

**The Perinatal Risk Factors for the Development of
Abnormal Glucose Metabolism in Women
with a Prior History of Gestational Diabetes Mellitus**

Thesis of the Master of Science (M.S.) Degree in Epidemiology

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April 2013

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Abstract

Background/Objective

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance diagnosed for the first time during pregnancy. Up to 60% of women who had a prior GDM will develop type II diabetes mellitus in the next 5 to 15 years after delivery. Our study aimed to examine perinatal factors associated with later development of impaired glucose metabolism in women with a recent history of GDM.

Methods

We conducted a retrospective cohort study based on a 2-year follow-up of women with or without prior GDM. We recruited 39 women from the previous case-control study, including 19 women with prior GDM and 20 women without prior GDM. All the subjects were taken a 75-g oral glucose tolerance test (OGTT) and were interviewed with a questionnaire by research nurses. Chi-square tests were used to examine differences in proportions. Multiple log-linear regression models were used to determine whether there was an association between the prenatal potential risk factors and glucose metabolic abnormalities, after adjustment of various potential confounding variables.

Results

Compared to women without a history of GDM, prior GDM women had significantly higher glucose and insulin concentration, increased insulin resistance and decreased β -cell function. Pre-pregnancy body mass index (BMI) and family history of diabetes were significantly reduced in early phase insulin responsiveness (IGI/HOMA-IR) and insulin secretion-sensitivity index (IS-SI) among women without prior GDM. Women's parity was statistically significant decreased in Matsuda insulin sensitivity index (IS_{OGTT}).

Conclusion

Women with history of GDM have a significant higher risk of developing glucose metabolic abnormalities about two years after delivery. Pre-pregnancy BMI may have an association with later developing abnormal glucose metabolism in women without history of GDM.

Introduction

Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM), one of the most common clinical issues of pregnancy, is defined as any degree of glucose intolerance with onset or first recognition during pregnancy (1). A pregnant woman would be diagnosed as GDM if a fasting plasma glucose level $\geq 7.0\text{mmol/L}$ and/or two-hour plasma glucose level $\geq 7.8\text{mmol/L}$ (2). In Pasadena June 2008, The International Association of Diabetes and Pregnancy Study Group assembled 225 experts, from 40 countries, to review the data of Hyperglycemia and Adverse Pregnancy Outcome study and other related studies, and decided to establish the new diagnostic criteria of GDM. The new diagnostic threshold for fasting blood glucose level is $\geq 5.1\text{mmol/L}$, 1-hour post-75-g glucose level $\geq 10.0\text{mmol/L}$, while the 2-hour post-75-g glucose level $\geq 8.5\text{mmol/L}$. If results of any one of these three levels shows abnormality, then subject should be considered as GDM (3).

GDM in the United States

Centers for Disease Control and Prevention reported GDM complicates approximately 2-10% of all pregnancies in the United States in 2010 (4), leading to more than 200,000 cases every year (5). About 18% of the pregnancies are affected according to the new diagnostic criteria. (4).

Potential Risk Factors of GDM

The risk of GDM typically increases with increasing maternal age when pregnancies are over 25 years old, especially for women over 35 years of age. The risk is about 2.59 (95% confidence interval: 1.84-3.67) among women between 25 and 29 years of age, 4.38 (3.13-6.13) among women 30-34 years of age, 10.85 (7.72-15.25) among women 35-39 years of age, and 15.90 (10.62-23.80) among women over 40 years of age (6).

The risks of GDM also differ between racial and ethnic groups. The prevalence of GDM was approximately 4.2% (4.1-4.3) among non-Hispanic white women, 4.4% (4.1-4.7) among African-American women, 5.4% (5.0-5.8) among other Hispanic women, 6.7% (5.0-8.3) among Korean women, 7.1% (6.8-7.4) among Mexican women, 7.2% (6.1-8.3) among Pacific Island women, 7.9% (7.3-8.5) Chinese women, 8.8% (7.7-9.0) Southeast Asian women, 9.6% (9.1-10.0) among Filipina women, and highest among Asian Indian women 11.1% (10.4-12.0) (7).

The risk of GDM also typically increases with increasing pre-pregnancy maternal body mass index (BMI). Compared to women with normal weight (BMI: 20-24.9), the odds ratio of developing GDM is 0.75 (0.69-0.82) for underweight women (BMI < 20), 1.97 (1.77-2.19) for overweight women (BMI: 25-29.9) , 3.01(2.34-3.87) for moderately obese women (BMI: 30-34.9), and 5.55 (4.27-7.21) for morbidly obese women. For every 1 kg/m² increase in pre-pregnancy maternal BMI, the prevalence of GDM increases by 0.92% (8).

The risk of gestation diabetes mellitus are also higher among women that have a

family history of type 2 diabetes on the maternal side, with a previous history of fetal macrosomia, and/or a previous pregnancy with gestational diabetes mellitus (9, 10).

Prognosis and Prevention of GDM

GDM can be controlled through eating healthy foods and regular exercise. Sometimes, a diabetic diet or exercise is inadequate to control glucose levels; therefore insulin therapy become necessary (11). However, if this condition is not well controlled, it can result in adverse maternal and fetal outcomes. Women with GDM are more likely to suffer preeclampsia, hypoglycemia, cesarean delivery and having fetal macrosomia. The offspring of women with GDM are at increased risk for birth trauma, obesity, glucose intolerance and early adulthood (1, 9).

For most women with gestational diabetes mellitus, glucose homoeostasis is restored to normal level soon after delivery (12). Among 5% to 10% of women with gestational diabetes mellitus, the glucose level is not back to the pre-pregnancy level - the condition becomes type II diabetes mellitus. Even if the glucose level is resolved, 15% to 60% of women who have had GDM will develop type II diabetes mellitus in next 5 to 15 years of delivery (13).

Research Questions

There are several potential risk factors that attribute to type II diabetes mellitus, such as age, race, family history of type II diabetes mellitus, smoking status and so on. Previous history of GDM is one of the potential risk factors of type II diabetes mellitus. This provides a window of opportunity for early identification of risk factors that contribute to later development of type II diabetes mellitus and for early interventions to prevent later development of type II diabetes mellitus in young women. However, it is unclear why some women with prior GDM develop type II diabetes mellitus later in life while others do not, and little is known regarding which risk factors contribute to the development of type II diabetes mellitus later in life in women with GDM history.

There were two questions that we intended to address in this study. Firstly, what perinatal factors are significant predictors for abnormal glucose metabolism at about 2 years after delivery? Secondly, what perinatal factors are significant predictors for abnormal glucose metabolism in women with a prior history of GDM at about 2 years after delivery?

In this study, we assessed fourteen potential perinatal risk factors, including maternal age, pre-pregnancy BMI, maternal race, maternal educational level, marital status, family income, parity, family history of type II diabetes mellitus, status of abortion, status of stillbirth, periodontal disease in pregnancy, prior depression during pregnancy, status of smoking prior to pregnancy and status of smoking now.

We hypothesized one or more aforementioned potential risk factors can be used to

identify women who are at higher risk of later developing abnormal glucose metabolism (toward to type II diabetes mellitus) than women without. In addition, we also speculated that among women with the potential risk factors, those with history of previous GDM tend to have much higher risk of later developing abnormal glucose metabolism than women without previous history of GDM.

Methods

Study Population

We conducted a retrospective cohort study based on a follow-up of women with and without prior GDM until about 2 year after delivery (12) at Woman's Hospital in Baton Rouge, Louisiana. In the follow-up study, we recruited subjects from a previous case-control study of the relationship between periodontal disease and GDM at Woman's Hospital, Baton Rouge (14). A total of 53 cases and 106 controls of previous case-control study were contacted to ask if they would be interested in participating in this follow-up study. At last, 39 women agreed to participate in the follow-up study, including 19 women with prior history of GDM and 20 women without prior history of GDM. The Informed Consent Form has been signed by each participant. Those women were scheduled for a standard 75-g OGTT and an interview by research nurses. The questionnaire involved socioeconomic status, lifestyle, breastfeeding, and any medications and treatments before and during pregnancy, as well as after their delivery.

Definition of GDM

In the case-control study (14), all pregnant women took a laboratory screening test for GDM between 20-30 weeks of their gestational age, which was based upon the American College of Obstetricians and Gynecologists' guidelines (1). Thus, the status of GDM was identified in the previous case-control study. Firstly, women were

screened for glucose intolerance by performing a standard 1-hour 50-g oral glucose challenge test. If the level of glucose was higher than 135 mg/dl, meaning that glucose challenge test was positive, they would undergo a 3-hour and a 100-g OGTT after 10-12 hours overnight fast. The diagnostic threshold for fasting blood glucose level is 90 mg/dl, and for 1-, 2-, and 3-hours thresholds are 180 mg/dl, 155 mg/dl and 140.5 mg/dl, respectively (3). The cases where subject's glucose levels exceeded any two or more threshold values of all tests were defined as having GDM. The controls were defined as subjects who passed the glucose challenge test at 20-30 weeks of their gestational age and did not have any other types of diabetes mellitus during pregnancy (12).

Measurements and Definitions of Potential Risk Factors

Age --- Maternal age in pregnancy

Pre-pregnancy body mass index (BMI) --- The BMI measures human body shape based on weight and height, defined as the individual's body weight in kilograms divided by the square of their height in meters (15). We collected the information of pre-pregnancy weight from the interview with the questionnaire by a research nurse, and the height measurement was taken barefoot in light clothing when women came to take the OGTT. We classified BMI into three levels, underweight/normal (BMI less than 25), overweight (BMI between 25 and 30), and obese (BMI over 30) (16).

Race --- We categorized race into three groups: White, Black or other.

Education, marital status, family income and parity --- For education, there were three levels: high school degree or lower, some college education or college degree, and some graduate education or graduate degree. For marital status, we categorized women into two groups, one group including women who were married or living with a partner, the other group including women who were either separated, divorced or never married. Family income measured the combined incomes of all people in a family. There were three levels of family total income (less than 20 thousands per year, between 20 and 75 thousands per year, and more than 75 thousands per year). For status of parity, we classified them into primiparous (defined as no prior child) or multiparous (defined as one or more prior child).

Family history of diabetes --- This variable described whether mother or sisters of the subjects ever have any type of diabetes mellitus or not.

Prior abortion and prior stillbirth --- Abortion is the termination of pregnancy by the removal or expulsion from the uterus of a fetus or embryo prior to viability (17), including spontaneous miscarriage and induced abortion. Stillbirth was defined as a fetus has died in the uterus (18). We collected the information from the questionnaires about whether the subjects ever have abortion or stillbirth prior to pregnancy.

Periodontal disease in pregnancy --- The participants were requested to undergo a full-mouth periodontal examination, with periodontitis diagnosed when the presence of any sites exhibiting probing depth ≥ 4 mm or clinical attachment loss ≥ 4 mm was confirmed (12).

Depression --- The information that whether a participant had ever been diagnosed with depression or not during their pregnancy. Maternal depression was assessed by using the Edinburgh Depression Scale (EDS). The EDS was first developed for the assessment of postpartum depression under the name of the “Edinburgh Postnatal Depression Scale” (19). It was then validated in childbearing women and in non-postnatal women (20, 21). EDS has 10 items (questions). Each item is scored on a four-point scale (from 0 to 3), with minimum and maximum overall scores ranging 0 to 30. The internal consistency of this scale was found to be good in pregnant women (Cronbach’s $\alpha=0.85$) (22). A cutoff value of 12 (22) was used to define depression in the present study.

Status of smoking currently and prior to pregnancy --- Through the questionnaire, we collected the information about subject’s smoking status in two periods, before and during pregnancy and at the two years after delivery, as well as the approximate number of cigarette they smoked per week.

Measurements of Insulin Resistance Indices

There are four indices that we use to express the function of pancreatic β -cell.

1) **The homeostasis model assessment for insulin resistance (HOMA-IR)** was based on baseline fasting glucose and insulin concentrations to calculate the insulin resistance (23).

2) **The Matsuda insulin sensitivity index (IS_{OGTT})** was derived from the OGTT, which is a well estimate of the result of insulin clamp technique (24).

3) **The corrected early phase insulin secretion index (IGI/HOMA-IR)** derived from recalculation of the insulinogenic index (IGI), an index of first phase β -cell activity, to adjust insulin secretion for degree of insulin resistance (23-25).

4) **The insulin secretion-sensitivity index (IS-SI)**, obtained over the 2-hour OGTT, was a critical measurement of overall ability of the β -cell to increase its secretion rate relative to insulin resistance in response to a glucose stimulus (26).

Statistical Analysis

1) What perinatal factors were significant predictors for abnormal glucose metabolism at 2 years after delivery?

The analysis for potential risk factors of developing abnormal glucose metabolism at about 2 years after delivery involved descriptions of baseline characteristics by percentages. The baseline characteristics included maternal age, race, education, marital status, pre-pregnancy BMI, family income, parity, history of GDM, family history of diabetes, prior abortion, prior stillbirth, periodontal disease in pregnancy, depression, status of smoking prior to pregnancy and current smoking status. The differences in means of these variables between and among groups were examined by one-way analysis of variance. Multivariable linear regressions were applied to adjust for other potential risk factors for every glucose metabolism indices.

2) What perinatal factors were significant predictors for abnormal glucose metabolism in women with a prior history of GDM at about 2 years after delivery?

For potential risk factors of developing abnormal glucose metabolism in women with prior GDM at about 2 years after delivery, the descriptions of baseline characteristics were performed in women with and without prior GDM. The differences in proportions were analyzed by Chi-square tests. One-way analysis of variance was used to examine the difference of means among groups. Finally, the multivariable linear regressions were performed to test if there were interactions

between pre-pregnancy BMI, or parity, and family history of diabetes or history of prior GDM, respectively. Multivariable linear regressions were also applied by adjusting for maternal age, race, education and family income.

Due to the small sample size and skewed distribution, all the glucose metabolism indices (baseline fasting glucose and insulin concentrations, glucose and insulin concentrations at 1/2-, 1-, 2-hour, HOMA-IR, IS_{OGTT}, IGI/HOMA-IR and IS-SI) were transformed into natural logarithmic format. In our model, the regression coefficients (β) were estimated by the least squares method (12). Due to the logarithmic formula $\ln A - \ln B = \ln(A/B)$, the regression coefficients (β) were representative of logged ratios. All the numbers in the attached tables were performed in exponential form.

Statistical analysis was performed using SPSS 20.0 software. A p-value of less than 0.05 was considered statistically significant. For the regression analysis, we chose the backward method, with a p-value of 0.05 for exclusion threshold and 0.10 for entrance criteria.

Results

Characteristics of the study population

Table 1 shows the baseline characteristics of all 39 subjects in the study as a group and according to the previous GDM diagnosis. Women younger than or equal to 35 years of age comprised 61.5% of the study population, while women over 35 years of age comprised 38.5%. 53.8% of the women in the study population were underweight or normal ($BMI < 25$), while 25.6% were overweight ($25 \leq BMI \leq 30$), and 20.5% were obese ($BMI > 30$). There were 53.8% of study subjects being non-Hispanic white, 41.0% being non-Hispanic black, and 5.1% being other races. The highest level of education completed during pregnancy was fairly heterogeneous in the study population with 33.3% of the women having high school degree or lower, 59.0% having some college education or college degree, 7.7% having some graduate education or graduate degree. There were 59.0% of the women in the study population married or living with a partner during their pregnancy, while 41.0% of the women were either separated, divorced or never married. Family income was also fairly heterogeneous in the study population with 12.1% of the women reporting a total family income of less than \$20,000/year, 51.5% reporting a total family income of \$20,000-\$75,000/year, and 36.4% reporting a total family income of greater than \$75,000/year. 41.0% of the studied women were primiparous while 59.0% were multiparous. There were 15.8% of women in the study population having family history of diabetes, while 84.2% do not having. Among the women in the study population, 10.3% reporting had a prior abortion, also 10.3% reporting had a prior

stillbirth, 66.7% reporting suffered periodontal disease during their pregnancy, 15.4% reporting having depression during their pregnancy, 23.1% reporting smoked before or/and during pregnancy and only 5.1% reporting smoking currently.

There were 48.7% of studied women had a history of GDM, while 51.3% did not. All of the variables among groups with or without prior GDM history did not show any significant differences: the subjects were similar in terms of maternal age, race, education, marital status, pre-pregnancy BMI, family income, parity, family history of diabetes, prior abortion, prior stillbirth, periodontal disease in pregnancy, depression during pregnancy, status of smoking during pregnancy and current smoking status.

Perinatal risk for the abnormal glucose metabolism in women at two years

postpartum --- Univariate analysis

Table 2 represents the baseline fasting glucose and the concentrations of glucose at 1/2-, 1-, 2-hour after the 75g OGTT among groups of variables at two years postpartum. As shown, women with a history of GDM have significantly higher glucose concentrations in all four points of time (P-value < 0.05) than women without prior GDM. The differences among the groups in other variables were not statistically significant (P-value > 0.05).

The baseline fasting insulin and insulin at 1/2-, 1-, 2-hour after 75g OGTT among groups according to the study variables are given in table 3. Compared to the women who were primiparous, women who were multiparous had significantly higher

insulin concentrations at baseline fasting, 1/2-hour and 1-hour after test (P-value < 0.05). The concentration of insulin at 2-hour among women who were multiparous was also higher than women who were primiparous, though the difference was not statistically significant (P-value = 0.074). The insulin concentrations were still significantly higher in women with history of GDM than women without GDM in all four time points (P-value < 0.05). Other variables did not show any significant difference.

Table 4 shows the means of metabolic parameters among groups according to the study variables. As shown, except for parity and prior GDM, the differences among the groups were not statistically significant. For parity, the HOMA-IR was significantly higher among women who were multiparous compared to women who were primiparous (P-value < 0.05). The IS_{OGTT} was significantly lower in multiparous group (P-value < 0.05). The IGI/HOMA-IR which expressed early phase insulin responsiveness was significantly reduced in women who were multiparous (P-value < 0.05). Though the IS-SI score between the two groups was not statistically different (P-value = 0.074), the score in primiparous women were high in multiparous women. For subjects with previous history of GDM, the insulin resistant score (HOMA-IR) was significantly lower in multiparous women compared to primiparous women (P-value < 0.05). The measurement of insulin sensitivity (IS_{OGTT}), early phase insulin responsiveness (IGI/HOMA-IR) and insulin secretion-sensitivity (IS-SI) among women who were multiparous were all statistically significantly higher than women who were primiparous (P-value < 0.05).

Perinatal risk for the abnormal glucose metabolism in women at two years

postpartum --- Multivariate analysis

Multivariate linear regression analyses in all women showed correlations between a potential risk factor and glucose metabolism indices after adjusting for other variables. As table 5 presents, most of values were not significant (P-value > 0.05). For example, the correlation between IS-SI and family history of diabetes mellitus was 1.140, means that the score of IS-SI in women with family history of diabetes mellitus (coded: 1) was 1.140 times more than in women without family history of diabetes (coded: 0), but this result was not significant (P-value = 0.592). Prior GDM was significantly associated with glucose metabolism indices. After adjusting for other potential risk factors, the glucose concentrations at 1/2-, 1-, 2-hour after 75-g OGTT in women with prior GDM (coded: 1) were 2.128, 1.984 and 1.811 times significantly higher than in women without prior GDM (coded: 0) (P-value < 0.05), respectively. Compared to women without prior GDM, early phase insulin responsiveness (IGI/HOMA-IR) and IS-SI were 0.529 and 0.548 times significantly reduced in women with previous GDM (P-value < 0.05). The associations between previous GDM history and other metabolism parameters were not significant. The association between prior stillbirth and 1/2-hour glucose concentration was significant (P-value = 0.017) - the glucose concentration in women with prior stillbirth (coded: 1) were 0.557 times lower than in women without prior stillbirth (coded: 0), but the values between prior stillbirth and other indices were not statistically significantly different.

Table 6 shows results from multiple linear regression models. For instance, the predictors of IS-SI were pre-pregnancy BMI, prior GDM, prior stillbirth, depression during pregnancy and current smoking status. The regression coefficients were 0.119, 0.534, 1.481, 1.485 and 6.517, respectively. Adjusted R square was 0.384. The prior GDM, family history of diabetes and maternal education were the major predictors of glucose metabolism indices.

Perinatal risk for the abnormal glucose metabolism in women with prior GDM at two years postpartum --- Univariate analysis

Associations of the study variables with baseline fasting glucose and glucose at 1/2-, 1-, 2-hour after 75g OGTT according to prior GDM are represented in table 7 and table 8. Women with or without previous GDM did not show significant differences in most of the variables studied. One of three significant values was in women without prior GDM, the concentrations of baseline fasting glucose were significantly different among groups of pre-pregnancy BMI (P-value = 0.013), but these three means of concentration did not show an incremented association from the underweight/normal group, overweight group, to the obese group (i.e., Underweight/normal: 82.220 ± 1.057 ; Overweight: 79.391 ± 1.060 ; Obese: 89.783 ± 1.080). Among women who had GDM, compared to women without family history of diabetes, the concentrations of glucose at 1/2-hour and 1-hour after OGTT significantly reduced in women with family history of diabetes (P-value_{1/2-hour} = 0.048; P-value_{1-hour} = 0.042).

Table 9 and table 10 show the baseline insulin and the insulin metabolic parameters after OGTT categorized by prior GDM status. Among women who had previous history of GDM, the concentrations of baseline fasting insulin, 1/2 hour and 1 hour after test in women who were multiparous were significantly higher than women who were primiparous (P-value_{fasting} = 0.021; P-value_{1/2-hour} = 0.008; P-value_{1-hour} = 0.033). In women with prior GDM, the value of 1/2-hour insulin after test among women who had depression during their pregnancy were significantly reduced in contrast to women without depression during pregnancy (P-value = 0.023). However, the differences in the indices relating to depression were not statistically significant.

Table 11 displays the mean scores of insulin resistance (HOMA-IR) and insulin sensitivity (IS_{OGTT}) categorized by feature of prior GDM. Other than women's parity, the differences in IS_{OGTT} were not statistically significant. In women with prior GDM, the IS_{OGTT} among women who were primiparous were significant higher than multiparous women (P-value = 0.021). However, the differences among the scores of HOMA-IR were not statistically significant.

The mean of early phase insulin secretion index (IGI/HOMA-IR) and insulin secretion-sensitivity index (IS-SI) classified by status of prior GDM are represented in table 12. In women without prior GDM, both of IGI/HOMA-IR and IS-SI were significantly different among groups of pre-pregnancy BMI (P-value IGI/HOMA-IR = 0.005; P-value IS-SI = 0.005), and mean scores decreased from underweight/normal group to obese group consistently (i.e., Underweight/normal IGI/HOMA-IR: $2.268 \pm$

2.006 > Overweight IGI/HOMA-IR: 0.885 ± 1.730 > Obese IGI/HOMA-IR: 0.616 ± 2.014 ; Underweight/normal IS-SI: 1305.707 ± 2.010 > Overweight IS-SI: 503.005 ± 1.858 > Obese IS-SI: 356.060 ± 1.824). Also among women without prior GDM, IGI/HOMA-IR and IS-SI were significantly lower in women with family history of diabetes than women without family history of diabetes (P-value IGI/HOMA-IR = 0.008; P-value IS-SI = 0.018).

Interactions between perinatal risk factors for abnormal glucose metabolism and history of GDM --- Multivariate analysis

Through the previous analysis, pre-pregnancy BMI, women's parity and family history of diabetes were considered as the most feasible potential risk factors for glucose metabolic abnormalities in women with prior GDM. Tables 13-15 present the results whether there was an interaction between these potential risk factors and prior GDM. Most of the results were not significant in these three tables. As the tables show, there were interactions between women's parity and history of GDM in adjusted models of baseline fasting insulin ($\beta = 2.351$), HOMA-IR ($\beta = 2.342$) and IS_{OGTT} ($\beta = 0.460$). Also, the interactions between family history of diabetes and prior GDM existed in crude models of baseline fasting glucose ($\beta = 0.608$), glucose concentration at 1/2-, 1-, 2-hour after OGTT ($\beta_{1/2-h} = 0.568$; $\beta_{1-h} = 0.563$; $\beta_{2-h} = 0.670$), insulin concentration at 1-hour after test ($\beta = 0.646$), IS_{OGTT} ($\beta = 1.568$), IGI/HOMA-IR ($\beta = 1.954$) and IS-SI ($\beta = 1.893$). However, the models after adjusting for maternal age, race, education and family income did not show any significant

interaction between prior GDM and family history of diabetes.

Discussion

For identifying what perinatal factors are significant predictors for abnormal glucose metabolism, we conducted a retrospective cohort study based on a follow-up of women with and without GDM until about 2 year after delivery. Our study had four findings: a) women with a history of GDM maintained a significant higher risk of developing glucose metabolic abnormalities at about two years after delivery; b) pre-pregnancy BMI alone was associated with lower early phase insulin secretion and poorer β -cell function; c) family history of diabetes was related to weaker early phase insulin responsiveness and weaker β -cell function among women without a history of GDM, but had an opposite association in women with prior GDM; d) Multiparous was associated with increased insulin resistance and lower insulin sensitivity in women with a prior GDM.

Association between prior GDM and glucose metabolic abnormalities

As expected, our findings revealed that subjects with previous GDM had a markedly increased risk for developing abnormal glucose metabolism. Our finding shows that women with a history of GDM had increased 1.5 times in insulin resistance contrast to women without prior GDM. Akinici B.et al. reported similar results that HOMA-IR was significantly elevated among previous GDM women at least 1 year follow-up after delivery (27). Our findings also indicated that insulin sensitivity and β -cell function were poorer in women with prior GDM that were

consistent with the results of Retnakaran. R et al. They found that women with GDM have decreased insulin sensitivity and declining β -cell function in the 1st year postpartum that may contribute to their future risk of developing type II diabetes mellitus (28, 29).

Association between pre-pregnancy BMI and glucose metabolic abnormalities

Pre-pregnancy BMI was demonstrated by our study as a potential risk of glucose metabolic abnormalities. Our results show that higher pre-pregnancy BMI could predict reducing early phase insulin secretion and declining β -cell function among whole study population. Moreover, they had significant association in women without a history of GDM. The study of Hypponen et al has also concluded that BMI is the most important risk factor for type 2 diabetes mellitus developing by early midlife (30). However, no significant relationship has been founded in our study between pre-pregnancy BMI and any abnormal glucose metabolism among women with prior GDM. Several studies concluded that BMI was a significant predictor of developing abnormal glucose metabolism among women with prior GDM (31-33). Pallardo et al found that among women with a history of GDM, compared to women with a pre-pregnancy BMI ≤ 27 , women with a BMI > 27 had an 8-fold increased risk of developing type 2 diabetes mellitus (OR = 8.7, 95% CI: 2.3-32.9). This result was adjusted for the number of abnormal glucose results from the OGTT and C-peptide glucose score) (33). Nevertheless, Linne et al. doubted if these conclusions can be used for a clinical decision. They explained although the GDM women who

developed type 2 diabetes mellitus had statistically significant higher BMI, the result already indicates a pronounced risk for obesity-related glucose metabolic abnormalities (34). More interestingly, Lobner et al. found that BMI did not further influence risk in women with prior GDM who received insulin treatment, but it did influence risk in women with prior GDM who had diet treatment only during their pregnancy (35).

Association between family history of diabetes and glucose metabolic abnormalities

Arslanian S.A et al. have found that family history of diabetes is associated with reduced insulin sensitivity and a weakened balance between insulin sensitivity and insulin secretion (36). Jafar-Mohammadi B et al. and Permutt M.A et al have identified that there were several genes that had association with type II diabetes mellitus (37, 38). Many other studies but not all have found family history of diabetes increased the risk of abnormal glucose metabolism (39-41). Through our results, we found that the effects of family history of diabetes on risk of developing abnormal glucose metabolism are different in the status of prior GDM; among women with a history of GDM, early phase insulin responsiveness and β -cell function in women with family history of diabetes were weaker than women without prior GDM. Among women without a history of GDM, IGI/HOMA-IR and IS-SI were higher in women with family history of diabetes, but the difference in the results of these were not statistically significant. What's more, the influence of risk among women with prior

GDM was not consistent with other parameters of glucose metabolism (i.e., HOMA-IR, IS_{OGTT}). Therefore, it is likely that family history of diabetes was misestimated due to a relatively young age of the parents of subjects or recall bias, and these may bias findings with respect to type II diabetes mellitus outcome relative to family history of diabetes.

Association between women's parity and glucose metabolic abnormalities

In our findings, there was no association between women's parity alone and glucose metabolic abnormalities. However, multiparous women had markedly increased insulin resistance and lower insulin sensitivity in women with a prior GDM. In the systematic review study of Kim, Newton, and Knopp, they concluded only one study had found women's parity was associated with type II diabetes mellitus after adjustment for confounders, especially the association only existed in women had a history of five or more pregnancies. Other studies they reviewed have not shown any significant association between women's parity and type II diabetes mellitus or glucose metabolic abnormalities (42).

Limitations of the study

The primary limitation of this retrospect cohort study was the small sample size. Firstly, it made the study insufficiently powered to identify the significant difference in potential risk factors between with and without prior GDM. Secondly, effect of

small sample size was that the associations in our results may be observed by chance.

In addition, Type II diabetes mellitus is a result of a combination of insulin resistance and dysfunction of insulin producing pancreatic β -cell. However, the glucose levels do not steadily decreased from onset of β -cell dysfunction to the final development of diabetes. As β -cell mass begin to fall and dysfunction emerges, β -cell compensates to increase mass and insulin secretion, the levels of glucose would be normal or increased (43). Moreover, the incidence of type II diabetes mellitus at 12 month postpartum is about 5% (44), and the incidence at 28 years after delivery approach 50% (45). However, the follow-up period of our study was only two years. Some of participants in our study may develop abnormal glucose metabolism in the future, or those currently having glucose metabolic abnormalities might not reflect on OGTT results. The information of several potential risk factors was collected from the interview by research nurses. There may be some recall bias and interviewer bias that would result the misclassification between the categories of risk factors, lead to incorrect association between risk factor and developing abnormal glucose metabolism. Since the subjects were from the previous case-control study, women with prior GDM may be more interested in participate to our study. Therefore, this may lead to bias from the true estimate of the association. Finally, we did not adjust for multiple comparison, which might result in some false positive associations.

Conclusion

Women with a previous pregnancy complicated by GDM have a significant higher risk of developing glucose metabolic abnormalities at about two years after delivery. Pre-pregnancy BMI may be associated with the development of abnormal glucose metabolism later among women with prior GDM. There was no strong evidence in our study to show any synergy of prior GDM and potential risk factors on glucose metabolic abnormalities. In order to decrease the frequency of abnormal glucose metabolism which leads to the development of type II diabetes mellitus, appropriate preventive strategies are required for women who have a previous history of GDM or who are obese. Further studies with sufficient sample size and follow-up period are needed for confirmation.

References

1. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994). Gestational diabetes. *Obstet Gynecol* 2001;98(3):525-38.
2. Sivaraman SC, Vinnamala S, Jenkins D. Gestational diabetes and future risk of diabetes. *J Clin Med Res* 2013;5(2):92-6.
3. Holt RI, Coleman MA, McCance DR. The implications of the new International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria for gestational diabetes. *Diabet Med* 2011;28(4):382-5.
4. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2011.
5. Gestational diabetes mellitus. *Diabetes Care* 2000;23 Suppl 1:S77-9.
6. Lao TT, Ho LF, Chan BC, Leung WC. Maternal age and prevalence of gestational diabetes mellitus. *Diabetes Care* 2006;29(4):948-9.
7. Hedderson MM, Darbinian JA, Ferrara A. Disparities in the risk of gestational diabetes by race-ethnicity and country of birth. *Paediatr Perinat Epidemiol* 2010;24(5):441-8.
8. Torloni MR, Betran AP, Horta BL, Nakamura MU, Atallah AN, Moron AF, et al. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. *Obes Rev* 2009;10(2):194-203.
9. Harder T, Franke K, Kohlhoff R, Plagemann A. Maternal and paternal family history of diabetes in women with gestational diabetes or insulin-dependent diabetes mellitus type I. *Gynecol Obstet Invest* 2001;51(3):160-4.
10. Ross G. Gestational diabetes. *Aust Fam Physician* 2006;35(6):392-6.
11. Ovidia C, Dixit A. The management of gestational diabetes. *Curr Diabetes Rev* 2012;8(4):247-56.
12. Xiong X, Elkind-Hirsch KE, Xie Y, Delarosa R, Maney P, Pridjian G, et al. Periodontal disease as a potential risk factor for the development of diabetes in women with a prior history of gestational diabetes mellitus. *J Public Health Dent* 2013;73(1):41-9.
13. Baptiste-Roberts K, Barone BB, Gary TL, Golden SH, Wilson LM, Bass EB, et al. Risk factors for type 2 diabetes among women with gestational diabetes: a systematic review. *Am J Med* 2009;122(3):207-214 e4.
14. Xiong X, Elkind-Hirsch KE, Vastardis S, Delarosa RL, Pridjian G, Buekens P. Periodontal disease is associated with gestational diabetes mellitus: a case-control study. *J Periodontol* 2009;80(11):1742-9.
15. Eknoyan G. Adolphe Quetelet (1796-1874)--the average man and indices of obesity. *Nephrol Dial Transplant* 2008;23(1):47-51.
16. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000;894:i-xii, 1-253.

17. Wikipedia. Abortion. In.
18. Wikipedia. Stillbirth. In.
19. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987;150:782-6.
20. Cox JL, Chapman G, Murray D, Jones P. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. *J Affect Disord* 1996;39(3):185-9.
21. Murray D CJ. Screening for depression during pregnancy with the Edinburgh depression scale. *J Reprod Infant Psychol* 1990;8:99-107.
22. Dayan J, Creveuil C, Herlicoviez M, Herbel C, Baranger E, Savoye C, et al. Role of anxiety and depression in the onset of spontaneous preterm labor. *Am J Epidemiol* 2002;155(4):293-301.
23. W.J.Sluiter DWE, W.D.Reitsma, H.Doorenbos. Glucose Tolerance and Insulin Release, A mathematical Approach I. Assay of the Beta-cell Response After Oral Glucose Loading. *Diabetes* 1976;25:241-44.
24. Wareham NJ, Phillips DI, Byrne CD, Hales CN. The 30 minute insulin incremental response in an oral glucose tolerance test as a measure of insulin secretion. *Diabet Med* 1995;12(10):931.
25. Hanson RL, Pratley RE, Bogardus C, Narayan KM, Roumain JM, Imperatore G, et al. Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. *Am J Epidemiol* 2000;151(2):190-8.
26. Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? *Diabetes Care* 2007;30(6):1544-8.
27. Akinci B, Celtik A, Genc S, Yener S, Demir T, Secil M, et al. Evaluation of postpartum carbohydrate intolerance and cardiovascular risk factors in women with gestational diabetes. *Gynecol Endocrinol* 2011;27(5):361-7.
28. Retnakaran R, Qi Y, Sermer M, Connelly PW, Hanley AJ, Zinman B. Beta-cell function declines within the first year postpartum in women with recent glucose intolerance in pregnancy. *Diabetes Care* 2010;33(8):1798-804.
29. Retnakaran R, Qi Y, Sermer M, Connelly PW, Hanley AJ, Zinman B. Glucose intolerance in pregnancy and future risk of pre-diabetes or diabetes. *Diabetes Care* 2008;31(10):2026-31.
30. Hypponen E, Power C, Smith GD. Prenatal growth, BMI, and risk of type 2 diabetes by early midlife. *Diabetes Care* 2003;26(9):2512-7.
31. Aberg AE, Jonsson EK, Eskilsson I, Landin-Olsson M, Frid AH. Predictive factors of developing diabetes mellitus in women with gestational diabetes. *Acta Obstet Gynecol Scand* 2002;81(1):11-6.
32. Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Molsted-Pedersen L, Hornnes P, et al. Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population. *Diabetes Care* 2004;27(5):1194-9.
33. Pallardo F, Herranz L, Garcia-Ingelmo T, Grande C, Martin-Vaquero P, Janez M, et al. Early postpartum metabolic assessment in women with prior

- gestational diabetes. *Diabetes Care* 1999;22(7):1053-8.
34. Linne Y, Barkeling B, Rossner S. Natural course of gestational diabetes mellitus: long term follow up of women in the SPAWN study. *BJOG* 2002;109(11):1227-31.
 35. Lobner K, Knopff A, Baumgarten A, Mollenhauer U, Marienfeld S, Garrido-Franco M, et al. Predictors of postpartum diabetes in women with gestational diabetes mellitus. *Diabetes* 2006;55(3):792-7.
 36. Arslanian SA, Bacha F, Saad R, Gungor N. Family history of type 2 diabetes is associated with decreased insulin sensitivity and an impaired balance between insulin sensitivity and insulin secretion in white youth. *Diabetes Care* 2005;28(1):115-9.
 37. Jafar-Mohammadi B, McCarthy MI. Genetics of type 2 diabetes mellitus and obesity--a review. *Ann Med* 2008;40(1):2-10.
 38. Permutt MA, Wasson J, Cox N. Genetic epidemiology of diabetes. *J Clin Invest* 2005;115(6):1431-9.
 39. Yeung EH, Pankow JS, Astor BC, Powe NR, Saudek CD, Kao WH. Increased risk of type 2 diabetes from a family history of coronary heart disease and type 2 diabetes. *Diabetes Care* 2007;30(1):154-6.
 40. Valdez R, Yoon PW, Liu T, Khoury MJ. Family history and prevalence of diabetes in the US population: 6-year results from the National Health and Nutrition Examination Survey (NHANES, 1999-2004). *Diabetes* 2007.
 41. Bjornholt JV, Erikssen G, Liestol K, Jervell J, Thaulow E, Erikssen J. Type 2 diabetes and maternal family history: an impact beyond slow glucose removal rate and fasting hyperglycemia in low-risk individuals? Results from 22.5 years of follow-up of healthy nondiabetic men. *Diabetes Care* 2000;23(9):1255-9.
 42. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002;25(10):1862-8.
 43. Weir GC, Bonner-Weir S. Five stages of evolving beta-cell dysfunction during progression to diabetes. *Diabetes* 2004;53 Suppl 3:S16-21.
 44. Mazze RS, Langer O. Primary, secondary, and tertiary prevention. Program for diabetes in pregnancy. *Diabetes Care* 1988;11(3):263-8.
 45. O'Sullivan JB. Diabetes mellitus after GDM. *Diabetes* 1991;40 Suppl 2:131-5.

Tables

Table 1: Baseline Characteristics of Study Population

	Whole Group (n [%])	Women without Gestational Diabetes Mellitus (n [%])	Women with Gestational Diabetes Mellitus (n [%])	P-value
Prior GDM History	39 (100)	20 (51.3)	19 (48.7)	
Age				
<=35 years old	24 (61.5)	14 (70.0)	10 (52.6)	0.265
>35 years old	15 (38.5)	6 (30.0)	9 (47.4)	
Pre-pregnancy Body Mass Index				
Underweight/Normal	21 (53.8)	9 (45.0)	12 (63.2)	0.521
Overweight	10 (25.6)	6 (30.0)	4 (21.1)	
Obese	8 (20.5)	5 (25.0)	3 (15.8)	
Race				
Non-Hispanic White	21 (53.8)	8 (40.0)	13 (68.4)	0.124
Non-Hispanic Black	16 (41.0)	10 (50.0)	6 (31.6)	
Other	2 (5.1)	2 (10.0)	0 (0.0)	
Education				
High School Degree or Lower	13 (33.3)	10 (50.0)	3 (15.8)	0.075
College	23 (59.0)	9 (45.0)	14 (73.7)	
Graduate School	3 (7.7)	1 (5.0)	2 (10.5)	
Marital Status				
Married	23 (59.0)	11 (55.0)	12 (63.2)	0.605
Single	16 (41.0)	9 (45.0)	7 (36.8)	
Family Income				
<20K	4 (12.1)	2 (12.5)	2 (11.8)	0.400
20-75K	17 (51.5)	10 (62.5)	7 (41.2)	
>75K	12 (36.4)	4 (25.0)	8 (47.1)	
Parity				
Primiparous	16 (41.0)	11 (55.0)	5 (26.3)	0.069
Multiparous	23 (59.0)	9 (45.0)	14 (73.7)	
Family History of Diabetes				
No	32 (84.2)	17 (85.0)	15 (83.3)	0.888
Yes	6 (15.8)	3 (15.0)	3 (16.7)	
Prior Abortion				
No	35 (89.7)	18 (90.0)	17 (89.5)	0.957
Yes	4 (10.3)	2 (10.0)	2 (10.5)	
Prior Stillbirth				
No	35 (89.7)	19 (95.0)	16 (84.2)	0.267
Yes	4 (10.3)	1 (5.0)	3 (15.8)	
Periodontal Disease During Pregnancy				
No	13 (33.3)	7 (35.0)	6 (31.6)	0.821
Yes	26 (66.7)	13 (65.0)	13 (68.4)	
Depression During Pregnancy				
No	33 (84.6)	17 (85.0)	16 (84.2)	0.946
Yes	6 (15.4)	3 (15.0)	3 (15.8)	
Smoked Before or/and During Pregnancy				
No	30 (76.9)	15 (75.0)	15 (78.9)	0.770
Yes	9 (23.1)	5 (25.0)	4 (21.1)	
Smoking Now				
No	37 (94.9)	20 (100.0)	17 (89.5)	0.136
Yes	2 (5.1)	0 (0.0)	2 (10.5)	

Table 2: Perinatal Risk for the Abnormal Glucose Metabolism < Glucose Concentration > in Women at Two Years Postpartum – Univariate Analysis

		Fasting Glucose (mg/dL)			1/2-hour Glucose (mg/dL)			1-hour Glucose (mg/dL)			2-hour Glucose (mg/dL)		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	85.089	1.115	0.412	117.026	1.258	0.367	98.170	1.326	0.207	90.315	1.266	0.373
	>35 years old	87.532	1.100		126.444	1.341		112.956	1.492		97.719	1.361	
Pre-pregnancy Body Mass Index	Underweight/Normal	86.444	1.104	0.505	119.522	1.331	0.447	105.130	1.473	0.569	92.499	1.313	0.968
	Overweight	83.421	1.104		113.693	1.232		94.642	1.287		92.731	1.336	
	Obese	88.279	1.134		132.569	1.244		111.698	1.326		95.126	1.278	
Race	Non-Hispanic White	86.436	1.106	0.528	121.231	1.306	0.821	105.478	1.442	0.772	98.445	1.337	0.288
	Non-Hispanic Black	86.384	1.116		121.340	1.292		103.317	1.375		88.597	1.250	
	Other	79.234	1.123		107.652	1.193		87.909	1.066		76.907	1.269	
Education	High School Degree or Lower	82.997	1.124	0.123	118.061	1.318	0.423	100.193	1.405	0.413	85.055	1.265	0.135
	College	88.464	1.096		124.649	1.287		108.603	1.416		99.823	1.323	
	Graduate School	81.126	1.091		101.982	1.154		83.563	1.062		80.632	1.038	
Marital Status	Married	86.852	1.098	0.502	120.542	1.294	0.998	102.125	1.426	0.751	94.585	1.332	0.660
	Single	84.868	1.126		120.518	1.295		105.795	1.369		90.995	1.267	
Family Income	<20K	81.117	1.119	0.376	102.576	1.194	0.335	103.670	1.283	0.821	85.237	1.276	0.612
	20-75K	86.589	1.088		119.591	1.256		103.235	1.316		94.619	1.352	
	>75K	88.227	1.130		129.067	1.392		111.976	1.588		100.026	1.295	
Parity	Primiparous	83.948	1.092	0.223	110.366	1.214	0.071	96.236	1.315	0.256	90.586	1.208	0.598
	Multiparous	87.514	1.119		128.150	1.320		109.082	1.446		94.879	1.363	
Prior Gestational Diabetes Mellitus History	No	83.171	1.079	0.035	109.826	1.213	0.017	89.228	1.264	0.003	81.435	1.243	0.001
	Yes	89.148	1.126		132.940	1.322		121.256	1.430		107.179	1.270	
Family History of Diabetes	No	86.522	1.108	0.584	122.034	1.310	0.522	104.575	1.420	0.534	93.476	1.325	0.931
	Yes	84.302	1.131		113.239	1.206		95.097	1.306		92.490	1.218	
Prior Abortion	No	85.790	1.114	0.626	119.462	1.301	0.525	103.131	1.405	0.803	34.244	1.303	0.995
	Yes	88.155	1.054		130.321	1.187		107.889	1.387		93.168	1.358	
Prior Stillbirth	No	86.600	1.109	0.244	122.132	1.296	0.348	105.099	1.393	0.440	94.000	1.304	0.504
	Yes	81.183	1.109		107.458	1.231		91.496	1.479		85.490	1.324	
Periodontal Disease During Pregnancy	No	86.332	1.111	0.884	118.132	1.224	0.732	97.009	1.314	0.392	90.450	1.246	0.637
	Yes	85.884	1.111		121.754	1.324		107.083	1.436		94.443	1.333	
Depression During Pregnancy	No	85.824	1.108	0.745	121.268	1.301	0.735	101.332	1.423	0.337	93.504	1.312	0.811
	Yes	87.147	1.127		116.618	1.250		117.097	1.207		90.858	1.279	
Smoked Before or/and During Pregnancy	No	86.557	1.108	0.510	122.010	1.289	0.594	105.267	1.406	0.596	93.831	1.328	0.737
	Yes	84.302	1.117		115.746	1.310		98.288	1.388		90.659	1.224	
Smoking Now	No	86.427	1.110	0.236	121.219	1.297	0.561	103.493	1.406	0.925	93.047	1.311	0.957
	Yes	78.973	1.036		108.625	1.124		105.943	1.321		94.019	1.153	

Table 3: Perinatal Risk for the Abnormal Glucose Metabolism < Insulin Concentration > in Women at Two Years Postpartum – Univariate Analysis

		Fasting Insulin (uU/mL)			1/2-Hour Insulin (uU/mL)			1-Hour Insulin (uU/mL)			2-Hour Insulin (uU/mL)		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	8.575	2.062	0.804	54.272	2.103	0.885	52.442	1.694	0.740	46.768	2.056	0.828
	>35 years old	9.091	1.992		56.120	1.869		55.924	1.945		49.338	2.173	
Pre-pregnancy Body Mass Index	Underweight/Normal	9.536	2.155	0.720	60.582	2.159	0.651	57.940	1.721	0.293	53.234	2.164	0.581
	Overweight	7.726	1.853		48.999	1.858		41.963	1.705		39.837	2.135	
	Obese	8.247	1.960		49.186	1.810		60.166	1.993		44.966	1.862	
Race	Non-Hispanic White	8.923	2.137	0.933	60.334	2.082	0.666	54.217	1.844	0.525	51.152	2.216	0.466
	Non-Hispanic Black	8.770	1.953		49.784	1.979		56.244	1.749		47.059	1.898	
	Other	7.320	1.871		45.755	1.231		34.199	1.008		25.943	2.345	
Education	High School Degree or Lower	7.480	2.142	0.321	42.216	2.082	0.214	48.395	1.917	0.139	37.883	2.239	0.107
	College	10.055	1.813		64.380	1.947		61.008	1.655		58.178	1.965	
	Graduate School	6.128	3.280		51.424	1.637		32.095	1.762		28.574	1.353	
Marital Status	Married	8.356	1.994	0.612	56.843	1.951	0.723	50.189	1.795	0.380	45.911	2.057	0.695
	Single	9.402	2.086		52.394	2.104		59.323	1.764		50.501	2.158	
Family Income	<20K	9.883	1.778	0.833	60.153	1.582	0.620	52.258	1.249	0.959	48.456	1.643	0.440
	20-75K	8.556	1.774		52.082	1.734		52.268	1.628		43.630	1.883	
	>75K	9.834	2.226		66.048	2.220		55.473	2.075		61.887	2.373	
Parity	Primiparous	6.241	2.156	0.010	38.854	2.315	0.007	40.500	1.663	0.009	37.155	2.200	0.074
	Multiparous	11.113	1.738		69.986	1.561		65.457	1.727		56.838	1.921	
Prior Gestational Diabetes Mellitus History	No	6.854	1.969	0.022	44.447	2.227	0.048	42.721	1.752	0.009	34.550	2.128	0.003
	Yes	11.368	1.908		68.758	1.617		68.457	1.647		67.094	1.719	
Family History of Diabetes	No	8.784	2.092	0.900	55.880	2.073	0.780	53.672	1.772	0.945	48.096	2.182	0.939
	Yes	9.146	1.801		51.131	1.784		52.699	2.011		46.871	1.730	
Prior Abortion	No	8.690	2.047	0.814	53.453	2.040	0.462	52.541	1.794	0.472	47.252	2.141	0.799
	Yes	9.500	1.899		70.253	1.596		65.634	1.700		52.253	1.598	
Prior Stillbirth	No	8.668	2.047	0.761	53.796	2.067	0.570	53.250	1.778	0.768	48.192	2.125	0.816
	Yes	9.724	1.890		66.453	1.208		58.352	1.952		43.974	1.809	
Periodontal Disease During Pregnancy	No	7.532	2.049	0.345	47.356	1.806	0.348	44.732	1.748	0.162	40.642	1.925	0.339
	Yes	9.464	2.005		59.228	2.089		58.927	1.774		51.744	2.156	
Depression During Pregnancy	No	8.897	2.071	0.769	56.764	2.075	0.504	53.490	1.787	0.902	49.829	2.131	0.400
	Yes	8.104	1.794		46.076	1.539		55.230	1.830		37.732	1.787	
Smoked Before or/and During Pregnancy	No	8.493	2.130	0.608	53.560	1.963	0.674	53.458	1.768	0.914	45.540	2.000	0.470
	Yes	9.764	1.648		59.955	2.189		54.757	1.883		55.874	2.408	
Smoking Now	No	8.736	2.045	0.882	53.893	2.010	0.469	52.710	1.793	0.366	46.684	2.086	0.420
	Yes	9.437	1.694		78.093	1.858		77.339	1.322		72.168	2.150	

Table 4: Perinatal Risk for the Abnormal Glucose Metabolism < Insulin Resistance Indices > in Women at Two Years Postpartum – Univariate Analysis

		HOMA-IR			ISOGTT			IGI/HOMA-IR			IS-SI		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	1.799	2.189	0.734	5.719	2.010	0.678	0.976	2.636	0.395	559.979	2.607	0.376
	>35 years old	1.964	2.151		5.176	2.153		0.724	3.288		407.443	3.497	
Pre-pregnancy Body Mass Index	Underweight/Normal	2.034	2.319	0.709	4.978	2.101	0.556	0.965	3.270	0.332	556.741	3.318	0.306
	Overweight	1.590	1.941		6.745	1.987		1.040	2.297		590.636	2.434	
	Obese	1.793	2.100		5.556	2.056		0.530	2.418		293.096	2.387	
Race	Non-Hispanic White	1.903	2.255	0.889	5.200	2.124	0.694	0.862	3.146	0.878	464.983	3.169	0.779
	Non-Hispanic Black	1.867	2.121		5.643	2.028		0.840	2.750		505.577	2.822	
	Other	1.434	2.096		8.180	1.709		1.267	1.788		822.542	2.200	
Education	High School Degree or Lower	1.530	2.345	0.256	6.883	2.235	0.131	0.916	2.966	0.475	533.629	3.087	0.568
	College	2.194	1.884		4.568	1.846		0.774	2.950		441.068	3.007	
	Graduate School	1.230	3.549		8.722	2.318		1.708	1.745		877.432	1.812	
Marital Status	Married	1.790	2.102	0.712	5.645	2.001	0.796	0.905	3.009	0.786	498.748	3.094	0.965
	Single	1.967	2.277		5.308	2.162		0.823	2.762		490.929	2.802	
Family Income	<20K	1.976	1.949	0.843	5.562	1.773	0.700	1.654	2.998	0.437	1011.229	3.323	0.350
	20-75K	1.826	1.822		5.721	1.749		0.808	2.510		482.043	2.534	
	>75K	2.144	2.444		4.608	2.378		0.727	3.853		384.701	3.915	
Parity	Primiparous	1.292	2.252	0.011	7.855	2.052	0.008	1.229	2.828	0.088	715.871	2.673	0.074
	Multiparous	2.399	1.888		4.297	1.852		0.684	2.769		383.638	2.954	
Prior Gestational Diabetes Mellitus History	No	1.405	2.055	0.017	7.532	1.972	0.004	1.235	2.341	0.032	708.748	2.338	0.031
	Yes	2.502	2.051		3.956	1.843		0.602	3.134		339.984	3.251	
Family History of Diabetes	No	1.874	2.241	0.968	5.423	2.117	0.856	0.876	3.040	0.912	495.120	3.132	0.962
	Yes	1.901	1.905		5.757	1.895		0.830	2.425		506.893	2.325	
Prior Abortion	No	1.839	2.191	0.780	5.603	2.090	0.652	0.887	2.996	0.739	508.162	3.032	0.671
	Yes	2.064	1.994		4.710	1.750		0.734	1.880		397.462	2.232	
Prior Stillbirth	No	1.852	2.191	0.906	5.511	2.087	0.973	0.843	2.972	0.588	478.569	2.993	0.557
	Yes	1.944	2.016		5.439	1.842		1.146	2.066		672.162	2.590	
Periodontal Disease During Pregnancy	No	1.603	2.166	0.398	6.610	2.042	0.265	0.836	2.431	0.870	475.658	2.367	0.869
	Yes	2.005	2.158		5.022	2.043		0.888	3.142		505.779	3.267	
Depression During Pregnancy	No	1.883	2.210	0.824	5.410	2.094	0.729	0.846	2.805	0.706	472.057	2.872	0.516
	Yes	1.743	1.953		6.052	1.880		1.013	3.562		647.164	3.503	
Smoked Before or/and During Pregnancy	No	1.812	2.288	0.700	5.610	2.109	0.765	0.865	2.790	0.954	489.361	2.900	0.896
	Yes	2.033	1.734		5.164	1.907		0.886	3.355		516.668	3.244	
Smoking Now	No	1.862	1.633	0.982	5.546	2.078	0.781	1.287	2.934	0.597	624.593	3.007	0.759
	Yes	1.838	2.191		4.784	1.621		0.852	1.607		489.361	1.625	

Table 5: Perinatal Risk for the Abnormal Glucose Metabolism in Women at Two Years Postpartum – Multivariate Analysis

	Fast Glucose		Half-hour Glucose		One-hour Glucose		Two-hour Glucose		Fast Insulin		Half-hour Insulin		One-hour Insulin		Two-hour Insulin		HOMA-IR		ISOGTT		IGI/HOMA-IR		IS-SI	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Age	0.876	0.563	0.845	0.376	0.913	0.691	0.791	0.303	0.964	0.882	0.850	0.552	1.020	0.937	0.841	0.513	0.949	0.836	1.093	0.718	0.957	0.850	0.977	0.921
Pre-pregnancy Body Mass Index	1.250	0.488	1.404	0.209	1.285	0.442	1.784	0.081	0.688	0.300	0.614	0.212	0.865	0.679	0.958	0.907	0.732	0.389	1.251	0.518	0.710	0.299	0.664	0.212
Race	0.988	0.978	0.925	0.831	0.773	0.569	0.502	0.130	1.269	0.629	1.287	0.635	0.976	0.960	0.957	0.932	1.246	0.659	0.925	0.872	1.064	0.891	1.212	0.667
Education	0.777	0.422	0.845	0.514	0.719	0.305	0.883	0.687	0.722	0.352	0.910	0.800	0.623	0.180	0.652	0.249	0.717	0.347	1.430	0.296	1.100	0.764	1.099	0.764
Marital Status	0.901	0.822	1.054	0.889	1.189	0.712	1.735	0.236	0.897	0.832	0.674	0.477	0.871	0.786	1.099	0.861	0.891	0.823	1.115	0.827	0.699	0.449	0.689	0.425
Family Income	1.094	0.804	0.958	0.887	1.001	0.998	1.197	0.616	0.844	0.674	0.706	0.427	0.868	0.724	1.283	0.558	0.867	0.725	1.150	0.723	0.939	0.864	0.890	0.749
Parity	1.338	0.268	1.247	0.305	1.095	0.726	0.950	0.841	1.388	0.261	1.365	0.318	1.254	0.429	1.063	0.838	1.406	0.247	0.739	0.285	0.969	0.907	0.963	0.881
Prior Gestational Diabetes Mellitus History	1.696	0.063	2.128	0.004	1.984	0.022	1.811	0.037	1.481	0.197	1.347	0.356	1.530	0.161	1.508	0.198	1.553	0.156	0.590	0.083	0.529	0.031	0.548	0.038
Family History of Diabetes	0.704	0.163	0.852	0.428	0.731	0.215	1.013	0.957	0.676	0.160	0.890	0.687	0.662	0.136	0.783	0.391	0.664	0.147	1.446	0.174	1.204	0.455	1.140	0.592
Prior Abortion	0.909	0.699	0.984	0.937	1.034	0.893	1.188	0.479	0.884	0.651	0.972	0.924	1.094	0.737	0.968	0.908	0.880	0.641	1.057	0.837	1.024	0.923	0.990	0.969
Prior Stillbirth	0.647	0.119	0.557	0.017	0.732	0.261	0.679	0.156	1.067	0.826	0.918	0.787	1.102	0.742	1.003	0.992	0.995	0.986	1.087	0.773	1.369	0.259	1.409	0.214
Periodontal Disease During Pregnancy	0.843	0.508	0.977	0.915	1.007	0.980	1.220	0.435	0.969	0.910	1.081	0.800	1.057	0.846	0.976	0.935	0.946	0.848	0.991	0.975	1.112	0.684	1.106	0.697
Depression During Pregnancy	1.201	0.498	0.737	0.181	1.013	0.963	0.951	0.851	0.929	0.804	0.742	0.357	0.953	0.871	0.860	0.630	0.958	0.887	1.123	0.689	1.358	0.272	1.426	0.201
Smoked Before or/and During Pregnancy	0.914	0.736	0.933	0.754	0.984	0.951	0.821	0.455	1.326	0.346	1.050	0.877	1.051	0.864	0.947	0.861	1.280	0.412	0.876	0.647	0.872	0.612	0.978	0.933
Smoking Now	0.737	0.271	0.688	0.110	0.697	0.202	0.770	0.335	0.948	0.859	1.221	0.539	1.082	0.791	1.170	0.619	0.910	0.756	1.055	0.855	1.571	0.116	1.490	0.157
Adjusted R Square	0.098		0.387		0.072		0.128		-0.109		-0.281		-0.088		-0.219		-0.132		-0.057		0.070		0.092	

Table 6: Perinatal Risk for the Abnormal Glucose Metabolism in Women at Two Years Postpartum – Linear Regression Models

	Fast Glucose		Half-hour Glucose		One-hour Glucose		Two-hour Glucose		Fast Insulin		Half-hour Insulin		One-hour Insulin		Two-hour Insulin		HOMA-IR		ISOGTT		IGI/HOMA-IR		IS-SI	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Age																								
Pre-pregnancy Body Mass Index			11.156	0.024							0.739	0.085									0.088	0.023	0.119	0.044
Race																								
Education					0.676	0.033			0.632	0.021			0.656	0.026	0.665	0.037	0.637	0.021	1.523	0.023				
Marital Status																					0.738	0.071		
Family Income																								
Parity											1.496	0.025												
Prior Gestational Diabetes Mellitus History	1.747	0.003	2.125	0.000	1.822	0.001	1.887	0.000	1.548	0.016			1.657	0.004	1.647	0.006	1.587	0.010	0.582	0.002	0.513	0.000	0.534	0.001
Family History of Diabetes					0.722	0.064			0.670	0.036			0.640	0.016	0.700	0.058	0.662	0.029	1.545	0.016				
Prior Abortion																								
Prior Stillbirth	0.657	0.017	0.026	0.001			0.747	0.080													1.511	0.019	1.481	0.023
Periodontal Disease During Pregnancy																								
Depression During Pregnancy			0.725	0.021																	1.496	0.016	1.485	0.014
Smoked Before or/and During Pregnancy																								
Smoking Now	0.714	0.044	0.078	0.017																	1.495	0.019	6.517	0.073
Adjusted R Square	0.300		0.523		0.332		0.326		0.231		0.173		0.301		0.245		0.254		0.329		0.386		0.384	

Table 7: Perinatal Risk for the Abnormal Glucose Metabolism < Glucose Concentration > in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		Fasting Glucose (mg/dL)						1/2-hour Glucose (mg/dL)					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	83.999	1.089	0.386	86.652	1.149	0.284	112.460	1.192	0.416	123.717	1.337	0.247
	>35 years old	81.272	1.044		92.010	1.093		103.897	1.269		144.005	1.295	
Pre-pregnancy Body Mass Index	Underweight/Normal	82.220	1.057	0.013	89.756	1.116	0.849	100.847	1.218	0.087	135.775	1.325	0.687
	Overweight	79.392	1.060		89.864	1.114		110.167	1.196		119.200	1.309	
	Obese	89.783	1.080		85.824	1.225		127.549	1.134		141.373	1.425	
Race	Non-Hispanic White	82.245	1.061	0.474	89.113	1.117	0.985	105.036	1.194	0.673	132.410	1.323	0.929
	Non-Hispanic Black	84.733	1.086		89.220	1.158		114.263	1.243		134.115	1.355	
	Other	79.234	1.123					107.652	1.193				
Education	High School Degree or Lower	82.583	1.095	0.889	84.394	1.234	0.270	111.989	1.221	0.910	140.808	1.594	0.327
	College	83.957	1.066		91.496	1.097		107.889	1.231		136.770	1.270	
	Graduate School	81.998	1.000		80.697	1.130		105.996	1.000		100.023	1.218	
Marital Status	Married	83.329	1.060	0.906	90.206	1.111	0.585	106.070	1.177	0.389	135.545	1.321	0.704
	Single	82.980	1.102		87.357	1.156		114.583	1.256		128.612	1.348	
Family Income	<20K	87.383	1.076	0.258	75.301	1.109	0.097	97.349	1.297	0.146	108.083	1.132	0.257
	20-75K	83.864	1.062		90.640	1.101		113.318	1.158		129.166	1.360	
	>75K	80.455	1.039		92.388	1.132		93.056	1.208		152.003	1.291	
Parity	Primiparous	82.591	1.080	0.663	86.999	1.114	0.607	104.941	1.218	0.256	123.334	1.155	0.499
	Multiparous	83.881	1.081		89.927	1.133		116.106	1.202		136.551	1.369	
Family History of Diabetes	No	82.352	1.070	0.171	91.506	1.115	0.102	106.837	1.204	0.134	141.897	1.319	0.048
	Yes	87.962	1.118		80.786	1.153		128.355	1.214		99.893	1.057	
Prior Abortion	No	82.914	1.082	0.602	88.943	1.133	0.813	109.300	1.224	0.750	131.263	1.339	0.577
	Yes	85.490	1.025		90.913	1.064		114.652	1.117		148.131	1.105	
Prior Stillbirth	No	83.229	1.081	0.854	90.786	1.119	0.127	109.870	1.220	0.970	138.490	1.312	0.146
	Yes	81.998	1.000		80.915	1.134		108.995	1.000		106.943	1.289	
Periodontal Disease During Pregnancy	No	84.175	1.056	0.615	88.917	1.155	0.950	113.296	1.079	0.611	124.039	1.340	0.477
	Yes	82.632	1.090		89.255	1.118		107.997	1.266		137.277	1.321	
Depression During Pregnancy	No	82.914	1.062	0.680	89.032	1.134	0.917	108.723	1.187	0.594	136.169	1.346	0.864
	Yes	84.622	1.171		89.756	1.095		116.257	1.405		116.991	1.099	
Smoked Before or/and During Pregnancy	No	84.074	1.084	0.281	89.113	1.123	0.979	113.148	1.226	0.243	131.565	1.326	0.762
	Yes	80.520	1.052		89.273	1.158		100.424	1.148		138.241	1.359	
Smoking Now	No				90.432	1.124	0.131				136.142	1.329	0.292
	Yes				78.973	1.036					108.625	1.124	

Table 8: Perinatal Risk for the Abnormal Glucose Metabolism < Glucose Concentration > in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		1-hour Glucose (mg/dL)						2-hour Glucose (mg/dL)					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	92.250	1.228	0.346	107.093	1.431	0.112	83.154	1.196	0.527	101.393	1.303	0.298
	>35 years old	82.558	1.228		139.218	1.377		77.556	1.355		114.000	1.226	
Pre-pregnancy Body Mass Index	Underweight/Normal	80.721	1.250	0.107	128.163	1.446	0.583	78.202	1.276	0.538	104.920	1.254	0.776
	Overweight	89.739	1.253		102.504	1.355		79.854	1.253		116.048	1.265	
	Obese	106.155	1.214		121.583	1.541		89.667	1.180		104.983	1.438	
Race	Non-Hispanic White	84.546	1.310	0.688	120.856	1.430	0.954	80.511	1.311	0.894	111.419	1.262	0.310
	Non-Hispanic Black	93.448	1.262		122.156	1.478		83.121	1.207		98.534	1.286	
	Other	87.909	1.066					76.907	1.269				
Education	High School Degree or Lower	92.666	1.260	0.740	129.970	1.763	0.371	82.517	1.217	0.958	94.085	1.450	0.101
	College	86.730	1.292		125.487	1.386		80.632	1.300		114.514	1.215	
	Graduate School	78.996	1.000		85.944	1.051		77.999	1.000		81.974	1.035	
Marital Status	Married	82.484	1.217	0.098	124.213	1.432	0.713	78.602	1.235	0.438	112.067	1.273	0.300
	Single	98.239	1.286		116.373	1.461		85.021	1.260		99.295	1.260	
Family Income	<20K	110.002	1.144	0.430	97.700	1.481	0.401	94.869	1.394	0.645	76.585	1.159	0.070
	20-75K	91.597	1.226		122.474	1.328		81.483	1.307		117.144	1.234	
	>75K	70.945	1.192		140.682	1.463		77.960	1.038		113.307	1.253	
Parity	Primiparous	88.102	1.254	0.796	116.863	1.338	0.796	85.345	1.189	0.299	103.275	1.180	0.698
	Multiparous	90.631	1.293		122.867	1.473		76.892	1.299		108.603	1.303	
Family History of Diabetes	No	85.987	1.245	0.093	130.543	1.410	0.042	79.321	1.253	0.207	112.584	1.245	0.154
	Yes	110.090	1.278		82.146	1.259		94.500	1.076		90.523	1.350	
Prior Abortion	No	89.837	1.280	0.711	119.367	1.448	0.591	82.508	1.253	0.434	105.763	1.281	0.497
	Yes	83.990	1.017		138.587	1.302		72.363	1.092		119.953	1.145	
Prior Stillbirth	No	90.378	1.263	0.300	125.713	1.414	0.323	81.786	1.250	0.709	110.908	1.240	0.155
	Yes	70.000	1.000		100.043	1.532		75.001	1.000		89.300	1.387	
Periodontal Disease During Pregnancy	No	91.909	1.227	0.690	103.306	1.415	0.192	84.809	1.217	0.554	97.505	1.270	0.252
	Yes	87.821	1.291		130.569	1.419		79.671	1.263		111.967	1.265	
Depression During Pregnancy	No	86.091	1.249	0.105	120.494	1.473	0.932	82.072	1.253	0.714	107.404	1.286	0.124
	Yes	109.322	1.259		125.437	1.158		77.906	1.225		105.975	1.220	
Smoked Before or/and During Pregnancy	No	92.684	1.273	0.218	119.546	1.468	0.748	81.345	1.268	0.971	108.245	1.294	0.738
	Yes	79.615	1.206		127.894	1.313		81.687	1.182		103.275	1.192	
Smoking Now	No				123.199	1.447	0.587				108.842	1.279	0.428
	Yes				105.943	1.321					94.019	1.153	

Table 9: Perinatal Risk for the Abnormal Glucose Metabolism < Insulin Concentration > in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		Fasting Insulin (uU/mL)						1/2-hour Insulin (uU/mL)					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	7.516	2.052	0.367	10.315	2.065	0.505	45.682	2.380	0.823	69.075	1.590	0.966
	>35 years old	5.528	1.760		12.666	1.764		41.700	1.992		68.402	1.694	
Pre-pregnancy Body Mass Index	Underweight/Normal	7.279	2.122	0.867	11.678	2.107	0.964	52.668	2.821	0.642	67.296	1.676	0.684
	Overweight	6.018	1.673		11.239	1.862		34.796	1.454		81.892	1.780	
	Obese	7.191	2.280		10.366	1.375		43.939	2.119		59.359	1.149	
Race	Non-Hispanic White	6.323	2.145	0.918	11.030	2.019	0.773	49.685	2.788	0.874	67.993	1.636	0.886
	Non-Hispanic Black	7.216	1.973		12.139	1.744		40.423	2.043		70.443	1.647	
	Other	7.320	1.871					45.755	1.231				
Education	High School Degree or Lower	6.842	2.219	0.939	10.067	1.956	0.399	36.866	2.178	0.488	66.301	1.380	0.974
	College	7.053	1.832		12.632	1.616		56.707	2.334		69.853	1.715	
	Graduate School	5.400	1.000		6.527	5.327		32.201	1.000		64.981	1.486	
Marital Status	Married	6.296	1.717	0.549	10.832	2.076	0.682	49.269	2.288	0.540	64.806	1.618	0.498
	Single	7.605	2.312		12.351	1.665		39.193	2.217		76.104	1.648	
Family Income	<20K	14.276	1.951	0.215	6.841	1.075	0.580	65.151	2.152	0.776	55.540	1.147	0.806
	20-75K	6.616	1.620		12.353	1.664		44.532	1.710		65.144	1.694	
	>75K	7.246	1.866		11.456	2.390		55.026	3.426		72.363	1.762	
Parity	Primiparous	6.104	2.241	0.412	6.552	2.144	0.021	36.948	2.668	0.265	43.397	1.586	0.008
	Multiparous	7.897	1.623		13.842	1.632		55.712	1.589		81.037	1.461	
Family History of Diabetes	No	6.338	1.939	0.228	12.713	1.926	0.250	43.913	2.278	0.878	73.420	1.652	0.363
	Yes	10.680	2.035		7.832	1.710		47.594	2.258		54.927	1.491	
Prior Abortion	No	6.768	2.043	0.809	11.325	1.888	0.942	42.713	2.308	0.519	67.789	1.598	0.718
	Yes	7.684	1.096		11.745	2.780		63.612	1.051		77.595	2.188	
Prior Stillbirth	No	6.976	1.996	0.624	11.216	1.971	0.840	43.939	2.273	0.788	68.409	1.686	0.919
	Yes	4.900	1.000		12.220	1.721		55.301	1.000		70.647	1.193	
Periodontal Disease During Pregnancy	No	5.556	2.153	0.322	10.739	1.646	0.803	37.720	1.989	0.516	61.744	1.403	0.523
	Yes	7.675	1.871		11.671	2.057		48.555	2.384		72.255	1.714	
Depression During Pregnancy	No	6.433	1.939	0.333	12.556	1.909	0.124	42.927	2.323	0.656	76.394	1.557	0.023
	Yes	9.815	2.203		6.691	1.415		54.141	1.790		39.217	1.244	
Smoked Before or/and During Pregnancy	No	6.443	2.067	0.494	11.194	2.020	0.846	41.717	2.097	0.554	68.772	1.666	0.997
	Yes	8.252	1.692		12.048	1.548		53.769	2.810		68.697	1.508	
Smoking Now	No				11.621	1.952	0.679				67.735	1.622	0.704
	Yes				9.437	1.694					78.093	1.858	

Table 10: Perinatal Risk for the Abnormal Glucose Metabolism < Insulin Concentration > in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		1-hour Insulin (uU/mL)						2-hour Insulin (uU/mL)					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	47.021	1.767	0.253	61.099	1.561	0.308	38.896	2.239	0.296	60.534	1.668	0.398
	>35 years old	34.158	1.676		77.680	1.735		26.206	1.801		75.234	1.788	
Pre-pregnancy Body Mass Index	Underweight/Normal	44.683	1.695	0.471	70.408	1.627	0.719	38.795	2.518	0.744	67.498	1.759	0.998
	Overweight	34.080	1.560		57.340	1.741		28.250	1.923		66.720	1.917	
	Obese	51.682	2.116		77.502	1.863		35.712	1.845		66.010	1.646	
Race	Non-Hispanic White	39.555	1.904	0.686	65.818	1.690	0.628	33.845	2.776	0.839	65.957	1.671	0.845
	Non-Hispanic Black	47.503	1.748		74.537	1.604		37.196	1.709		69.644	1.912	
	Other	34.199	1.008					25.943	2.345				
Education	High School Degree or Lower	42.462	1.852	0.516	74.851	1.974	0.221	31.582	2.031	0.729	69.463	2.610	0.101
	College	46.122	1.670		73.032	1.526		39.773	2.364		74.284	1.478	
	Graduate School	22.801	1.000		38.077	1.979		23.901	1.000		31.243	1.443	
Marital Status	Married	38.575	1.713	0.382	63.886	1.710	0.445	32.750	2.212	0.736	62.571	1.646	0.478
	Single	48.400	1.811		77.069	1.553		36.885	2.110		75.626	1.878	
Family Income	<20K	53.006	1.277	0.688	51.522	1.344	0.751	58.774	2.151	0.525	39.949	1.073	0.430
	20-75K	41.763	1.444		72.024	1.610		31.877	1.682		68.313	1.671	
	>75K	36.288	2.248		68.587	1.884		44.420	3.400		73.047	1.937	
Parity	Primiparous	38.248	1.688	0.343	45.929	1.660	0.033	33.886	2.468	0.903	45.499	1.591	0.059
	Multiparous	48.906	1.833		78.949	1.534		35.378	1.781		77.084	1.666	
Family History of Diabetes	No	40.061	1.593	0.231	74.776	1.658	0.123	32.622	2.139	0.433	74.679	1.725	0.164
	Yes	61.516	2.743		45.146	1.435		47.837	2.173		45.925	1.467	
Prior Abortion	No	42.645	1.795	0.966	65.536	1.666	0.279	34.429	2.221	0.952	66.069	1.766	0.727
	Yes	43.445	1.475		99.166	1.114		35.673	1.098		76.531	1.299	
Prior Stillbirth	No	43.450	1.770	0.571	67.803	1.640	0.853	35.195	2.162	0.645	69.986	1.731	0.449
	Yes	31.000	1.000		72.046	1.889		24.301	1.000		53.592	1.718	
Periodontal Disease During Pregnancy	No	32.944	1.581	0.131	63.918	1.587	0.696	28.318	1.857	0.402	61.954	1.516	0.675
	Yes	49.141	1.779		70.661	1.700		38.455	2.275		69.616	1.827	
Depression During Pregnancy	No	39.793	1.642	0.184	73.244	1.654	0.180	34.543	2.137	0.998	73.538	1.718	0.088
	Yes	63.892	2.357		47.746	1.401		34.588	2.450		41.157	1.143	
Smoked Before or/and During Pregnancy	No	44.208	1.737	0.650	64.644	1.714	0.347	32.246	1.909	0.494	64.315	1.763	0.525
	Yes	38.563	1.895		84.885	1.284		42.504	2.954		78.642	1.591	
Smoking Now	No				67.485	1.687	0.726				66.526	1.717	0.847
	Yes				77.339	1.322					72.168	2.150	

Table 11: Perinatal Risk for the Abnormal Glucose Metabolism < HOMA-IR and ISOGTT > in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		HOMA-IR						ISOGTT					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	1.556	2.141	0.348	2.206	2.241	0.436	6.805	2.034	0.320	4.483	1.889	0.362
	>35 years old	1.107	1.834		2.877	1.861		9.544	1.801		3.442	1.799	
Pre-pregnancy Body Mass Index	Underweight/Normal	1.474	2.194	0.782	2.590	2.293	0.944	7.032	2.068	0.643	3.842	1.952	0.965
	Overweight	1.179	1.732		2.491	1.838		9.411	1.721		4.093	1.834	
	Obese	1.590	2.423		2.192	1.672		6.525	2.245		4.249	1.786	
Race	Non-Hispanic White	1.281	2.177	0.902	2.428	2.141	0.798	7.974	2.203	0.927	3.997	1.860	0.917
	Non-Hispanic Black	1.507	2.100		2.670	1.968		7.079	1.952		3.868	1.912	
	Other	1.434	2.096					8.180	1.709				
Education	High School Degree or Lower	1.393	2.389	0.935	2.094	2.381	0.338	7.825	2.180	0.794	4.490	2.433	0.223
	College	1.459	1.836		2.851	1.670		6.912	1.856		3.499	1.574	
	Graduate School	1.090	1.000		1.307	5.961		11.150	1.000		7.714	3.159	
Marital Status	Married	1.292	1.722	0.580	2.414	2.214	0.786	8.105	1.764	0.607	4.051	1.909	0.831
	Single	1.556	2.503		2.659	1.856		6.887	2.275		3.797	1.811	
Family Income	<20K	3.076	2.101	0.193	1.270	1.034	0.449	4.140	2.187	0.391	7.474	1.160	0.358
	20-75K	1.367	1.644		2.760	1.650		7.742	1.505		3.713	1.586	
	>75K	1.438	1.836		2.617	2.665		7.622	2.373		3.583	2.228	
Parity	Primiparous	1.242	2.314	0.413	1.408	2.304	0.330	8.461	2.165	0.412	6.670	1.876	0.021
	Multiparous	1.633	1.738		3.072	1.773		6.534	1.741		3.282	1.655	
Family History of Diabetes	No	1.286	1.996	0.199	2.872	2.068	0.188	8.132	1.894	0.239	3.427	1.813	0.077
	Yes	2.318	2.263		1.559	1.656		4.879	2.426		6.795	1.482	
Prior Abortion	No	1.383	2.137	0.777	2.487	2.037	0.921	7.628	2.046	0.811	4.041	1.868	0.669
	Yes	1.619	1.125		2.630	2.963		6.725	1.167		3.298	1.893	
Prior Stillbirth	No	1.431	2.086	0.631	2.514	2.115	0.946	7.416	2.002	0.665	3.874	1.891	0.743
	Yes	0.990	1.000		2.435	1.932		10.140	1.000		4.419	1.732	
Periodontal Disease During Pregnancy	No	1.152	2.241	0.379	2.358	1.763	0.816	9.241	2.025	0.336	4.471	1.708	0.568
	Yes	1.563	1.971		2.571	2.222		6.747	1.947		3.739	1.927	
Depression During Pregnancy	No	1.314	1.989	0.337	2.760	2.077	0.175	7.965	1.903	0.395	3.586	1.843	0.108
	Yes	2.051	2.577		1.481	1.461		5.487	2.570		6.675	1.316	
Smoked Before or/and During Pregnancy	No	1.335	2.192	0.595	2.461	2.174	0.853	7.755	2.019	0.749	4.058	1.935	0.735
	Yes	1.639	1.682		2.661	1.688		6.900	1.955		3.594	1.557	
Smoking Now	No				2.594	2.102	0.537				3.868	1.884	0.655
	Yes				1.838	1.633					4.784	1.621	

Table 12: Perinatal Risk for the Abnormal Glucose Metabolism <IGI/HOMA-IR and IS-SI> in Women with Prior GDM at Two Years Postpartum – Univariate Analysis

		IGI/HOMA-IR						IS-SI					
		Women Without Prior GDM			Women With Prior GDM			Women Without Prior GDM			Women With Prior GDM		
		MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value	MEAN	SD	P-Value
Age	<=35 years old	1.144	2.479	0.553	0.783	2.877	0.305	652.427	2.439	0.520	452.144	2.869	0.279
	>35 years old	1.476	2.102		0.450	3.402		859.714	2.184		247.695	3.632	
Pre-pregnancy Body Mass Index	Underweight/Normal	2.268	2.006	0.005	0.509	2.930	0.303	1305.707	2.010	0.005	293.771	3.018	0.306
	Overweight	0.885	1.730		1.325	3.324		503.005	1.858		751.446	3.548	
	Obese	0.616	2.014		0.413	3.539		356.060	1.824		211.876	3.646	
Race	Non-Hispanic White	1.388	2.296	0.879	0.643	3.463	0.720	745.832	2.067	0.931	347.686	3.641	0.907
	Non-Hispanic Black	1.119	2.622		0.521	2.663		660.436	2.760		323.889	2.708	
	Other	1.267	1.788					822.542	2.200				
Education	High School Degree or Lower	1.087	2.679	0.763	0.517	4.234	0.249	658.128	2.697	0.763	265.284	4.472	0.275
	College	1.451	2.131		0.517	2.963		810.134	2.102		298.360	3.115	
	Graduate School	1.030	1.000		2.199	1.625		446.215	1.000		1230.407	1.158	
Marital Status	Married	1.441	1.994	0.384	0.591	3.513	0.927	804.403	1.903	0.476	321.790	3.736	0.798
	Single	1.022	2.786		0.622	2.743		607.165	2.918		373.643	2.677	
Family Income	<20K	2.328	5.700	0.268	1.175	1.413	0.599	1658.386	5.866	0.223	616.587	1.595	0.572
	20-75K	1.022	2.017		0.577	3.120		599.622	1.988		352.905	3.270	
	>75K	1.983	1.913		0.440	3.848		1079.982	1.923		229.591	3.869	
Parity	Primiparous	1.517	2.410	0.242	0.774	3.724	0.582	884.215	2.406	0.206	449.799	3.136	0.552
	Multiparous	0.960	2.201		0.550	3.048		540.827	2.169		307.661	3.378	
Family History of Diabetes	No	1.507	2.083	0.008	0.474	3.212	0.080	850.224	2.147	0.018	268.298	3.351	0.081
	Yes	0.399	1.763		1.726	1.204		252.725	1.734		1016.784	1.162	
Prior Abortion	No	1.237	2.442	0.975	0.624	3.342	0.704	706.272	2.436	0.957	358.633	3.433	0.580
	Yes	1.212	1.547		0.445	1.016		731.575	1.612		215.961	1.594	
Prior Stillbirth	No	1.207	2.382	0.621	0.551	3.305	0.447	694.228	2.380	0.647	307.661	3.317	0.409
	Yes	1.890	1.000		0.970	2.202		1050.477	1.000		579.172	3.025	
Periodontal Disease During Pregnancy	No	0.963	1.775	0.352	0.709	3.316	0.684	533.895	1.617	0.285	415.673	3.353	0.627
	Yes	1.411	2.617		0.558	3.181		825.509	2.656		309.854	3.328	
Depression During Pregnancy	No	1.243	1.989	0.934	0.563	3.291	0.565	702.749	1.912	0.919	309.265	3.482	0.435
	Yes	1.187	5.794		0.865	2.544		743.523	6.471		563.349	1.859	
Smoked Before or/and During Pregnancy	No	1.152	2.305	0.544	0.650	3.139	0.587	641.494	2.367	0.378	373.269	3.333	0.519
	Yes	1.519	2.615		0.452	3.525		955.753	2.278		239.535	3.225	
Smoking Now	No				0.551	3.228	0.334				316.524	3.400	0.456
	Yes				1.287	1.607					624.593	1.625	

Table 13: The Interactions between Prior GDM and Potential Risk Factors on Glucose Concentration -- Multivariate Analysis

	Fast Glucose				Half-hour Glucose				One-hour Glucose				Two-hour Glucose			
	Crude		Adjusted		Crude		Adjusted		Crude		Adjusted		Crude		Adjusted	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Gestational Diabetes Mellitus History	1.994	0.324	1.423	0.656	1.714	0.423	1.742	0.423	2.184	0.239	2.465	0.207	1.461	0.547	1.361	0.663
Pre-pregnancy Body Mass Index	1.278	0.277	1.203	0.477	1.330	0.191	1.363	0.177	1.250	0.293	1.195	0.441	1.146	0.502	1.149	0.549
Gestational Diabetes Mellitus * Body Mass Index	0.714	0.627	0.986	0.986	0.879	0.847	0.935	0.923	0.739	0.643	0.705	0.623	1.190	0.781	1.231	0.771
Gestational Diabetes Mellitus History	1.288	0.347	1.002	0.995	1.379	0.221	1.519	0.173	1.533	0.098	1.728	0.078	1.441	0.135	1.357	0.306
Parity	1.077	0.736	0.833	0.490	1.219	0.356	1.249	0.358	1.043	0.839	0.972	0.907	0.822	0.322	0.733	0.193
Gestational Diabetes Mellitus * Parity	1.087	0.801	1.616	0.231	1.001	0.997	0.975	0.944	1.033	0.919	1.029	0.936	1.328	0.337	1.448	0.298
Gestational Diabetes Mellitus History	1.664	0.003	1.626	0.027	1.744	0.001	1.848	0.003	1.870	0.000	2.028	0.001	1.939	0.000	1.908	0.002
Family Diabetes History	1.262	0.273	0.905	0.710	1.300	0.200	1.006	0.982	1.311	0.166	0.990	0.966	1.274	0.216	1.123	0.634
Gestational Diabetes Mellitus * Family Diabetes History	0.608	0.030	0.780	0.367	0.568	0.011	0.726	0.205	0.563	0.007	0.698	0.138	0.670	0.055	0.739	0.228

*Adjusted result were calculated after adjustment by maternal age, race, education and family income.

Table 14: The Interactions between Prior GDM and Potential Risk Factors on Insulin Concentration -- Multivariate Analysis

	Fast Insulin				Half-hour Insulin				One-hour Insulin				Two-hour Insulin			
	Crude		Adjusted		Crude		Adjusted		Crude		Adjusted		Crude		Adjusted	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Gestational Diabetes Mellitus History	1.115	0.876	0.665	0.609	0.853	0.821	0.457	0.338	0.945	0.933	0.748	0.702	0.824	0.769	0.488	0.332
Pre-pregnancy Body Mass Index	0.905	0.656	0.751	0.276	0.794	0.310	0.633	0.094	0.893	0.605	0.791	0.350	0.827	0.373	0.739	0.215
Gestational Diabetes Mellitus * Body Mass Index	1.292	0.714	2.266	0.314	1.605	0.501	2.883	0.204	1.619	0.479	2.266	0.291	1.939	0.317	3.274	0.119
Gestational Diabetes Mellitus History	1.052	0.836	0.769	0.392	1.125	0.641	0.745	0.372	1.175	0.510	1.004	0.990	1.226	0.411	0.937	0.831
Parity	1.201	0.369	0.850	0.503	1.344	0.158	1.064	0.813	1.236	0.290	0.999	0.995	1.029	0.885	0.786	0.321
Gestational Diabetes Mellitus * Parity	1.405	0.265	2.351	0.025	1.162	0.627	1.872	0.117	1.284	0.404	0.999	0.101	1.379	0.291	2.009	0.062
Gestational Diabetes Mellitus History	1.642	0.005	1.793	0.007	1.449	0.042	1.339	0.207	1.718	0.002	1.886	0.003	1.759	0.001	1.727	0.011
Family Diabetes History	1.313	0.212	0.873	0.598	1.043	0.853	0.731	0.289	1.313	0.200	0.790	0.344	1.210	0.362	0.855	0.544
Gestational Diabetes Mellitus * Family Diabetes History	0.678	0.094	0.723	0.222	0.866	0.548	1.030	0.922	0.646	0.053	0.781	0.330	0.726	0.150	0.841	0.510

*Adjusted result were calculated after adjustment by maternal age, race, education and family income.

Table 15: The Interactions between Prior GDM and Potential Risk Factors on Insulin Resistance Indices -- Multivariate Analysis

	HOMA-IR				ISOGTT				IGI/HOMA-IR				IS-SI			
	Crude		Adjusted		Crude		Adjusted		Crude		Adjusted		Crude		Adjusted	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Gestational Diabetes Mellitus History	1.218	0.777	0.725	0.687	0.918	0.897	1.435	0.634	0.389	0.160	0.439	0.258	0.442	0.224	0.474	0.299
Pre-pregnancy Body Mass Index	0.943	0.794	0.789	0.367	1.108	0.633	1.296	0.300	0.643	0.044	0.666	0.092	0.664	0.062	0.674	0.099
Gestational Diabetes Mellitus * Body Mass Index	1.204	0.789	2.109	0.357	0.687	0.574	0.419	0.261	1.768	0.389	1.473	0.595	1.553	0.507	1.372	0.661
Gestational Diabetes Mellitus History	1.087	0.737	0.788	0.434	0.845	0.479	1.121	0.696	0.724	0.225	0.664	0.213	0.728	0.231	0.670	0.217
Parity	1.195	0.382	0.839	0.467	0.835	0.357	1.137	0.581	0.806	0.321	0.625	0.642	0.796	0.295	0.843	0.503
Gestational Diabetes Mellitus * Parity	1.377	0.292	2.342	0.025	0.737	0.296	0.460	0.033	1.055	0.868	1.020	0.960	1.052	0.875	1.042	0.914
Gestational Diabetes Mellitus History	1.689	0.003	1.833	0.005	0.547	0.000	0.516	0.002	0.579	0.001	0.543	0.004	0.586	0.002	0.571	0.009
Family Diabetes History	1.324	0.191	0.871	0.585	0.771	0.202	1.200	0.452	0.632	0.026	0.798	0.375	0.663	0.048	0.825	0.456
Gestational Diabetes Mellitus * Family Diabetes History	0.655	0.064	0.716	0.201	1.568	0.039	1.346	0.234	1.954	0.003	1.643	0.062	1.893	0.005	1.526	0.115

*Adjusted result were calculated after adjustment by maternal age, race, education and family income.

Acknowledgements

Special acknowledge is given to Xu Xiong, MD, DrPH and Shengxu Li, MD, PhD. They contributed to the overall study design, data analysis, and interpretation, without which this work would not have been possible. I also thank all the professors and faculty who have taught me during the last two years. They will remain my mentors.