12-Month Postpartum Metabolic Follow-Up of β-cell function in Women with Pregnancy-related Glucose Intolerance

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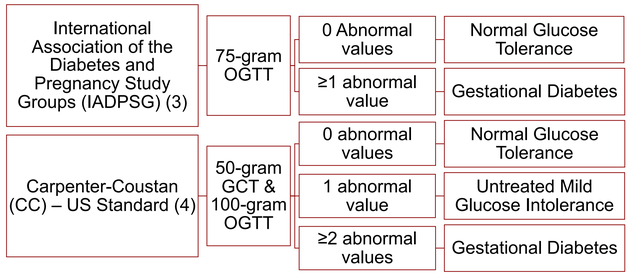
Introduction

1. Gestational Diabetes Mellitus (GDM) is associated with increased perinatal risks including preeclampsia during pregnancy, Caesarean section delivery, and numerous postnatal effects on the mother and child including T2DM and dyslipidemia (1,2).
2. GDM evaluated by two criteria, IADPSG and CC. Debate continues about which screening is most effective for GDM. Per GDM[2] study, IADPSG is less selective, while CC fails to diagnose patients with mild glucose intolerance (MGI) (3). This is a follow-up study, reviewing impact of not diagnosing MGI in CC.

Figure 1. Criteria and Process for Diagnosing GDM, MGI



3. Patients with MGI, compared to normal patients, are at risk for metabolic impairments, they have shown increased risk for cardiovascular events (4) and metabolic syndrome (5).
4. Glucose intolerance conditions in pregnancy have been shown to predispose to progression to T2DM, including a seven-fold increase in patients with GDM within 10 years (6).

Methods

Participants: 407 women, 305 with no GDM, 49 with Mild Glucose Intolerance, 53 with treated GDM.

Settings: Follow up to the Gestational Diabetes Diagnostic Methods (GDM[2]) trial, which randomized pregnant individuals to either IADPSG or CC OGTTs at 24-28 weeks pregnancy at University of Pittsburgh Medical Center. All MGI, GDM, and half the normal patients were invited to return for a 75g OGTT at fasting, 1-hr, 2-hr time points to collect insulin/glucose measurements at 12 months postpartum (3).

Data Analysis: Statistics were calculated and tabulated using SAS. Statistical significance was calculated using Kruskal-Wallis test for continuous variables or Wilcoxon Tests for pairwise comparisons. Linear and logistic regression models were adjusted for participants characteristics for metabolic recovery and progression to diabetes analyses, respectively.

Results

Table 1. Maternal Demographics Compared Between No GDM, MGI, & GDM

Characteristics	
Significant	age, BMI, glucose measurements, history of GDM
Not Significant	race, history of family diabetes, prenatal smoker

Table 2. Maternal Glucose and Metabolic Characteristics during Pregnancy and 12 Months Postpartum

Characteristic	Timeline	Total (N=407)	No GDM (n=305)	MGI (CC) (n=49)	Treated GDM (n=53)	P-value*
Stumvoll Index	Pregnancy	1,507.5 (667.4)	1,470.5 (607.6)	1,465.5 (750.9)	1,755.6 (848.3)	**0.037**
	12 mo. PP	1,383.9 (809.6)	1,371.9 (876.4)	1,350.2 (594.8)	1,475.8 (567.0)	0.25
Matsuda Index	Pregnancy	20.4 (17.2)	23.5 (18.3)	13.3 (8.1)	9.4 (8.4)	**<0.001**
	12 mo. PP	36.7 (38.2)	41.0 (41.6)	28.7 (26.6)	20.0 (15.9)	**<0.001**
Disposition Index	Pregnancy	24,370.9 (14,508.6)	27,936.7 (14,892.2)	15,358.6 (5,479.1)	12,518.9 (5,222.3)	**<0.001**
	12 mo. PP	32,641.3 (20,229.5)	35,421.5 (20,973.7)	27,441.2 (17,559.3)	22,328.3 (13,175.0)	**<0.001**
Triglycerides (mg/dl)	Pregnancy	170.8 (63.9)	160.3 (57.3)	200.4 (73.5)	203.8 (71.7)	**<0.001**
	12 mo. PP	89.9 (50.6)	83.8 (47.4)	103.4 (53.8)	111.6 (57.5)	**<0.001**
Cholesterol (mg/dl)	Pregnancy	234.8 (44.6)	235.7 (43.2)	231.4 (46.8)	233.0 (50.7)	0.75
	12 mo. PP	176.6 (35.5)	174.5 (35.7)	175.4 (24.6)	189.8 (40.6)	**0.024**
Leptin (ng/ml)	Pregnancy	61.4 (78.1)	52.2 (50.6)	81.1 (125.6)	97.2 (128.2)	**<0.001**
	12 mo. PP	47.4 (80.9)	36.8 (53.4)	71.2 (144.7)	81.3 (108.9)	**<0.001**
Adiponectin (µg/ml)	Pregnancy	19.0 (12.4)	20.2 (13.4)	16.6 (8.2)	14.6 (6.9)	**<0.001**
	12 mo. PP	19.1 (9.0)	20.2 (9.4)	17.3 (8.2)	15.3 (6.0)	**<0.001**
A1c (%)	12 mo. PP	5.3 (0.3)	5.3 (0.3)	5.3 (0.4)	5.4 (0.3)	0.27

Table 3. Metabolic Recovery Between Pregnancy and 12 Months Postpartum

Outcome	No GDM	CC Mild	Treated GDM (IADPSG/CC)	P-value
Stumvoll Index	-48.26	-108.94	-285.99	0.20
Matsuda Index	16.26	16.88	13.51	0.87
Disposition Index	9257.12	13497.3	11796.6	0.37
Triglycerides (mg/dl)	-73.94	-95.00	-89.75	0.06

Table 4. Pairwise Comparisons of Indices

Characteristic	No GDM vs MGI P-value*	No GDM vs GDM P-value*	MGI vs GDM P-value*
12-month postpartum Stumvoll Index	0.93	0.10	0.24
12-month postpartum Matsuda Index	0.026	<0.001	0.07
12-month postpartum Disposition Index	0.006	<0.001	0.05

Table 5. Development Prediabetes/T2DM Based on Maternal Glucose Outcome at 12 Months Postpartum

Characteristic	Measure	Total (N=407)	No GDM (n=305)	MGI (CC) (n=49)	Treated GDM (n=53)	P-value*
Diabetes Status at 12 months PP	Normal glucose tolerance	310 (82.0%)	238 (84.7%)	34 (72.3%)	38 (76.0%)	0.09
	Prediabetes	65 (17.2%)	41 (14.6%)	12 (25.5%)	12 (24.0%)	
	Type 2 Diabetes	3 (0.8%)	2 (0.7%)	1 (2.1%)	0 (0.0%)	

Results

- **β-cell Function**: Best measured by Disposition Index, the function is significantly decreased in patients with MGI and GDM. This index is a strong indicator for progression to T2DM (7).
- **Insulin Secretion**: Measured by Stumvoll Index (8), there were differences during pregnancy but not in the postpartum period. This suggests that deficits in insulin secretion may contribute to MGI and GDM during pregnancy, but this does not persist into the postpartum period.
- **Insulin Resistance**: Measured primarily by Matsuda Index (9) and secondarily by adiponectin (10), significantly decreased levels during pregnancy and 12 months postpartum ($p<0.001$) indicate insulin resistance is the main impairment contributing to GDM and long-term metabolic impairment. Both MGI and GDM demonstrate similar levels of insulin resistance in the postpartum period ($p=0.07$).
- **Metabolic Recovery**: The Stumvoll, Matsuda, and Disposition Indices experienced similar rates of change between pregnancy and 12 months postpartum. This indicates that the glucose intolerance seen in pregnant individuals likely represents their baseline physiology rather than a pregnancy specific metabolic disorder (Table 3).
- **A1c**: This did not differ significantly among groups and indicates that HbA1c is not sensitive enough to assess differences in glucose metabolism during pregnancy or the postpartum period (11).
- **Diabetes Risk**: The study was underpowered but indicated a trend towards development of prediabetes/T2DM in patients with MGI and GDM (Table 5). Both MGI and GDM demonstrate similar levels of progression to prediabetes.

Conclusion

Patients with mild glucose intolerance have impairments in β-cell function, specifically insulin resistance one year postpartum and should receive follow-up for potential progression to T2DM. Metabolic recovery back to baseline levels is reflective of systematic differences in β-cell function not specifically attributable to pregnancy impairments.

References & Acknowledgements

This IMPRS project was funded, in part, with support from the Indiana Clinical and Translational Sciences Institute Grant funded, in part by UL1TR002529 from the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. References can be accessed via the QR code.