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Comparing Early and Late Postpartum Glucose Tolerance Test in Patients With Gestational Diabetes Mellitus

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Abstract

Objectives: The present study aimed to evaluate if postpartum diabetes mellitus screening can be performed during post-delivery hospitalization.

Materials and Methods: This case series study was conducted on 130 women with gestational diabetes mellitus (GDM) who had normal blood sugar after the delivery. They took 75 g oral glucose tolerance test (OGTT) before hospital discharge and repeated the test 6-12 weeks later.

Results: Totally, 107 (82.3%) patients out of the total participated women were analyzed. Early OGTT, prediabetes, and diabetes were abnormal in 46 (43.0%), 34 (31.8%), and 12 (11.2%) cases, respectively. In addition, they above-mentioned variables were found to be abnormal in 28 (25.2%) 22 (20.6%), and 6 (5.6%) cases 6-12 weeks later. Further, 6-12 weeks later, the OGTT was abnormal (prediabetes and diabetes) in 5 patients (4.7%) with normal early OGTT. Therefore, there was a significant association between the results of early OGTT and those of 6-12 weeks later (P = 0.00). It implies that early OGTT could detect prediabetes and diabetes (abnormal results) with a sensitivity of 82.14% (95% CI, 63.11-93.94) and specificity of 70.89% (95% CI, 59.58-80.57).

Conclusions: In general, early postpartum screening effectively diagnosed women who were at high risk of diabetes mellitus and needed undergoing OGTT 6 weeks later. Identifying high-risk patients who need to return later facilitates the management of patients and sensitizes patients to refer for further examination.

Keywords: Gestational diabetes, Postpartum screening, Glucose tolerance test

Introduction

Insulin resistance during pregnancy is due to diabetogenic hormones which have a major role in gestational diabetes mellitus (GDM) including placental lactogen, corticotropin-releasing hormone, growth hormone, and progesterone (1).

As traditionally defined, the prevalence of gestational diabetes is about 6%-7% (2-4). In addition, its global incidence differs based on race, age, and body composition along with the screening and diagnostic criteria (2). According to a study implemented in Iran, the incidence of GDM is 4.8% (2). There are several risk factors for GDM such as maternal age, body mass index (BMI), past history of gestational diabetes, previous unexplained stillbirth, specified ethnic groups, macrosomia in a previous pregnancy, polyhydramnios, previous unexplained stillbirth, polycystic ovary syndrome, type 2 diabetes mellitus in a first degree relative, and metabolic syndrome (2, 4).

The effects of gestational diabetes on the outcomes of mothers and offspring increase the risk of preeclampsia, shoulder dystocia, macrosomia (>4000 g), stillbirth (if elevating fasting glucose level), and cesarean delivery (2,4).

The majority of women nearly immediately revert back to their prepregnancy glycemic status almost after the delivery. Several women with GDM may have previously unrecognized type 2 diabetes mellitus. Recommendations for postpartum evaluation are based on up to 30% of women developing persistent postpartum dysglycemia after the pregnancy (5-7). The endocrine society recommendation is to check glucose concentration for 24-72 hours after the delivery in order to exclude the hyperglycemia (8).

If fasting plasma glucose (FPG) concentrations suggest overt diabetes (FPG ≥126 mg/dL or random glucose ≥200 mg/dL), then treatment is warranted. To diagnose diabetes or prediabetes in women who have FPG levels below 126 mg/dL after delivery, they should have a 2-hour 75-gram oral glucose tolerance test (OGTT) 6-12 weeks postpartum(9).

A large number of women are not screened for persistent GDM during postpartum despite the recommendations

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for postpartum screening in women with a history of GDM (4,10). The rate of postpartum screening in GDM patients is about 9%-95% (5,10). Further, there is no agreement on employing appropriate methods to increase the rate of women who attend the postpartum screening test. Several ways and reminder systems are suggested for women with gestational diabetes during their pregnancy in order to improve their attendance rate for OGTT 6 weeks after giving birth.

Detecting GDM and abnormal glucose tolerance during the pregnancy is important to identify patients with a high probability of type 2 diabetes and cardiovascular complications associated with dyslipidemia, hypertension, and abdominal obesity. After diagnosis, physicians could help patients change their lifestyle, lose weight, or get antiglycemic drugs. Early postpartum OGTT improves the rate of the postpartum screen when the patients are in the hospital. Therefore, the early postpartum screen of diabetes and its consistency with the standard test of 6-12 weeks later the OGTT were evaluated in the present study.

Materials and Methods

A total of 130 postpartum women with known GDM who delivered in Taleghani and Alzahra hospitals during February 2017-2018 participated in this study. All pregnant women underwent FPG test as the prenatal routine test (FPG ≥ 92 was abnormal) in a prenatal clinic. The pregnant women were then screened with 75 g OGTT at 24-28 weeks (11). If 1 or more than 3 glucose measurements were found abnormal (FPG ≥ 92, 1 hour ≥ 180, 2 hours ≥ 153 mg/dL), then GDM was diagnosed. Moreover, women with GDM underwent dietary management and blood glucose measurements. If the glycemic goal (FPG <92, 1-hour postprandial <140) was not achieved, they were referred to endocrinology clinic, to receive metformin or insulin. The blood glucose level was estimated by the glucose oxidase method with BT1500 machine.

After delivery, intermittent glucose was evaluated every 6 hours during the fasting period and 1-hour postprandial after oral intake for 24-48 hours (5,8,10). All patients were breastfeeding during the hospital stay. After 24-48 hours if FG < 100 and 2-hour <140 (8,12,11), then they underwent a 75 OGTT (OGTT1) 24-48 hours after delivery in the immediate postpartum hospitalization period (the day after vaginal delivery and 2 days after cesarean section), FPG and blood glucose were checked 2 hours after receiving 75-g glucose. Patients were instructed to eat or drink nothing except for water after 11:00 PM before the OGTT. The first blood sample was taken at 7:00 AM and then 75-g anhydrous glucose was given to the patient with a glass of water to rinse and drink, and then the second blood sample was taken at 9:00 AM. An abnormal FPG level was considered diabetes if it was more than 126 mg/dL or impaired FPG if it was more than 100-125 mg/dL. Additionally, an abnormal 2-hour value was considered diabetes if it was more than 200 mg/dL and the value of 140-199 mg/dL was regarded as impaired glucose tolerance (12).

The exclusion criteria were overt diabetes before pregnancy, FPG ≥100 and blood glucose ≥200 in regular postpartum control, and using corticosteroids in the past 5 days. In patients with postpartum hemorrhage and other obstetrical complications such as fever and preeclampsia the test was performed after the condition subsides and before hospital discharge.

If the first OGTT was normal, the patients were advised to undergo 75 g OGTT 6-12 weeks after the delivery. However, if the first OGTT was abnormal then the patients were referred to endocrinology outpatient clinic and followed by phone 4-6 weeks later by an educated midwife. In addition, if the patients took no medication for diabetes and had normal glucose tests, they were advised to conduct the OGTT (OGTT2) test, 6-12 weeks after the delivery and share the result with the postpartum clinic. Further, after 6 weeks postpartum, a midwife contacted the patients by phone calls, several times during 12 weeks in order to ask them to refer to the clinic and perform the test. Several patients who were unable to return for the routine test at 6-12 weeks later, performed the test at other standard laboratories which were convenient for them and sent the results by Telegram software. In the case the patients had problems to refer, the researchers called a taxi.

Statistical Analysis

The obtained data were analyzed using the SPSS software, version 16. Furthermore, the Pearson correlation coefficient chi-square was applied to analyze the correlations and relationships between the qualitative variables. Moreover, *t* test and ANOVA were employed to evaluate the quantitative variables. OGTT results were compared using the chi-square test for diagnosing normal, prediabetes, and diabetes conditions. Receiver operating characteristic (ROC) curves were illustrated accordingly. The area under the curve (AUC) with 95% confidence intervals (CI) was reported to determine the sensitivity, specificity, and positive and negative predictive values at different cut-off values. The sample size was computed for a power of 80% and an α error of 0.05. The 95% CI and $P < 0.05$ were considered statistically significant in all analyses.

Results

A total of 130 postpartum women participated in the study while 23 (17.6%) of them were excluded due to the lack of follow up. All the excluded patients had a normal OGTT1 results ($P = 0.00$) and did not refer for the second test in spite of telephone call or their phone numbers were wrong. Finally, 107 patients were analyzed. The mean ± standard deviations for the patients' characteristics are provided in Table 1. As shown in Table 1, there is no statistically significant difference between the patients'

Table 1. Baseline Characteristics

Variable (Mean ± SD)	GTT2: nl[a]	GTT2: anl[b]	*P* Value	GTT1: nl	GTT1: anl	*P* Value
Maternal age (y)	32.4 ± 5.4	34.5 ± 4.9	0.06	32.2 ± 5.3	33.9 ± 4.7	0.10
Parity	1.2 ± 1.0	1.3 ±1.1	0.54	1.1 ± 1.3	1.1 ± 0.9	0.50
Abortion	0.2 ± 0.6	0.4 ± 0.9	0.28	0.3 ± 0.7	0.3 ± 0.8	0.80
Pre-pregnancy BMI (kg/m^2)	29.1 ± 5.0	30.5 ± 4.0	0.19	29.4 ± 4.8	29.5 ± 4.9	0.86
Weight gain (kg) in pregnancy	10.0 ± 4.5	10.6 ± 5.1	0.59	9.9 ± 5.0	11.1 ± 4.9	0.22

[a]Normal; [b]Abnormal.

characteristics in groups with positive and negative results of OGTT1 and 2. Additionally, based on the variables listed in Table 2, complications of pregnancy are preeclampsia (3 mild cases vs. 1 severe case), pregnancy-induced hypertension (6 cases), abruption (2 cases), intrauterine growth restriction (2 cases), preterm labor (2 cases of 34 and 36 weeks of gestation), and thrombocytopenia (2 cases). In addition, past medical history includes epilepsy (1 case), hypertension (3 cases), hypothyroidism (2 cases), depression (2 cases), and asthma (1 case).

The mean of FPG level in OGTT1 was 99.2 mg/dL, (89.0, 107.9, and 128.1 for normal, prediabetic, and diabetic results, respectively) while the mean 2-hour glucose level was 127.7 mg/dL (106.8, 147.6, and 179.0 for normal, prediabetic, and diabetic results). Further, as regards OGTT2, the mean FPG level was 103.7 mg/dL (95.5, 118.4, and 127.8 for normal, prediabetic, and diabetic results) whereas the mean 2-hour glucose level was 136.1 mg/dL (128.5, 147.5, and 163.1 for normal, prediabetic, and diabetic results).

Based on the findings, the OGTT1 results were abnormal in 46 (43.0%), prediabetes in 34 (31.8%), diabetes in 12 (11.2%) cases. Furthermore, the OGTT2 results were found abnormal, prediabetes, and diabetes in 28 (25.2%), 22 (20.6%), and 6 (5.6%) cases, respectively. Moreover, the OGTT2 was abnormal (i.e., either prediabetes or diabetes) in 5 patients (4.7%) with normal OGTT1. Additionally, the OGTT2 was considered normal in 23 patients (21.5%) with abnormal OGTT1. Finally, the OGTT2 was either abnormal in 23 patients (21.5%) with abnormal OGTT1.

Using Pearson chi-square, a significant association was observed between the results of OGTT1 and OGTT2 (P = 0.00). OGTT1 could predict prediabetes and diabetes (the abnormal results) with a sensitivity of 82.14% (95% CI, 63.11-93.94), specificity of 70.89% (95% CI, 59.58-80.57), positive predictive value of 50.00% (95% CI, 40.49-59.51), and negative predictive value of 91.80% (95% CI, 83.33-96.17).

In addition, antihyperglycemic drugs were used to control the diabetes in 26 cases (42.6%) in normal OGTT1 group and 29 cases (63.0%) in abnormal OGTT1 group (P = 0.03). Further, in OGTT2, 37 patients (34.6%) with a normal result and 17 (15.9%) other patients with an abnormal result employed antihyperglycemic drugs during pregnancy (P = 0.25).

The ROC curve was constructed for FPG, 2-hour glucose level of OGTT1, and the results of OGTT2 (Figure 1). ROC analysis of first FPG indicated an AUC of 0.80, (95% CI, 0.70-0.90) and P = 0.00 for a prediabetes condition, as well as an AUC of 0.84, (95% CI, 0.66-1.01) and P = 0.00 for diabetes condition. Both conditions were considered optimal for separating the patients. As regards the first 2-hour glucose level, AUC was diagnosed 0.63 (95% CI, 0.48-0.78), P = 0.06 for prediabetes while it was diagnosed 0.77 (95% CI, 0.63-0.91) and P = 0.02 for the diabetes due to OGTT2. The first 2-hour glucose level was considered fair at separating the diabetic patients while it failed to diagnose the prediabetes.

The cut-off value determined by the ROC for diagnosing the prediabetes by the first FPG was more than 96 mg/dL with a sensitivity of 90.0% and a specificity of 65.9%. Furthermore, the cut-off value for diagnosing the diabetes was more than 96.5 mg/dL for the first FPG with a sensitivity of 83.3% and a specificity of 56.4% and 127 mg/dL for 2-hour glucose level with a sensitivity equal to 83.0% and a specificity of 60.6%.

Table 2. Comparison of Variables Between the Groups

Variable	GTT1: anl[a] No. (%)	GTT1: nl[b] No. (%)	*P* Value	GTT2: anl No. (%)	GTT2: nl No. (%)	*P* Value
Cesarean	36 (33.6)	52 (48.6)	0.34	22 (20.6)	66 (61.7)	0.90
FH	24 (22.4)	37 (34.6)	0.67	14 (13.1)	47 (43.9)	0.52
Complication	8 (7.5)	10 (9.3)	0.89	7 (6.5)	11 (10.3)	0.17
PMH	6 (5.7)	3 (2.9)	0.14	4 (3.8)	5 (4.8)	0.20
Antiglycemic drugs	29 (27.1)	25 (23.4)	0.02	17 (15.9)	37 (34.6)	0.13

[a]Abnormal; [b]Normal.
FH: Family history of DM; PMH: past medical history.

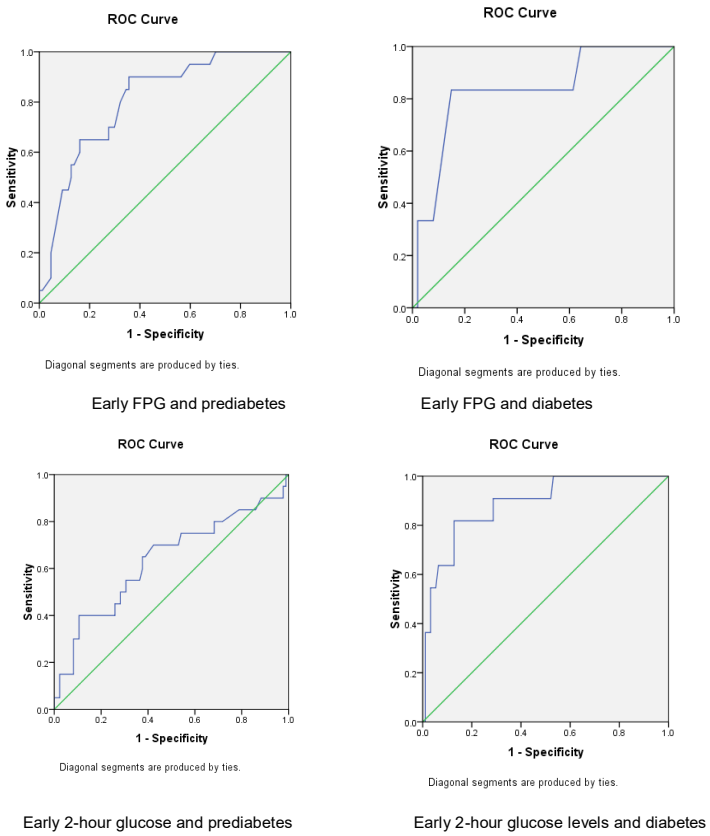

Figure 1. Receiver Operating Characteristic Curve for Early FPG and 2-Hour Glucose Levels and the Results of OGTT2. FPG: fasting plasma glucose; OGTT2: Oral glucose tolerance test 2.

Discussion

The prenatal care of women with GDM includes routine pregnancy care, as well as diagnosis and management of conditions which are common in these patients. Moreover, other common complications include macrosomia, preeclampsia, polyhydramnios, stillbirth, and neonatal morbidity. The risks related to GDM increase after the pregnancy and this is a marker for maternal development of type 2 diabetes. Therefore, glycemic control is the key intervention to control diabetic pregnancy. Glucose monitoring, nutritional therapy, and the use of insulin or other antiglycemic agents are the main methods for managing these patients. The early postpartum period is an important time to identify the risk of diabetes mellitus in women with GDM. The OGTT can help guide the lifestyle management and reduce the future risk of type 2 diabetes mellitus.

In two previous studies, Nabuco et al and Werner et al evaluated postpartum women with second-day OGTT (13,14). The number of patients who presented for OGTT2 in these studies was fewer than the patients of the current study.

The performance of OGTT1 increased the attendance rate for OGTT2 in the present study. Identifying high-risk patients who need to refer after 6 weeks facilitates the process of patient management and raises the patients' awareness to return for a further check-up. Werner et al reported that only less than half of the patients completed a GTT during 6-12 weeks postpartum. The frequency of postpartum follow-up of diabetes for women with gestational diabetes was low (5,20,21). However, the rate of postpartum follow-up was higher in the current study. Additionally, none of the patients with positive OGTT1 result refused the follow-up. Conversely, a low proportion of patients with normal OGTT1 were reluctant to be followed up in spite of phone call contact and training programs (P = 0.02). Considering the importance of the disease with early OGTT, education on taking the next OGTT, the following phone calls by the same midwife, and free transport facilities is considered the reason for the high rate of performing the second test by the patients.

The possibility of screening before discharging the women increases the chances for detecting women at higher risk of diabetes mellitus and persuading the patients to return for postpartum follow-up.

The result of the present study revealed that early OGTT is a useful screen test and its negative results are consistent with those of the routine test after 6 weeks. The prevalence of abnormal results in OGTT1 and 2 was prediabetes in 31.8% and 20.6%, diabetes in 11.2% and 5.6% respectively. In the study of Nabuco et al results of OGTT1 and 2 were 32.9% and 20.7% for prediabetes, which were consistent

with the present study (13).

However, the rate of diabetes in OGTT2 in the present study is inconsistent with that of the other studies (10, 15).

Risk factors of postpartum diabetes (type 2) or prediabetes were a family history of diabetes, advanced maternal age, high-risk ethnic group (e.g., South Asian), higher prepregnancy or postpartum BMI (>25 kg/m^2), or patients who require insulin during the pregnancy. (5, 10) These risk factors could be the reason for the different frequency of diabetes and prediabetes. Based on the findings, the only risk factor for postpartum diabetes was the use of antiglycemic drugs during pregnancy which was significantly related to a higher rate of abnormal OGTT1 results (P = 0.02). Werner et al found that previous GDM was a risk factor for the positive first OGTT.

The OGTT2 was abnormal (i.e., prediabetes and diabetes) in 5 patients (4.7%) with normal OGTT 1, which was considered a false negative result. This is possibly due to the fasting during the labor or postcesarean and poor nutrition during hospitalization.

In addition, there was a significant relationship between the results of the first FPG and prediabetes and diabetes in OGTT2. If the OGTT1 result was normal, then with a high probability the OGTT2 was either normal, with a good negative predictive value (91.8%). Further, if the result of OGTT1 was abnormal, then the OGTT2 was significantly abnormal with a positive predictive value of 50.0%. The OGTT1 could detect prediabetes and diabetes (abnormal results) with a sensitivity of 82.14% (95% CI: 63.11-93.94) and a specificity of 70.89% (95% CI: 59.58-80.57). Werner et al reported that the 2-day postpartum OGTT was 100% sensitive (95% CI: 2.5-100) and 94% specific (95% CI: 83-99) for diabetes. Both specificity and sensitivity were higher compared to those of the current study.

With an abnormal early test, the patient should be encouraged to modify their lifestyle patterns and attend the second test at 6 weeks postpartum. As regards early 2-hour glucose levels, an AUC was 0.63 (P = 0.06) and 0.77% (P = 0.02) for prediabetes and diabetes, which was diagnosed due to OGTT2. Furthermore, early 2-hour glucose level was considered fair at separating the diabetic patients due to the AUC of ROC analysis while it failed to diagnose the prediabetes. ROC analysis of the early FPG was considered optimal at separating prediabetes and diabetes from the normal people.

Based on the findings, less than half of the patients had positive OGTT1 who were advised to perform OGTT 6-12 weeks later. OGTT1 results have more false positive for diabetes than for the prediabetes. This result regarding the positive rate was in conformity with the results of Nabuco et al regarding the positive OGTT1.

Moreover, the normal results of OGTT1 obtained by Nabuco et al are in line with normal results of standard 75 OGTT after 6 weeks postpartum. They concluded that early OGTT during hospitalization is feasible and useful in identifying the high-risk patients (13).

The false positive results of OGTT1 corroborate with the results of placental hormones in maternal circulation after the delivery. During pregnancy, placental diabetogenic hormones such as placental lactogen hormone, growth hormone, corticotropin-releasing hormone, and progesterone led to insulin resistance (16-18). These hormones caused increased resistance in the early postpartum period. After the delivery, placental hormones decreased abruptly and reached prepregnancy levels within a few days to weeks. (16, 19) The majority of women returned to their prepregnancy glycemic status almost immediately. However, the endocrine society recommendation is to check glucose concentration 24-72 hours after the delivery in order to exclude the permanent hyperglycemia since several women with GDM may suffer from previously unrecognized type 2 diabetes mellitus.

In this study, nearly half of the patients used antiglycemic drugs and thus OGTT1 rather than OGTT2 was significantly positive in these patients. This is probably due to the severity of diabetes in these patients and therefore they are prone to diabetes mellitus after delivery.

This study has several limitations which need to be acknowledged. Several patients with mild gestational diabetes were probably ignored and did not report their diabetes and thus only those with severe diabetes were included in the study. Additionally, a number of patients who were unable to refer for the routine test 6 weeks later, performed the test at other standard laboratories and delivered the results via Telegram software.

Conclusions

In general, early postpartum screening can effectively diagnose the women who are high-risk candidates for diabetes and need to undergo OGTT 6 weeks later. Finally, early OGTT can be an effective tool in order to persuade pregnant patients to perform OGTT at 6 weeks postpartum

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

The present case series study was approved by the Ethics Committee of Tabriz University of Medical Sciences. All the women provided written informed consent.

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