68 Obesity in pregnancy: what's next? Long-term cardiovascular morbidity in a follow-up period of more than a decade

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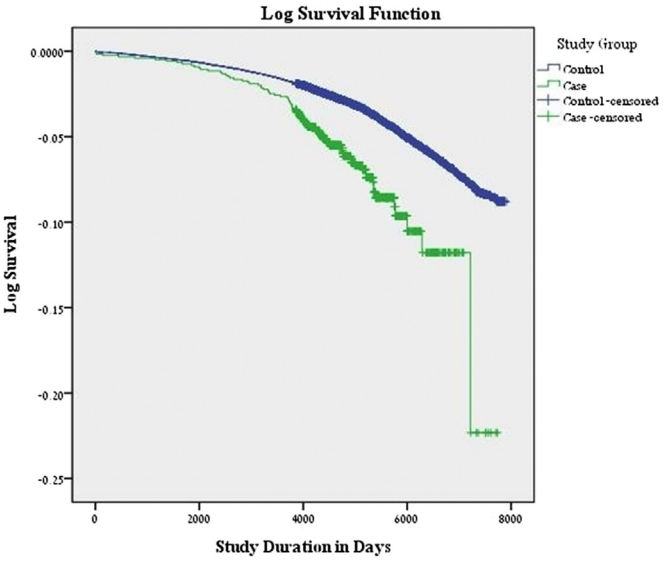
OBJECTIVE: To investigate whether obesity in pregnancy is an independent risk factor for subsequent long-term cardiovascular morbidity during a follow-up period of more than a decade.

STUDY DESIGN: Data were analyzed from consecutive pregnant women who delivered between 1988 and 1999, and were followed-up retrospectively until 2010. Long-term cardiovascular morbidity was compared among women with and without obesity in pregnancy (defined as maternal pre-pregnancy body mass index (BMI) of 30 kg/m2 or more). Cardiovascular morbidity was divided into four categories including simple and complex cardiovascular events and invasive and noninvasive cardiac procedures. Kaplan-Meier survival curves were used to compare cumulative incidence of cardiovascular hospitalizations. Cox proportional hazards models were used to estimate the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for long term cardiovascular hospitalizations.

RESULTS: During the study period 46,688 women met the inclusion criteria; 1221 (2.6%) suffered from obesity during pregnancy. During a follow up period of more than ten years, patients with obesity had higher risk for cardiovascular hospitalizations (Kaplan-Meier survival analysis, P<0.001; Figure). Specifically, obese patients had higher rates of simple cardiovascular events and non-invasive procedures (Table). These complications tended to occur at a younger age (mean 4871±950 days vs. 5060±1140 days from their pregnancy; p=0.001). In a Cox proportional hazards model, adjusted for diabetes mellitus, preeclampsia and maternal age, obesity was independently associated with long-term cardiovascular hospitalizations (adjusted HR 1.33, 95% CI 1.17-1.5).

CONCLUSION: Obesity during pregnancy is an independent risk factor for long-term cardiovascular morbidity, and these complications tend to occur at a younger age. Obese parturients might benefit from cardiovascular risk screening that could lead to early detection and secondary prevention of cardiovascular morbidity.

Kaplan-Meier hazard function analysis curve for cardiovascular associated hospitalization of patients with and without obesity



Cardiovascular hospitalizations in patients with and without obesity

	Obesity (n= 1213)	No obesity (n= 46,498)	OR	CI (95%)	P value
Cardiac non invasive diagnostic procedures	2.0%	1.1%	1.9	1.2-2.8	0.002
Invasive diagnostic procedures	0.7%	0.4%	1.6	0.72-3.28	0.182
Simple cardiovascular events	5.1%	2.6%	2.0	1.53-2.6	0.001
Complex cardiovascular events	0%	0.1%	0.97	0.97-0.98	0.212
Total cardiovascular hospitalizations	6.6%	3.6%	1.8	1.4-2.3	0.001

69 Excess gestational weight gain (GWG) is associated with alterations in metabolic function of the microbiome

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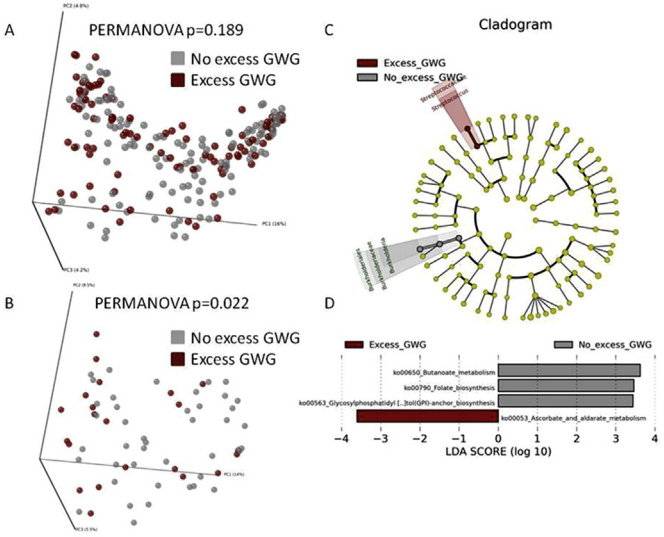
OBJECTIVE: Pathologic states (obesity) and physiologic states (pregnancy) are accompanied by changes in the microbiome. Unique to pregnancy is a physiologic state of increasing adiposity, although this can cross-over to pathologic if weight gain is excessive. Our aim was to investigate whether excess gestational weight gain affects the microbiome in pregnancy and, if so, the biologic significance.

STUDY DESIGN: Placentas (n=243) were rigorously and uniformly collected from term and preterm gravidae and stratified by IOM GWG guidelines. Genomic DNA was extracted (MoBIO), and metagenomic libraries (n=26) were subjected to shotgun sequencing (WGS; Illumina).

RESULTS: 16S rRNA pyrosequencing (1A) revealed no significant difference in between-subject beta-diversity by virtue of obesity (p=0.22), nor excess GWG (p=0.189). However, among gravidae with preterm births, there was significant clustering by excess GWG (p=0.022), and species richness (abundance across multiple taxa) was notably decreased. Among all gravidae, detailed analysis of WGS with linear discriminant analysis (LDA) identified microbial genus

that were significantly differentially abundant among placentas from gravidae with excess GWG (1B.) This detailed analysis also uncovered significant differences in the metabolic function; excess GWG associated with decreased activity of placental microbial folate biosynthesis pathways and decreased butanoate metabolism (1C).

CONCLUSION: Overall, while there were no alterations in the microbiome by virtue of obesity, excess weight gain did alter the microbiome among those with preterm birth. Deeper metagenomic sequencing revealed excess GWG was associated with alterations in the abundance of certain genuses and functional pathways in the placental microbiome. Some of these pathways may affect the inflammatory milieu; for example, butanoate is posited to suppress colonic inflammation in the gut. We speculate that these alterations may contribute to increased morbidity among gravidae with excess gain.



A. Principal coordinates analysis (PCoA) shows beta-diversity of the microbiome community on operational taxonomic unit level with Canberra distance.
B. PCoA among preterm gravidae with and without excess GWG.
C. Cladogram reveals significant genus differences between subjects with excess GWG and non-excess GWG among certain genus.
D. The relative abundance of functional pathways was generated and compared by MG-RAST and LEfSe. Folate biosynthesis pathways and butanoate metabolism were less active in the placentas of women with excess GWG.

70 The joint effects of pre-pregnancy body mass index (ppBMI) and gestational diabetes mellitus (GDM) on pregnancy outcomes and inpatient healthcare costs in Florida, 2004-2009

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OBJECTIVE: To examine the joint effects of maternal ppBMI and GDM on adverse pregnancy/ birth outcomes and hospitalization costs.

STUDY DESIGN: We conducted a retrospective cohort study using a linked maternal-infant database covering over 1.2 million infant born alive to Florida-resident mothers from 2004-09. Births were classified according to maternal ppBMI (underweight, normal, overweight, and obese classes I-III) and GDM status. Outcomes were identified using a combination of International Classification of Diseases, 9th Edition, codes in hospital discharge records and indicators on the birth certificate. Using multivariable logistic regression, we compared the adjusted odds of each outcome across different levels of ppBMI and GDM. We also converted hospital charges into refined cost estimates and compared hospitalization costs among these groups. We excluded multiple births, infants with chromosomal anomalies, and mothers with pre-pregnancy diabetes.

RESULTS: Among 1,057,678 pregnancies 52,000 (4.9%) had GDM, 43.6% were either overweight or obese, and 3.3% were overweight/ obese with GDM. GDM and ppBMI tended to have a synergistic effect on the odds of adverse birth outcomes (e.g., macrosomia, brachial plexus injury, congenital heart defect, hypoglycemia, shoulder dystocia [Table 1]), and maternal conditions (e.g., depression, eclampsia, gestational hypertension, sleep apnea, and delivery by cesarean section [Table 2]). Women with GDM and severe/morbid obesity experienced the highest rates of poor outcomes, which translated into significantly higher mean maternal (GDM/ obese III: $5614 vs. No GDM/normal BMI: $4297) and infant (GDM/obese III: $4393 vs. No GDM/normal BMI: $3177) hospitalization costs.

CONCLUSION: Women with high ppBMI and GDM are at an increased risk of adverse birth outcomes. These findings suggest the importance of extensive BMI reduction interventions for those at risk of GDM.

Adjusted odds ratios* and 95% confidence intervals for the joint effect of gestational diabetes and pre-pregnancy boday mass index (BMI), on selected fetal birth outcomes Florida, 2004-2009.

Groups	Infant birth outcomes							
	Macrosomia	LGA	PTB	BP injury	Congenital HD	Hypoglycemia	SIDM	Dystocia
Normal weight no GDM	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Normal weight with GDM	1.26(1.18-1.34)	1.47(1.39-1.56)	1.32(1.25-1.39)	2.99(2.06-4.33)	1.15(1.06-1.25)	0.76(0.66-0.88)	226.46(197.24-26.01)	1.36(1.19-1.55)
Underweight no GDM	0.51(0.48-0.53)	0.52(0.49-0.54)	1.35(1.31-1.39)	0.48(0.30-0.78)	1.05(1.00-1.11)	1.11(1.04-1.19)	0.58(0.34-0.99)	0.75(0.68-0.83)
Underweight with GDM	0.66(0.49-0.91)	0.81(0.61-1.06)	1.32(1.10-1.59)	2.66(0.66-10.72)	1.07(0.78-1.47)	0.51(0.26-0.98)	175.33(135.79-226.37)	1.58(1.01-2.46)
Overweight no GDM	1.54(1.51-1.57)	1.57(1.54-1.60)	0.98(0.96-0.99)	1.82(1.56-2.13)	1.07(1.04-1.10)	1.12(1.07-1.16)	2.02(1.68-2.42)	1.14(1.09-1.19)
Overweight with GDM	2.11(2.00-2.23)	2.46(2.34-2.59)	1.38(1.31-1.46)	3.21(2.20-4.67)	1.34(1.23-1.45)	1.06(0.93-1.21)	276.659(241.08-317.48)	1.77(1.56-2.00)
Obese class I no GDM	1.80(1.76-1.85)	1.90(1.85-1.94)	1.01(0.98-1.03)	2.03(1.67-2.46)	1.106(1.07-1.15)	1.29(1.23-1.36)	2.786(2.27-3.43)	1.14(1.07-1.21)
Obese class I with GDM	2.76(2.60-2.93)	3.36(3.19-3.55)	1.58(1.49-1.67)	5.91(4.23-8.26)	1.52(1.39-1.66)	1.20(1.03-1.38)	362.46(315.35-416.61	1.61(1.38-1.88)
Obese class II no GDM	2.05(1.98-2.12)	2.19(2.12-2.26)	1.05(1.01-1.09)	2.54(1.98-3.25)	1.24(1.18-1.30)	1.45(1.36-1.55)	3.52(2.72-4.56)	1.06(0.97-1.16)
Obese class II with GDM	3.19(2.97-3.44)	4.02(3.76-4.30)	1.62(1.50-1.75)	5.19(3.26-8.27)	1.74(1.56-1.95)	1.34(1.11-1.61)	403.30(348.37- 466.89)	1.58(1.29-1.93)
Obese class III no GDM	2.28(2.18-2.37)	2.47(2.38-2.57)	1.05(1.01-1.10)	2.62(1.95-3.54)	1.35(1.28-1.44)	1.74(1.61-1.87)	5.24(4.01-6.85)	1.08(0.97-1.21
Obese class III with GDM	4.33(4.00-4.68)	5.12(4.76-5.51)	1.77(1.63-1.93)	6.90(4.33-10.99)	2.21(1.97-2.48)	1.92(1.61-2.30)	503.37(433.41 584.62)	1.60(1.27-2.01)

OR=odds ratio, CI=confidence interval, LGA=large for gestational age, PTB=preterm birth, BP injury=brachial plexus, HD=heart defect, SIDM=syndrome of infant born to diabetes mellitus mother.

*Adjusted for age, education, race, nativity, parity, infants gender, adequacy of antenatal care, smoking, alcohol, and drug use (No gestational diabetes, normal pre-pregnancy BMI is the reference group).

Table2. Adjusted odds ratios* and 95% confidence intervals for the joint effect of gestational diabetes and pre-pregnancy boday mass index (BMI), on selected maternal birth outcomes Florida, 2004-2009

Groups	Maternal birth outcomes					
	Depression	Eclampsia	All Eclampsia	Gest HPN	OSA	CS
Normal weight no GDM	Ref	Ref	Ref	Ref	Ref	Ref
Normal weight with GDM	1.44(1.26-1.65)	1.10(0.79-1.53)	1.60(1.48 - 1.73)	1.68(1.59-1.79)	0.94(0.13 -6.91)	1.37(1.33- 1.41)
Underweight no GDM	1.09(1.00-1.18)	0.92(0.76-1.12)	0.81(0.76- 0.86	0.74(0.70 -0.77)	0.38(0.05-2.82)	0.78(0.77-0.80)
Underweight with GDM	1.17(0.70-1.95)	0.81(0.20-3.24)	1.06(0.76- 1.48)	0.99(0.76- 1.29)	-	0.97(0.86- 1.10)
Overweight no GDM	1.16(1.11- 1.22)	1.43(1.30-1.57)	1.51(1.47 -1.55)	1.69(1.65-1.72)	3.04(1.86- 4.95)	1.35(1.34-1.37)
Overweight with GDM	1.52(1.32 - 1.76)	1.91(1.46-2.50)	2.58(2.40 -2.76)	2.87(2.72 -3.03)	9.93(4.67 -21.13)	1.80(1.74-1.86)
Obese class I no GDM	1.27(1.19 - 1.35)	1.78(1.58-1.99)	2.00(1.94- 2.07)	2.33(2.27- 2.38)	8.49(5.32- 13.55)	1.73(1.71- 1.75)
Obese class I with GDM	1.58(1.34-1.86)	2.53(1.91-3.33)	3.28(3.04 -3.53)	3.75(3.54- 3.97)	16.83(8.34-33.96)	2.38(2.29- 2.48)
Obese class II no GDM	1.52(1.40- 1.65)	2.13(1.83-2.47)	2.45(2.35 -2.55)	2.95(2.86- 3.04)	12.17(7.24-20.47)	2.16(2.11- 2.20)
Obese class II with GDM	1.97(1.63 -2.37)	3.21(2.31-4.44)	3.89(3.55- 4.26)	4.56(4.25-4.89)	29.51(14.61-59.61)	2.98(2.83-3.15)
Obese class III no GDM	1.65(1.49 -1.82)	2.72(2.30-3.21)	2.90(2.77 -3.05)	3.68(3.55 -3.82)	69.29(45.26- 106.08)	2.84(2.77- 2.91)
Obese class III with GDM	2.00(1.62- 2.46)	3.13(2.16-4.54)	4.60(4.173- 5.07)	5.41(5.01-5.84)	97.24(56.98- 165.95)	4.20(3.93 - 4.48)

OR=odds ratio, CI=confidence interval, LGA=large for gestational age, PTB=preterm birth, BP injury=brachial plexus, HD=heart defect, SIDM=syndrome of infant born to diabetes mellitus mother
**Adjusted for age, education, race, nativity, parity, infants gender, adequacy of antenatal care, smoking, alcohol, and drug use (No gestational diabetes, normal pre-pregnancy BMI is the reference group)*