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Early versus 6–12 week Postpartum Glucose Tolerance Testing for Women with Gestational Diabetes

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Abstract

Objective—To estimate the accuracy of early oral glucose tolerance testing (GTT) to predict impaired glucose tolerance.

Study Design—This was a prospective cohort study. Women received an early 75-gram 2-hour GTT between postpartum days 2–4 and again 6–12 weeks postpartum. The ability of the early GTT to accurately detect impaired glucose tolerance and diabetes was assessed by calculating sensitivity, specificity, positive predictive value and negative predictive values. The routine 6–12 week postpartum GTT was considered the gold standard.

Results—The early GTT was completed by 100% of subjects while only 31 of 58 (53%) women returned to complete the 6–12-week postpartum GTT. The early GTT had modest sensitivity for impaired glucose tolerance (62.5%) and overt diabetes (50%). However, it had excellent specificity (100%), PPV (100%) and NPV (96.7%) for diabetes. The NPV for impaired glucose tolerance with the early GTT was 80%.

Conclusion—Rates of 6–12 week postpartum GTT completion among patients with gestational diabetes is poor. Appropriate postpartum management may improve by using the early GTT as a screening test.

INTRODUCTION

Gestational diabetes (GDM) complicates 3 – 5% of pregnancies in the United States and rates continue to increase. (1) Women with GDM are at significant risk for developing type 2 diabetes, hypertension and cardiovascular disease.(2, 3) While carbohydrate intolerance associated with pregnancy improves in most women with GDM following delivery, up to 30% will have impaired glucose tolerance at the time of postpartum screening.(4) The American Congress of Obstetricians and Gynecologists, American Diabetes Association,

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CONFLICT OF INTEREST:

The authors report no conflicts of interest.

and several professional organizations recommend screening women with GDM 6–12 weeks after delivery, to roughly coincide with the timing of the first postpartum visit.(5–11) Unfortunately, less than 50% of women with GDM receive glucose screening postpartum.(12) Even among women who present to the routine postpartum visit, health care providers do not always offer postpartum glucose testing to their patients with GDM.(13) Strategies to reverse this trend have included reminder systems, which have shown limited effectiveness and improved postpartum screening rates from approximately 14% to 28%.(14) Women who complete postpartum glucose screening are more likely to be older, nulliparous, have higher income or education, receive prenatal care, be treated with insulin during pregnancy or complete a 6 week postpartum visit.(15) Yet, none of these are easily modifiable factors to improve screening rates.

The choice of 6 – 12 weeks for postpartum screening is a somewhat arbitrary endpoint and insulin resistance may normalize much earlier following delivery. This is because levels of the placental factors (*human placental lactogen, progesterone, prolactin, cortisol, tumor necrosis factor*) responsible for the insulin resistance in pregnancy quickly decline after delivery.(16) Therefore, one strategy to improve postpartum screening rates after GDM would be to test women following delivery and prior to hospital discharge. The purpose of this study was to investigate whether an early glucose tolerance test (GTT), following delivery and prior to hospital discharge, accurately diagnoses impaired glucose tolerance and diabetes using the routine, 6–12 week postpartum GTT as the gold standard.

MATERIALS AND METHODS

This was a prospective cohort study including women with gestational diabetes at our institution from May, 2014–June, 2016. Institutional review board approval was obtained from Washington University School of Medicine. Patients were eligible if they were diagnosed with GDM by early or routine two-step screening and were less than 72 hours postpartum. Women with pre-gestational diabetes or a history of gastric bypass surgery were excluded.

Trained obstetrics research assistants approached women with GDM on the postpartum service and consented patients who were willing to participate. Consenting subjects underwent a 2-hour 75 g oral GTT during their hospitalization for delivery and repeated this test at 6–12 week postpartum as part of their routine medical care with their obstetric provider. Women were reminded to return for further testing at 6–12 weeks postpartum, prior to leaving the hospital, and received up to 3 reminder phone calls between 4–8 weeks postpartum at 2-week intervals. Postpartum reminders to obtain a GTT after hospital discharge are not part of the standard of care at our institution. Medical records were requested from the primary obstetrician or laboratory following completion of the 6–12-week postpartum GTT. Information on maternal demographics, medical history, antepartum course, and labor and delivery records were extracted from the medical record. The primary outcome was the ability of the early GTT to diagnose diabetes mellitus using the 6–12 week routine postpartum GTT as the gold standard.

GDM was defined by laboratory criteria with ≥2 abnormal values on 100g antenatal GTT using National Diabetes Data Group criteria(5) after exceeding a screening threshold of 140 mg/dL on screening glucose challenge test with a 50 g glucose load. Women with a value ≥ 200 mg/dL on glucose challenge test were also considered GDM, even without an antepartum glucose challenge test. On postpartum GTT, impaired glucose tolerance was defined as having a fasting blood glucose of 110–125 mg/dL or 2 hour value of 140–199 mg/dL on 75-g postpartum GTT or diabetes mellitus.(5) Diabetes mellitus was defined on postpartum GTT as a fasting value > 125 mg/dL or 2 hour value ≥ 200 mg/dL.(5)

The *a priori* sample size calculation was based on a 15% prevalence of a positive test for diabetes, based on unpublished institutional data, with sensitivity and specificity of 90% and 10% precision. This estimate required 50 patients and the goal for recruitment was 58 patients due to an estimated 18% loss-to-follow-up. A lower loss-to-follow-up than seen in other studies was chosen because prior studies in the same setting showed high postpartum follow-up rates.(17) Data analysis was performed with descriptive and bivariate statistics with the unpaired Student t- test or Mann-Whitney U test for continuous variables and Chi-square or Fisher exact test for categorical variables. Normality of distribution was tested with the Kolmogorov-Smirnov test. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for impaired glucose tolerance and diabetes mellitus. Sensitivity represents the percentage of women who are correctly diagnosed with pre-diabetes or diabetes on the early GTT, among those with the condition, while specificity is the percentage of women who are not diagnosed as having either condition, among those who did not have the condition. The PPV is the proportion of women with pre-diabetes or diabetes accurately diagnosed, according to the routine GTT, while NPV is the proportion of negative early GTTs, according to the routine GTT. Analysis was performed with STATA software (version 11, College Station, TX).

RESULTS

The early GTT was completed by 100% of subjects while 31 of 58 (53%) women returned to complete the routine GTT at 6–12 week postpartum. Subjects completing both tests were more likely to undergo cesarean delivery (80% vs. 56%; p=0.047), attend their postpartum visit (100% vs. 44%; p<0.001) and breastfeed at 6–12 weeks (53% vs 8%; p=0.001) (Table 1). Women with impaired glucose tolerance on the early GTT were less likely to have public insurance with Medicare or Medicaid (48% vs. 84%; p=0.004) and more likely to have a cesarean delivery (85% vs. 53%; p=0.010) (Table 2), but these differences were no longer present on the routine GTT. The only risk factor for a positive test result on routine GTT was tobacco use. Both smokers who returned for the test 6–12 weeks postpartum had impaired glucose tolerance. All women with a vaginal delivery had the early GTT on postpartum days one or two while the majority of women with cesarean deliveries had the early GTT on post-operative days two or three (Table 3).

The early GTT had modest test characteristics for impaired glucose tolerance (Table 4) with a sensitivity of 63%, PPV of 31% and area under the curve of 0.57. The routine 6–12 week GTT had modest sensitivity for diabetes (50%). However, early GTT had excellent

specificity (100%), PPV (100%) and NPV (96.7%) for diabetes and an area under the curve of 0.75 (Table 5).

Of 58 patients completing the early GTT, 27 (47%) had impaired glucose tolerance (pre-diabetes or diabetes) and 3 (5%) had diabetes mellitus. Only 1 of the 3 patients with diabetes on the early GTT returned for the routine GTT and diabetes was confirmed at that time. Of 31 patients completing both the early and routine test, 8 (26%) had impaired glucose tolerance and 2 (7%) had diabetes mellitus on the routine GTT. Among the 2 patients diagnosed with diabetes 6–12 weeks postpartum (Table 5), one had impaired glucose tolerance and the other had diabetes on the early GTT (Table 4). No patients with normal testing on the early GTT had diabetes on the routine GTT. However, 3 patients with normal early GTT's had impaired glucose tolerance on the routine GTT.

DISCUSSION

Our findings suggest an early postpartum GTT may be a reasonable initial postpartum screening test for patients with GDM for diabetes mellitus, especially since nearly 50% of the patients in our study failed to return for the routine GTT 6–12 weeks postpartum even with aggressive follow-up strategies.

Our results are consistent with those of Werner et al. who had a similarly low rate of return for the routine 6 week postpartum GTT of 46%.(18) Test characteristics were similar with regard to diagnosis of diabetes mellitus with a NPV>86% for the early GTT in their study. Use of an early GTT in our study population would have identified all patients with diabetes and missed 3 patients with a normal GTT who would have gone on to have impaired glucose tolerance testing on routine GTT. We posit that informing patients of their abnormal result from the early GTT may increase follow-up rates for the highest risk subgroup.

A notable strength of our study is the rigorous methodology with minimal missing data. However, our findings should be considered in the context of the following limitations. First, our power calculation was based on an estimated 18% loss to follow-up based on other postpartum follow-up studies in our patient population. However, our loss to follow-up was actually 47%. While underscoring the potential importance of the early GTT, this suggests that it may be possible to obtain even greater precision with a larger sample size. We recruited patients on the postpartum floor who delivered at our institution, but not all of them returned to our institution for their postpartum care. While we obtained records for patients receiving postpartum care at other institutions, it means the routine GTT results were obtained from four different laboratories, which may introduce some heterogeneity. Lastly, our institution is a large tertiary referral center serving predominantly Caucasian and African American patients with a high acuity level; thus, our results may not be generalizable to all clinical settings.

Future research should employ a large, multi-center study to estimate more precise and generalizable early GTT test characteristics, use receiver-operating characteristics to identify the threshold of early screening timing to predict abnormal routine GTT results, and build a predictive model incorporating patient characteristics.

In conclusion, rates of 6–12 week postpartum GTT completion among patients with gestational diabetes is unacceptably low. Further studies are needed to determine whether appropriate postpartum assessment may be improved by using the early GTT as a screening test that triages women with normal results to routine care and heightens awareness in women with abnormal results regarding the need for follow-up testing and care. This strategy may provide the best hope of both capturing this high-risk population before they are lost to follow-up, and improving their long-term health status.

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Table 1

Baseline Characteristics of patients who completed routine 6–12 week postpartum GTT compared to those who did not

	Completed Routine 6–12 wk GTT (n=31)	Did not complete Routine 6–12 wk GTT (n=27)	p-value
Age (median, IQR)	32 (28–36)	30 (23–34)	0.095
Race			
-American Indian	1 (3.23)	0	0.346
-African American	14 (45.16)	12 (44.44)	0.956
-Hispanic	5 (16.13)	0	0.029
-White	13 (41.94)	13 (48.15)	0.635
-Other	3 (9.68)	2 (7.41)	0.759
Public Insurance	19 (61.29)	20 (74.07)	0.301
Nulliparous	4 (12.90)	9 (33.33)	0.063
History of GDM	5 (16.13)	3 (11.11)	0.580
Preterm Delivery	7 (22.58)	7 (25.93)	0.776
Cesarean delivery	24 (80.00)	15 (55.56)	**0.047**
Diabetes Type			0.219
-A1GDM	5 (16.13)	8 (29.63)	
-A2GDM	26 (83.87)	19 (70.37)	
Tobacco	2 (6.45)	3 (11.11)	0.528
Breastfeeding at Delivery	19 (61.29)	12 (44.44)	0.200
Breastfeeding at 6–12 weeks postpartum visit	15 (50.00)	2 (8.70)	**0.001**
Attended postpartum visit	31 (100.00)	12 (44.44)	**<0.001**

Bolded items denote significance p>0.05;

Data presented as n (%) unless otherwise noted

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Table 2

Demographic Characteristics of Normal vs. Impaired Glucose Tolerance on early and routine GTT

	Early GTT			Routine GTT		
	Normal (n=31)	**Impaired (n=27)**	**P-value**	**Normal (n=23)**	**Impaired (n=8)**	**p-value**
Age	31 (25–36)	33 (27–35)	0.727	33 (28–37)	30 (27–34)	0.338
Race						
-American Indian	0	1 (3.70)	0.280	1 (4.35)	0	0.549
-African American	14 (45.16)	12 (44.44)	0.956	9 (39.13)	5 (62.50)	0.253
-Hispanic	2 (6.45)	3 (11.11)	0.528	5 (21.74)	0	0.150
-White	16 (51.61)	10 (37.04)	0.266	11 (47.83)	2 (25.00)	0.260
-Other	1 (3.23)	4 (14.81)	0.117	2 (8.70)	1 (12.50)	0.754
Public Insurance	26 (83.87)	13 (48.15)	**0.004**	12 (52.17)	7 (87.50)	0.077
Nulliparous	5 (16.13)	8 (29.63)	0.219	0	4 (50.00)	>0.001
History of GDM	5 (16.13)	3 (11.11)	0.580	3 (13.04)	2 (25.00)	0.428
Preterm Delivery	7 (22.58)	7 (25.93)	0.766	6 (26.09)	1 (12.50)	0.429
Cesarean delivery	16 (53.33)	23 (85.19)	**0.010**	18 (81.82)	6 (75.00)	0.680
Diabetes Type						
-A1GDM	9 (29.03)	4 (14.81)	0.195	3 (13.04)	2 (25.00)	0.428
-A2GDM	22 (70.97)	23 (85.19)		20 (86.96)	6 (75.00)	
Tobacco	3 (9.68)	2 (7.41)	0.759	0	2 (25.00)	**0.013**
Breastfeeding at Delivery	15 (48.39)	16 (59.26)	0.408	15 (65.22)	4 (50.00)	0.447
Breastfeeding at 6–12 weeks postpartum visit	8 (27.59)	9 (37.50)	0.441	13 (56.52)	2 (28.57)	0.195

Bolded items denote significance p>0.05;

Data presented as n (%)

Table 3

Early GTT distribution by postpartum day and mode of delivery

Postpartum day of Early GTT	SVD n=19	Cesarean n=39
1	2 (10.53)	1 (2.56)
2	17 (89.57)	15 (38.46)
3	0	18 (46.15)
4	0	5 (12.82)

Data presented as n (%)

Table 4

Impaired glucose tolerance in Early vs. Routine Postpartum Testing

6–12 week Postpartum GTT	Early GTT		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Impaired Glucose Tolerance or Diabetes	Normal				
Impaired Glucose Tolerance or Diabetes	5	3	62.5	52.2	31.3	80.0
Normal	11	12				

ROC area=0.57

Table 5

Diabetes in Early vs. Routine Postpartum GTT Testing

6–12 week Postpartum GTT	Early GTT		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Diabetes	No Diabetes				
Diabetes	1	1	50	100	100	96.7
No Diabetes	0	29				

ROC area=0.75