pregnancy also ranges between regions from 11.8% to 23.1% in Western Pacific and Southeast Asia, respectively. National incidence of the hyperglycemia in pregnancy also ranges from 6.3% to 40.4% in countries such as Belgium and United Arab Emirates, respectively [6]. Increased rates of obesity in recent years and high prevalence of metabolic syndrome among Turkish people also make Turkish women at high risk for DM or GDM development throughout pregnancy [7]. Hence, screening of DM in the first trimester is crucial for earlier diagnosis and interventions to reduce neonatal and maternal morbidities. Undiagnosed overt DM is also strictly related to adverse perinatal outcomes including congenital malformations or early pregnancy losses, which may also be diagnosed initially at pregnancy [8,9]. Screening modalities for high risk patients have been defined previously in the literature [10,11]. One step (75-g Glucose Challenge Test) or two step (50-g and 100-g OGTT) approaches are available and widely used for detection of DM in the first trimester despite lack of consensus on an ideal screening regimen. One-step approach is found to be correlated with lower rates of fetal macrosomia, neonatal intensive care unit admission and lower mean birth weight compared to two-step approach. Despite these potential advantages, rate of patients diagnosed with GDM by one-step approach is much more higher than two-step approach [12].

In this study, we aim to show the utility of the 100-g OGTT in first trimester screening of high risk patients as an alternate screening modality and to demonstrate pregnancy outcomes of patients screened with this modality as a preliminary study.

Materials and Methods

This retrospective study consisted of pregnancies screened with 100-g OGTT in the first trimester due to increased risk of impaired glucose metabolism. This study was designed to demonstrate the obstetric outcomes of patients screened with 100-g OGTT in first trimester. Relevant data was acquired from electronic database of our institution and birth room registries. Patients delivered between 2014-2019 were included in data. Screening criteria of the American Diabetes Association and American Congress of Obstetrics and Gynecology were used for determination of the high-risk group including subsequent risk factors: a) GDM in previous pregnancy; b) Detected impaired glucose tolerance or fasting glucose levels; c) Family history of DM; d) History of cardiovascular disease or hypertension; e) Low levels of High-density lipoprotein or high levels of triglyceride; f) Polycystic ovary syndrome or any systemic disorder associated with insulin resistance; g) History of a macrosomic fetus weighing more than 4000 g in a previous pregnancy; h) Physical inactivity [10,11]. Patients fulfilling at least one criteria were screened with 100-g OGTT after detailed informed consent at the initial diagnosis of pregnancy. The 100-g OGTT was performed after a 3-day carbohydrate rich diet and overnight fasting. Results were evaluated according to Carpenter & Coustan criteria (95, 180, 155 and 140 mg/dL cutoffs for fasting, 1st, 2nd and 3rd hour postprandial) [13]. Lipid profiles or trigylceride levels of the patients were not evaluated in the routine screening as these parameters are not used for diagnosing patients with impaired glucose tolerance or GDM. Patients evaluated with DM or impaired glucose tolerance according to first trimester screening results were followed-up in the Division of Perinatology and Endocrinology and insulin treatment was administered in necessary cases. A second OGTT was offered to patients between the 24th and 28th gestational week according to national and international screening guidelines [11]. Carpenter & Coustan criteria were also used for defining patients with GDM, impaired glucose tolerance or normal glucose tolerance [13]. Patients with GDM and impaired glucose tolerance were also evaluated by the Division of Perinatology and Endocrinology. Patients with a maternal systemic disorder, fetal chromosomal abnormalities or major congenital anomalies were excluded from the study group.

Patients were classified into three groups as DM, impaired glucose tolerance and normal screening according to their first trimester screening results. Patients refusing the second OGTT between the 24th and 28th gestational weeks were also included in the final data. Further analysis included management of the patients, birthweek, route of delivery, rate of newborns with a birthweight greater than 90th percentile, APGAR score < 7 at the first ten minutes and NICU admissions.

The acquired data was evaluated via descriptive statistics. All statistical calculations were performed with the Statistical Package for Social Sciences (SPSS) for Windows (SPSS version 23; SPSS Inc., Chicago, IL) statistical software package. We have also performed one-sample Chi-square test to compare the results of first and second trimester screening test results.

This retrospective study was approved by the Hacettepe University Ethics Committee (GO 17-426).

Results

This study consisted of 125 patients fulfilling all the study criteria. First and second trimester OGTT results of the patients are summarized in Figure 1. Eleven out of 125 (8.8%) patients were diagnosed with DM according to first trimester screening results.

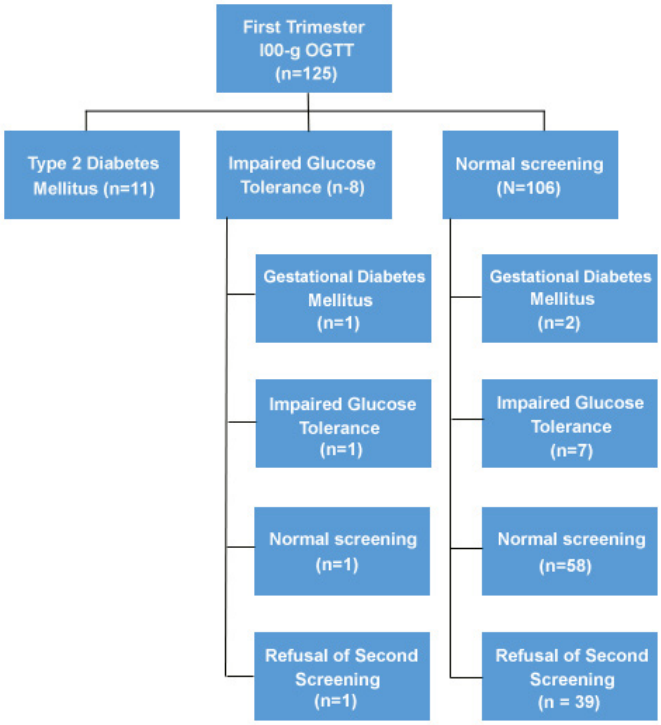

Figure 1: Summary of OGTT results at first and second trimeste

Five of 11 (45.4%) patients were followed-up with a carbohydrate restricted diet, while six (54.6%) patients required insulin administration throughout the pregnancy. Vaginal delivery rate of the patients with DM diagnosis was 45.5%. Only one newborn was macrosomic despite overt DM in mothers (9.1%). None of the newborns in this group necessitated NICU admission Table 1.

	Patients Diagnosed as Diabetes Mellitus at 1st trimester (n = 11)
Management‡	
Diet	6 (54.5 %)
Insulin Treatment	5 (45.5 %)
Birthweekγ	38 (36 – 40)
Route of Delivery‡	
Vaginal	5 (45.5 %)
Cesarean Section	6 (54.5 %)
Birthweightγ	3500 (2160 – 4190)
>90 percentile Newborns‡	1 (9.1 %)
APGAR score <7‡	1 (9.1 %)
NICU admission‡	0 (0 %)
Prematurity	0 (0 %)
Neonatal Jaundice	0 (0 %)
Hypoglycemia	0 (0 %)
Respiratory Problems	0 (0 %)

‡: Rate of event in whole group; γ: Median (Range) are given

Table 1: Obstetric outcomes of the patients diagnosed as Diabetes Mellitus in 1st trimester screening

Eight out of 125 patients (6.4%) were diagnosed with impaired glucose tolerance according to first trimester screening results. Only three of these patients were admitted for a second trimester glucose screening test and five refused to repeat the test. One patient with a normal second trimester screening had a 30 week preterm delivery with a birthweight of 1750 gr that necessitated NICU admission for prematurity. The second trimester screening test also defined two patients with impaired glucose tolerance and Gestational Diabetes Mellitus, which were followed-up with diet and insulin regimens, respectively. Five out of eight patients refused a second trimester OGTT, while two of them still necessitated diet for impaired glucose tolerance detected in the first trimester Table 2.

	Patients Diagnosed as Impaired Glucose Tolerance at 1st trimester (n = 8)			
2nd trimester Screening Results	**Normal screening (n = 1)**	**Impaired Glucose Tolerance (n = 1)**	**Gestational Diabetes Mellitus (n = 1)**	**Refusal of Second Screening (n = 5)**
Management‡				
Follow-up	1 (100 %)	0 (0 %)	0 (0 %)	3 (60 %)
Diet	0 (0 %)	1 (100 %)	0 (0 %)	2 (40 %)
Insulin Treatment	0 (0 %)	0 (0 %)	1 (100 %)	0 (0 %)
Birthweekγ	30	40	37	38 (36 – 40)
Route of Delivery‡				
Vaginal	1 (100 %)	0 (0 %)	0 (0 %)	3 (60 %)
Cesarean Section	0 (0 %)	1 (100 %)	1 (100 %)	2(40 %)
Birthweightγ	1750	4080	3190	3600 (2800 – 4170)
>90 percentile Newborns‡	0 (0 %)	0 (0 %)	0 (0 %)	1 (20 %)
APGAR score <7‡	1 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)
NICU admission‡	1 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)
Prematurity	1 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)
Neonatal Jaundice	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
Hypoglycemia	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
Respiratory Problems	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)

Table 2: Obstetric outcomes of the patients diagnosed as impaired glucose tolerance in 1st trimester screening

According to the first trimester screening results, 106 patients were evaluated as glucose tolerant. Second trimester screening results detected impaired glucose tolerance and Gestational Diabetes Mellitus in 7 and 2 cases, respectively. All of the patients diagnosed with impaired glucose tolerance were followed-up with a carbohydrate restricted diet, while one patient diagnosed with Gestational Diabetes Mellitus required insulin treatment. Thirty-nine out of 106 patients refused second trimester screening (36.7%). One patient in this group also necessitated a carbohydrate restricted diet due to detection of fetal macrosomia and polyhydramniosis at antenatal visits. None of the fetuses required NICU admission among mothers with impaired glucose tolerance and Gestational Diabetes Mellitus, while 12% and 12.8% of the cases required NICU admission in the normal glucose tolerance group and among patients refusing screening, respectively Table 3.

	Patients With a Normal Glucose Tolerance at 1st trimester (n = 106)			
2nd trimester Screening Results	**Normal screening (n = 58)**	**Impaired Glucose Tolerance (n = 7)**	**Gestational Diabetes Mellitus (n = 2)**	**Refusal of Second Screening (n = 39)**
Management‡				
Follow-up	58 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)
Diet	0 (0 %)	7 (100 %)	1 (50 %)	1 (2.5 %)
Insulin Treatment	0 (0 %)	0 (0 %)	1 (50 %)	0 (0 %)
Birthweekγ	38 (30 – 41)	39 (36 – 41)	37	38 (31 – 41)
Route of Delivery‡				
Vaginal	23 (39.7 %)	2 (28.6 %)	0 (0 %)	12 (30.8 %)
Cesarean Section	35 (60.3 %)	5 (71.4 %)	2 (100 %)	27 (69.2 %)
Birthweightγ	3300 (750 – 4100)	3040 (2170 – 3950)	3485 (3290 – 3780)	3220 (1930 – 4740)
>90 percentile Newborns‡	2 (3.4 %)	0 (0 %)	0 (0 %)	2 (5.1 %)
APGAR score <7‡	4 (6.8 %)	0 (0 %)	0 (0 %)	2 (5.1 %)
NICU admission‡	7 (12 %)	0 (0 %)	0 (0 %)	5 (12.8 %)
Prematurity	0 (0 %)	0 (0 %)	0 (0 %)	3 (7.6 %)
Neonatal Jaundice	5 (8.6 %)	0 (0 %)	0 (0 %)	1 (2.5 %)
Hypoglycemia	2 (3.4 %)	0 (0 %)	0 (0 %)	0 (0 %)
Respiratory Problems	1 (1.7 %)	0 (0 %)	0 (0 %)	1 (2.5 %)

Table 3: Obstetric outcomes of the patients diagnosed as normal glucose tolerance in 1st trimester screening

Additionally, in our series, 44 out of 114 patients refused second trimester OGTT screening (38.5%). Furhermore, comparison between the results of first trimester screening and second trimester screening showed statistically no significant difference between groups (p=0,110).

Discussion

The increasing prevalence of obesity and metabolic syndrome are resulting in increased risk of overt DM or GDM during pregnancy [14]. Therefore, early detection of these carbohydrate metabolism disorders is the objective of physicians for better obstetric outcomes. Screening modalities are shown to be a key point of management and for decreasing adverse outcomes including perinatal and maternal mortality [15]. Some certain pregestational risk factors such as maternal obesity or excess weight gain during pregnancy are strictly related to GDM or DM during pregnancy [16,17]. Thus, first trimester GTT is recommended for these patients worldwide despite lack of consensus on a definitive diagnostic screening test for this group of patients [18]. Alternate methods such as screening by HbA1c or fasting glucose levels have also been recommended in previous studies, despite recommendations focusing on lack of feasibility of a single laboratory test [19-21]. In our series, we have evaluated the obstetric outcomes of patients screened with a 100-g OGTT in the first trimester as an alternate approach.

Lower rates of false positivity indicate the superiority of the 100-g OGTT versus the 75-g Glucose Challenge Test despite the existence of conflicting gestational outcomes [22,23]. 75-g GTT was found to be diagnosing nearly two times more patients as impaired glucose metabolism or GDM compared to two-step approach which may create additional ecenomic burden or maternal anxiety fort he patients that would have been evaluated as normal by a two-step approach. In our cohort, none of the neonates had a major congenital anomaly that could be related to impaired carbohydrate metabolism. This is most likely due to early screening of patients and close follow-up of patients who had a diagnosis of impaired carbohydrate metabolism. Macrosomia and APGAR score less than 7 were observed in only one fetus for each complication in patients diagnosed with DM in the first trimester, which also shows the efficacy of early diagnosis.

The refusal rate of second trimester OGTT was unexpectedly high in our cohort (38.5%). This was most likely due to the effect of social media or the press recommending not to perform any OGTT during pregnancy especially in countries such as Turkey [24]. The most significant cause of this problem was reported as misinformation of the patients [25]. On the other hand, perinatal outcomes of patients who performed the OGTT in both first and second trimesters and refused second trimester OGTT were found to be similar in our cohort. This may also be explained by the existence of a first trimester screening that detects overt DM and impaired glucose tolerant patients in early pregnancy.

Single step 100-g OGTT in the first trimester must also be discussed in terms of financial burden. It is obvious that a false positive diagnosis may result in increased financial burden since a diagnosed case has a greater burden [26]. On the other hand, GDM prevention and early detection is the way to decrease economic burden, which is also acquired by early screening [27]. Thus, single step 100-g OGTT may be considered at further studies due to possible advantages over other screening modalities. Avoiding high false positivity of single step 75-g GCT may be superiority of this approach by decreasing rates of maternal anxiety and economic burden on health system. Performing this modality as a single step test may also be advantagous over 50-g GCT by avoiding a two step test which may increase the patient compatibility. One step test may be beneficial where patient's access to health services are limited or difficult due to various factors [28]. Nevertheless, all these possible advantages or disadvantages must be confirmed and discussed by further prospective studies.

The limitations of this study were the number of cases and the retrospective design of the study. This is a retrospective study with a limited number of cases as this is a specific screening modality and just applied to a certain number of patients for a certain period. On the other hand, this study focused on an alternate screening modality described for the first time in the literature, according to our search.

In conclusion, 100-g OGTT as a single step screening test may be an alternate approach for GDM and overt DM screening with favorable perinatal and maternal outcomes in high risk patients. Our findings must also be supported by prospective randomized studies focusing on comparison with other screening modalities.

Conflict of Interest

The authors have no conflict of interest to declare.

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