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Pregnancies After the Diagnosis of Mild Gestational Diabetes Mellitus and Risk of Cardiometabolic Disorders

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Abstract

Objective—To assess the association of subsequent pregnancy with subsequent metabolic syndrome and type II diabetes mellitus after a pregnancy complicated by mild gestational diabetes mellitus (GDM).

Methods—We conducted a prospective observational follow up study of women with mild GDM randomized from 2002–2007 to usual care or dietary intervention and glucose self-monitoring. Women were evaluated 5–10 years after the parent study. Participants were grouped according to the number of subsequent pregnancies (Group A, none [reference]; Group B, one; Group C, ≥ two). Serum triglycerides, glucose tolerance, HDL-cholesterol, blood pressure, and waist circumference were assessed. Metabolic syndrome was diagnosed by American Heart Association

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and National Heart Lung and Blood Institute criteria. Multivariable regression was used to estimate adjusted relative risks (RR) and 95% confidence intervals (CI).

Results—Of 905 eligible women from the original trial, 483 agreed to participate, 426 of whom were included in this analysis. Groups A, B, and C consisted of 212, 143, and 71 women, respectively. Of women with subsequent pregnancies, 32% (69/214) had another pregnancy complicated with GDM. No difference between groups was observed for metabolic syndrome (Group A, 34%; Group B, 33%; Group C, 30%). Subsequent pregnancies were associated with diabetes mellitus outside of pregnancy (Group A, 5.2%; Group B, 10.5%, RR 2.62, 95%CI 1.16–5.91; Group C, 11.3%, RR 2.83, 95%CI 1.06–7.59), and if complicated with GDM (no subsequent GDM pregnancy, RR 1.99, 95%CI 0.82–4.84; subsequent GDM pregnancy, RR 3.75, 95%CI 1.60–8.82).

Conclusions—In women with prior mild GDM, subsequent pregnancies did not increase the frequency of metabolic syndrome, but subsequent pregnancies with GDM increased the risk of diabetes mellitus outside of pregnancy.

INTRODUCTION

Hormonally mediated physiologic adaptations that occur during pregnancy, including increased insulin resistance, weight gain, atherogenic dyslipidemia, and inflammation, unmask a woman's predisposition to subsequent chronic diseases[1–3]. Women who develop gestational diabetes mellitus (GDM), for example, are known to be at increased risk of developing type II diabetes and cardiometabolic disorders, including metabolic syndrome[4]. Because it can often be diagnosed in a relatively short follow-up interval after pregnancy, and because it is associated with increased cardiovascular and metabolic disease risks, the diagnosis of metabolic syndrome in women who have experienced the aforementioned pregnancy complications has also been considered as a proxy for subsequent cardiometabolic disease[5–6].

Pregnancy complications and their associated future diseases share common pathophysiologies of inflammation and endothelial dysfunction[7–8]. If the pregnancy-associated changes play an etiologic role in subsequent cardiometabolic disease, we hypothesized that additional pregnancies occuring after a prior diagnosis of GDM, might increase the likelihood of subsequent metabolic syndrome.

The objective of this analysis was to assess the association of subsequent pregnancy with maternal cardiometabolic disorders at 5 – 10 years after an index pregnancy complicated by mild GDM.

MATERIALS AND METHODS

Women enrolled from October 2002 through mid-November 2007 in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network's Mild GDM trial were followed up 5–10 years later from February 2012 through September 2013. Details regarding the parent study have been previously described[9]. Mild GDM was defined with a 3-hour 100-gram oral glucose

tolerance test (OGTT) with a fasting glucose of less than 95 mg/dl but two of three timed measurements that exceeded established thresholds: one hour, 180 mg/dl: two hour, 155 mg/dl: and three hour, 140 mg/dl. Women did not have a prior history of pregestational or gestational diabetes mellitus, renal or cardiovascular disease or chronic hypertension, nor did they have preeclampsia at the time of enrollment in the original study. The mild GDM trial was approved by the institutional review board of all participating centers.

The prospective observational follow-up study[10], which was not planned at the time of the original study, was approved by the Institutional Review Boards of all participating centers. Eligibility included enrollment in the original GDM study at a center still participating in the MFMU Network at the time of the follow-up study (12 of 16 centers throughout the United States; 94% of the original trial patients), and the woman's index child participated in the follow-up study. Following informed consent, women underwent anthropometric and blood pressure measurements, and were queried about breastfeeding during the index pregnancy, pregnancies since their index pregnancy, medication use, physical activity, and diet. After an 8-hour fast, participants had their blood drawn, followed by a 2-hour 75-g oral glucose-tolerance test. Collection, processing and storage of specimens were conducted per a standardized approach prior to being shipped on dry ice to the Northwest Lipid Metabolism and Diabetes Research Laboratories for lipid panel and glucose laboratory measurements. Weight and height were measured using a hospital grade scale and a stationary stadiometer, respectively. Waist circumference was measured by trained personnel who received standardized anthropometric training, using an AcuFitness MyoTape just above the uppermost lateral border of the right ilium of the pelvis[11], and an average of three measurements was used in the analysis. Blood pressure was measured by trained personnel after the participant had not smoked or consumed coffee or alcohol for at least 30 minutes, and was sitting quietly for at least 10 minutes, by auscultation using aneroid sphygmomanometer instruments or a hospital grade blood pressure–pulse machine, and an average of two measurements was used in the analysis. To minimize bias, research staff involved in data collection and laboratory analyses were masked to the participant's exposures during the original study.

The primary outcome, metabolic syndrome, was defined per the American Heart Association and National Heart Lung and Blood Institute Scientific Statement as three or more of the following: high waist circumference (>88 cm), high triglycerides (≥150 mg/dL), low high-density lipoprotein cholesterol (HDL-C) (<50 mg/dL), blood pressure ≥130/85 mmHg, or fasting glucose ≥100 mg/dL, or relevant treatment for any of these components[12]. Diabetes mellitus outside of pregnancy was a secondary outcome and was defined as currently treated for diabetes with an oral agent or insulin or meeting American Diabetes Association diagnostic criteria for an abnormal 75-gram glucose tolerance test[13]. The primary exposure was the number of subsequent pregnancies since the index pregnancy and a secondary exposure was number of subsequent pregnancies that were, or were not, complicated with GDM.

Descriptive analyses used the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables. Components of the metabolic syndrome, OGTT results, and C-peptide were evaluated as continuous outcomes by constructing least squares means based

on linear multivariable regression. Metabolic syndrome, diabetes mellitus outside of pregnancy, and binomial components of metabolic syndrome were evaluated as binomial outcomes using log-Poisson multivariable regression to estimate relative risks and 95% confidence intervals. The multivariable models were adjusted for race–ethnicity, mild GDM treatment group in the index pregnancy, pregnancy associated hypertension (gestational hypertension or preeclampsia) in the index pregnancy, maternal age at follow-up, current self-reported daily servings of vegetables other than potatoes or corn, and current log body mass index (BMI). Continuous variables were assessed to evaluate whether they were normally distributed and log-transformed when appropriate. SAS software (SAS Institute, Cary, NC) was used for the analyses. All tests were two-tailed and $p < 0.05$ was used to define statistical significance. No imputation for missing data was performed.

RESULTS

Of the 905 eligible women with mild GDM from the original trial, 666 (74%) were successfully contacted, of whom 483 women consented and participated in the follow-up study. The maternal baseline characteristics were generally similar between women who did and did not participate in the follow-up study, although a higher percentage of the non-Hispanic white women participated in the follow-up study (Appendix 2, available online at http://links.lww.com/xxx). Of the 483 women who were included in the follow up, 26 were pregnant at the time of follow-up and 31 had missing laboratory data, leaving 426 included in this analysis. Of these, 212 had no subsequent pregnancies since the index pregnancy (Group A), 143 women had only one subsequent pregnancy (Group B) and 71 women had two or more subsequent pregnancies (Group C). There were 309 subsequent pregnancies among the 214 women in groups B and C, 8 of which were multiple gestations (twins).

Demographics of the three groups at the time of enrollment in the parent study and at the time of this follow-up evaluation are presented in Tables 1 and 2.. Overall, 59% of the participants were Hispanic. Women in Group A also had higher BMIs than did women in Groups B and C. There were no differences between groups in treatment group, race–ethnicity, or frequency of pregnancy-associated hypertension during the index pregnancy. When including all pregnancies before and after the index pregnancies, women in Group C had higher median parity.

At the time of enrollment in the follow-up study, women in Group A were significantly older (median = 38 years) than women in Groups B (median = 35 years) and C (median = 33 years) ($p < 0.001$). The interval from participation in parent study to participation in the follow-up study was longer for women in Group C (median = 8 years) than for women in Groups A or B (median for both = 7 years) ($p = 0.03$). There were no other significant differences between the groups in any other self-reported demographic information, smoking status, dietary intake, minutes per week of vigorous physical activity, or breastfeeding in the index pregnancy. Almost a third (69/214; 32%) of women with subsequent pregnancies (Groups B and C) had another pregnancy complicated with GDM.

Results for laboratory markers of vascular risk, by group and adjusted for various potential confounders, are presented in Table 3. Median unadjusted insulin concentrations were not

significantly different between groups, although mean adjusted insulin was highest in Group A. No other significant differences were observed.

The frequency of metabolic syndrome and diabetes mellitus at the time of follow-up evaluation was 32.9% (140/426) and 8.0% (34/426), respectively (Table 4). Among the 34 women diagnosed with diabetes, 5 were being treated with an oral agent or insulin prior to the follow-up visit; the remainder (N = 29, 6.8% of all participants) were diagnosed with an abnormal 75-gm OGTT at the follow-up visit.

The specific components of metabolic syndrome in each Group are shown in Table 4. In all three Groups the diagnosis of metabolic syndrome was primarily based on waist circumference and low HDL cholesterol. There were no differences between the groups in the diagnosis of metabolic syndrome (34%, 33%, 30%, respectively; relative risks 1.15 (95%CI 0.79–1.69) and 1.00 (0.60 – 1.68) for the second and third groups, respectively, compared with the first group), however there was a difference between groups in diabetes (5.2%, 10.5%, 11.3%, respectively; relative risks 2.62 (95%CI 1.16–5.91) and 2.83 (1.06 – 7.59) for the second and third groups, respectively, compared with the first group. The association with diabetes was driven mostly by having a subsequent pregnancy complicated with GDM, with relative risks 1.99 (95%CI 0.82–4.84) and 3.75 (1.60 – 8.82) for subsequent pregnancies without or with GDM, respectively, compared with women who did not have subsequent pregnancies (Table 5). BMI was the one risk factor consistently associated with all of the outcomes evaluated.

DISCUSSION

We found that pregnancies after a diagnosis of mild GDM did not increase a woman's risk of developing metabolic syndrome but were associated with an increased likelihood of diabetes mellitus outside of pregnancy at 5–10 years after the index pregnancy. The magnitude of the association with post-gestational diabetes was strongest in those having a subsequent pregnancy complicated with GDM. While this could be consistent with either a stronger genetic or an environmental predisposition to Type II diabetes, it could also represent confounders that were not measured in this prospective observational follow-up study

In women with a previous diagnosis of mild GDM, metabolic syndrome was common, being diagnosed in 32.9% of these women at 5–10 years. Subsequent pregnancies were not associated with an increased likelihood of developing metabolic syndrome at 5–10 years follow-up but were associated with an increased incidence of diabetes mellitus outside of pregnancy over the same interval. The association with diabetes was driven mostly by subsequent pregnancy(ies) complicated with GDM.

Women whose pregnancies are complicated by GDM are known to be at increased risk for subsequent metabolic syndrome and other long-term vascular disease. Several previous reports have identified metabolic syndrome rates in parous women with a prior diagnosis of GDM. Verma and colleagues evaluated 106 women with a previous diagnosis of GDM at 11 years after delivery and identified metabolic syndrome in twenty-nine (27.2%)[14]. A

subsequent report from Denmark evaluated 481 women with a previous diagnosis of GDM at a median of 9.8 years (interquartile range 6.4 – 17.2 years) after delivery and diagnosed metabolic syndrome in 38.4% [15]. Most recently, Li and colleagues reported on 1263 Chinese women with a previous diagnosis of GDM, with 23.8% of them having a diagnosis of metabolic syndrome at 1–5 years after delivery [16]. These incidence figures (23.8 – 38.4 percent) are similar to our findings (32.9%). However, none of these reports provided data on the number of intervening pregnancies from the index pregnancy to the time of metabolic syndrome diagnosis. Although we observed a high overall frequency of metabolic syndrome in our cohort, our data suggest that subsequent pregnancies do not increase a woman's risk of developing metabolic syndrome. Our data are limited, however, by the fact that we do not know how many patients had metabolic syndrome at the time of the index pregnancy.

Gunderson and associates have demonstrated that waist circumference increases with each birth while bodyweight increased only after the first birth[17]. However, we did not identify any significant differences in waist circumference between our study groups, perhaps because our Group A women older less likely to be nulliparous at entry into the parent study but our Group C women had higher overall parity by the time of the follow-up study.

The fact that participation in the parent study was limited to women with mild GDM could be seen as a limitation, particularly in light of the relatively low incidence of diabetes at the time of follow-up. Likewise, these findings may not apply to women with GDM diagnosed early in pregnancy. However, our frequency of metabolic syndrome is high and consistent with other reports in the literature[14–16]. Still, our results may not be generalizable to the full spectrum of GDM. In addition, this is a relatively small retrospective study that reported on less than half (426/905) of the participants in the parent study, We can thus not exclude the possibility of a selection bias. A higher percentage of the non-Hispanic white women participated in the follow-up study. Despite this, 59% of the women included in this analysis were Hispanic. Another limitation of this report is the lack of metabolic syndrome data from both the index pregnancy and prior to the index pregnancy. Likewise, given the lack of contact with study participants between the parent and follow-up studies, it is not possible to know when women with metabolic syndrome developed the condition, specifically in relation to any intervening pregnancies. Lastly, our limited significant findings should be interpreted in the context of multiple comparisons. Strengths of this report include the parent study's precise definitions of mild GDM and of metabolic syndrome components and diabetes in the follow-up study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Demographics of Follow-up Participants at the Time of Enrollment in the Parent Study, October 2002 – November 2007[13]

Characteristic	Number of Pregnancies Since the Index Pregnancy			P-Value*
	0 (n = 212) (Group A)	1 (n = 143) (Group B)	2+ (n = 71) Group C)	
Race/ethnicity				0.39
Hispanic	133 (62.7)	82 (57.3)	36 (50.7)	
Non-Hispanic, white	60 (28.3)	48 (33.6)	25 (35.2)	
Non-Hispanic, non-white	19 (9.0)	13 (9.1)	10 (14.1)	
Number of live births before the index pregnancy				<0.001
0	32 (15.1)	54 (37.8)	36 (50.7)	
1	67 (31.6)	52 (36.4)	23 (32.4)	
2+	113 (53.3)	37 (25.9)	12 (16.9)	
Treated mild GDM	111 (52.4)	75 (52.5)	41 (57.8)	.71
Body mass index at enrollment (kg/m^2)	30.3 (27.7–33.8)	29.1 (26.2–33.0)	28.9 (25.5–32.9)	0.03
Pregnancy associated hypertension†	22 (10.4)	12 (8.4)	10 (14.1)	0.44

Data are N (%) or median (interquartile range) unless otherwise noted.

*Based on the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables.

†Gestational hypertension or preeclampsia.

Table 2

Demographic and Lifestyle Information on Participants at Follow-Up, February 2012 – September 2013[14].

Characteristic	Number of Pregnancies Since the Index Pregnancy			P-Value*
	0 (n = 212) Group A)	1 (n = 143) Group B)	2+ (n = 71) Group C)	
Duration of follow-up (years)	7 (6–8)	7 (6–8)	8 (6–9)	0.03
Age (years)	38 (34–42)	35 (32–39)	33 (30–36)	<0.001
Marital status†				0.37
Never married	35 (16.6)	17 (11.9)	12 (16.9)	
Divorced/widowed/separated	34 (16.1)	21 (14.7)	6 (8.5)	
Married/living with partner	142 (67.3)	105 (73.4)	53 (74.6)	
Insurance				0.60
Self-pay/uninsured	75 (35.4)	46 (32.2)	25 (35.2)	
Private	66 (31.1)	52 (36.4)	28 (39.4)	
Government-assisted	71 (33.5)	45 (31.5)	18 (25.4)	
Smoking				0.77
Never	177 (83.5)	121 (84.6)	59 (83.1)	
Past	19 (9.0)	8 (5.6)	6 (8.5)	
Current	16 (7.6)	14 (9.8)	6 (8.5)	
Body mass index at follow-up (kg/m^2)	28.8 (25.8–33.4)	28.0 (24.2–32.6)	28.9 (23.3–33.4)	0.15
Lunch meals outside the home per week	1 (0–2)	1 (0–2)	1 (0–2)	0.92
Dinner meals outside the home per week	1 (0–2)	1 (0–2)	1 (0–1)	0.96
Cups of sugar-sweetened beverages per day	0.3 (0.0–1.0)	0.3 (0.0–1.0)	0.3 (0.0–1.0)	0.87
Servings of vegetables‡ per day	0.7 (0.4–1.4)	1.0 (0.4–2.0)	1.0 (0.4–2.0)	0.13
Servings of fruit per day	1.0 (0.6–2.0)	1.0 (0.6–2.0)	1.0 (0.7–2.0)	0.54
Vigorous physical activity minutes per week	0 (0–0)	0 (0–30)	0 (0–60)	0.32
Ever breastfed the index pregnancy	163 (76.9)	109 (76.2)	57 (80.3)	0.79
Duration breastfed the index pregnancy (months)	4 (0–4)	5 (0–5)	4 (1–4)	0.62
Pregnancies since the index pregnancy complicated with gestational diabetes mellitus				§
0	212 (100.0)	100 (69.9)	45 (63.4)	
1	0 (0.0)	43 (30.1)	17 (23.9)	
2+	0 (0.0)	0 (0.0)	9 (12.7)	
Total parity	3 (2–3)	3 (2–4)	4 (3–5)	<0.001

Data are N (%) or median (interquartile range) unless otherwise noted.

*Based on the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables.

†Missing in one participant.

‡Other than potatoes or corn.

§Not computed due to zero cells from lack of independence between variables.

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Table 3

Adjusted* results for laboratory and physical examination markers of vascular risk, by number of pregnancies after the index GDM pregnancy.

OUTCOME	NUMBER OF PREGNANCIES SINCE INDEX GDM PREGNANCY					
	0 (n = 212) (Group A)		1 (n = 143) (Group B)		≥2 (n = 71) (Group C)	
	Unadjusted median (interquartile range)	Adjusted* mean (95% CI)	Unadjusted median (interquartile range)	Adjusted* mean (95% CI)	Unadjusted median (interquartile range)	Adjusted* mean (95% CI)
Triglycerides (mg/dl)†	108 (75–152)	99 (89–110)	103 (68–163)	101 (90–114)	95 (60–152)	95 (82–109)
HDL-cholesterol (mg/dl)‡	47 (41–57)	49 (46–51)	44 (40–55)	48 (46–51)	41 (37–54)	46 (43–49)
Fasting blood glucose (mg/dl)‡	95 (90–102)	95 (92–99)	92 (87–99)	94 (90–97)	94 (89–101)	96 (92–101)
1-hr OGTT glucose (mg/dl)	165 (131–200)	155 (145 – 165)	152 (123–190)	153 (142 – 165)	150 (122–191)	154 (141 – 168)
2-hr OGTT glucose (mg/dl)	127 (104–158)	130 (121 – 140)	121 (96–155)	128 (118 – 139)	121 (93–153)	127 (113 – 140)
Insulin (mIU/ml)†‡	11.9 (7.4–16.4)	11.2 (10.1 – 12.4)	9.3 (5.7–14.2)	9.4 (8.4 – 10.5)§	11.2 (5.6–17.4)	9.6 (8.4 – 11.0)§
C-peptide (ng/ml)†	2.7 (2.1–3.4)	2.6 (2.5 – 2.8)	2.5 (1.9–3.3)	2.5 (2.3 – 2.7)	2.6 (1.9–3.8)	2.5 (2.3 – 2.7)
Waist circumference (cm)	90.8 (83.9–101.0)	94.9 (93.4 – 96.3)	90.5 (82.2–99.0)	95.8 (94.2 – 97.4)	93.1 (83.2–102.3)	96.8 (94.8 – 98.8)
Systolic blood pressure (mmHg)‡	115 (109–123)	122 (119 – 125)	111 (105–120)	120 (117 – 123)	112 (106–121)	120 (116 – 123)
Diastolic blood pressure (mmHg)‡	73 (67–80)	77 (74 – 79)	70 (65–78)	76 (73 – 78)	71 (66–77)	75 (72 – 78)

*Adjusted for race/ethnicity, mild GDM treatment group in the index pregnancy, pregnancy-associated hypertension (gestational hypertension or preeclampsia) in the index pregnancy, maternal age at follow-up, current daily servings of vegetables other than potatoes or corn, and current log body mass index. Blood pressure models also adjusted for hypertension treatment at follow-up.

†Log values back transformed.

‡$p < 0.05$ for the unadjusted comparison of the three groups based on the Kruskal-Wallis test.

§$p < 0.05$ compared with Group A (women who had no pregnancies since the index pregnancy).

GDM = gestational diabetes mellitus; HDL = high-density lipoprotein; OGTT = oral glucose tolerance test; CI = confidence interval

Table 4

Adjusted* results for metabolic syndrome and its components, and diabetes mellitus, by number of pregnancies after the index GDM pregnancy.

OUTCOME	NUMBER OF PREGNANCIES SINCE INDEX PREGNANCY						
	0 (n = 212) (Group A)	1 (n = 143) (Group B)			2+ (n = 71) (Group C)		
	n (%)	n (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	n (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*
Metabolic syndrome	72 (34.0)	47 (32.9)	0.97 (0.72–1.31)	1.15 (0.79–1.69)	21 (29.6)	0.87 (0.58–1.31)	1.00 (0.60 – 1.68)
Metabolic syndrome components							
Waist circumference >88 cm	135 (63.7)	84 (58.7)	0.92 (0.78–1.09)	1.02 (0.77–1.35)	42 (59.2)	0.93 (0.75–1.16)	0.97 (0.67–1.39)
Triglycerides ≥ 150 mg/dl	56 (26.4)	45 (31.5)	1.19 (0.86–1.66)	1.33 (0.88–2.00)	18 (25.4)	0.96 (0.61–1.52)	1.08 (0.62–1.90)
HDL-C < 50 mg/dl	121 (57.1)	88 (61.5)	1.08 (0.91–1.28)	1.10 (0.83–1.47)	48 (67.6)	1.18 (0.97–1.45)	1.18 (0.83–1.69)
Blood pressure ≥ 130.85 mmHg	46 (21.7)	23 (16.1)	0.74 (0.47–1.17)	0.90 (0.54–1.51)	6 (8.5)	0.39 (0.17–0.87)§	0.43 (0.18–1.05)
Fasting glucose ≥ 100 mg/dl	66 (31.1)	36 (25.2)	0.81 (0.57–1.14)	0.93 (0.61–1.41)	21 (29.6)	0.95 (0.63–1.43)	1.09 (0.64–1.84)
Diabetes mellitus	11 (5.2)	15 (10.5)	2.02 (0.96–4.27)	2.62 (1.16–5.91)§	8 (11.3)	2.17 (0.91–5.18)	2.83 (1.06–7.59)§

*Adjusted for race/ethnicity, index pregnancy treatment group, pregnancy associated hypertension in the index pregnancy, maternal age at follow-up, current daily servings of vegetables other than potatoes or corn, and current log BMI.

§p < 0.05 compared with Group A (women who had no pregnancies since the index pregnancy)RR = relative risk; CI = confidence interval.

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Table 5

Adjusted* results for metabolic syndrome and diabetes mellitus, by whether or not pregnancies after the index GDM pregnancy were complicated with GDM.

OUTCOME	SUBSEQUENT PREGNANCIES SINCE INDEX PREGNANCY NOT COMPLICATED OR COMPLICATED WITH GDM						
	No subsequent pregnancies (n = 212)	Subsequent pregnancies with none complicated with GDM (n = 145)			Subsequent pregnancies with at least one complicated with GDM (n = 69)		
	n (%)	n (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	n (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*
Metabolic syndrome	72 (34.0)	41 (28.3)	0.83 (0.60–1.15)	1.02 (0.68–1.52)	27 (39.1)	1.15 (0.81–1.63)	1.27 (0.81 – 2.00)
Diabetes mellitus‡	11 (5.2)	11 (7.6)	1.46 (0.65–3.28)	1.99 (0.82–4.84)	12 (17.4)	3.35 (1.55–7.25)§	3.75 (1.60–8.82)§

*Adjusted for race/ethnicity, mild GDM treatment group in the index pregnancy, pregnancy associated hypertension (gestational hypertension or preeclampsia) in the index pregnancy, current daily servings of vegetables other than potatoes or corn, and current log body mass index.

§$p < 0.05$ compared with Group A (women who had no pregnancies since the index pregnancy).

GDM = gestational diabetes mellitus; RR = relative risk; CI = confidence interval.