253 What is the association between insulin sensitivity and microarray differential gene expression in omental tissue of healthy non-obese pregnant women?

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OBJECTIVE: To determine correlations between insulin sensitivity and gene expression in omental tissue of non-obese pregnant women.

STUDY DESIGN: Microarray gene profiling using Illumina HumanHT-12 V4 Expression BeadChips was performed on omental adipose tissue obtained during non-laboring cesarean section in a fasting state from 11 non-obese non-diabetic pregnant women. Measuring transcript levels of selected genes using quantitative real-time PCR validated findings. Matusda-Insulin sensitivity Index (IS) was calculated from glucose and insulin levels obtained from a frequently sampled oral glucose tolerance test. homeostasis model assessment of insulin resistance (HOMA-R) was calculated and correlated with IS. Linear regression analysis was performed and list was filtered at $P<0.01$.

RESULTS: 510 genes significantly correlated with IS; of these 325 matched to known genes in NIH David. Twenty-three genes were determined to be involved in immune/inflammatory, vascular or metabolic pathways. Two insulin signaling pathways genes: insulin receptor (INSR) ($r=0.84$), which stimulates glucose uptake, and mitogen-activated protein kinase 3 (MAPK1) ($r=0.78$), which is anabolic, were strongly positively correlated with IS. Leptin which has been shown to suppress insulin gene expression and glucose transport was negatively correlated with IS. Of 13 genes with immune/inflammatory; 10 were positively correlated and 3 negatively correlated with IS.

CONCLUSION: Our findings suggest differential gene expressions that may be associated with cellular mechanisms modulating insulin sensitivity and resistance in visceral adipose tissue in healthy pregnancy. The unexpected finding of most immune/inflammatory genes correlating positively with insulin sensitivity indicates the need for further studies in clarifying relations between functional variants and local protein expressions.

Association between insulin sensitivity and microarray differential gene expression in omental tissue of healthy non-obese pregnant women

Gene Name	Gene Symbol	(ISI matsuda index)correlation	p-value(ISI matsuda index)	HOMA r, correlation	Function
CD48 molecule	CD48	0.75	0.007	-0.48	Facilitate interaction between activated lymphocytes.Regulation of T-cell activation
Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 3	KIR2DL3	0.74	0.010	-0.48	Inflammatory cells activation
CD19 molecule	CD19	-0.74	0.010	0.42	Facilitate interaction between activated lymphocytes. regulating T-cell activation
Leptin	LEP	-0.80	0.003	0.58	Suppresses insulin expression, secretion & glucose transport into the β-cell. Signaling pathway inhibit food intake &/or regulate energy expenditure to maintain adipose mass. Linked to type 2 diabetes mellitus. Mutations cause obesity & hypogonadism
Chemokine (C-C motif) ligand 19	CCL19	0.87	0.000	-0.64	Inflammatory and immunological responses; normal lymphocyte recirculation and homing
p21 protein (Cdc42/Rac)-activated kinase 2	PAK2	0.79	0.004	-0.45	Cell survival and cell growth
Chemokine (C-X-C motif) ligand 11	CXCL11	0.78	0.004	-0.55	Proinflammatory
Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	GZMB	0.78	0.004	-0.61	Proinflammatory, target cell lysis in cell-mediated immune responses,involved in stroke, Alzheimer's disease, myocardial infarction, cancer, inflammatory disease.
Mitogen-activated protein kinase 3	MAPK1	0.78	0.004	-0.52	Protein synthesis;cell growth, adhesion, survival

254 Gestational weight gain in excess of IOM guidelines associated with macrosomia in obese women with GDM

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OBJECTIVE: To determine whether adherence to Institute of Medicine (IOM) weight gain guidelines modifies risk of macrosomia among women with GDM.

STUDY DESIGN: We conducted a retrospective cohort study of singleton term pregnancies diagnosed with GDM (50g 1-hr >140 mg/dL; 100g 3-hr OGTT, NDDG criteria) that delivered at UNC Hospitals, January 2002 - May 2010. We calculated body mass index (BMI) using height and self-reported pre-pregnancy or measured first prenatal visit weight <20 weeks. We used last visit weight > 37 weeks - baseline weight to calculate gestational weight gain (GWG). We modeled the odds (OR, aOR) with 95% confidence intervals (95%CI) of macrosomia >4000g by BMI category and 2009 IOM guidelines. Women meeting IOM guidelines were the reference group. Final adjusted models include ethnicity and gestational age at delivery.

RESULTS: Among 577 eligible women, 85% (466/548) comprised the cohort with complete data, and 19% (89/466) delivered infants >4000g. Obese women were more likely than overweight or normal weight women to gain above IOM guidelines (52% v 41% v 31%). Overweight women were more likely than obese or normal weight women to meet IOM guidelines (31% v 20% v 15%). Normal weight

women were more likely than obese or overweight women to gain under IOM guidelines (55% v 19% v 28%) (all p<.001). Exceeding IOM guidelines was associated with macrosomia in obese women (aOR 2.51 95%CI 1.01, 6.26). In overweight women, adjusted odds of macrosomia (aOR 2.82 95%CI 2.82, 8.75) were of similar magnitude to those for obese women, but findings were not significant. Individual OGTT values were not associated macrosomia.

CONCLUSION: Exceeding IOM weight gain guidelines is associated with infant macrosomia among obese GDM women, independent of OGTT results. Gestational weight gain is a modifiable risk factor that influences macrosomia risk. Interventions that optimize gestational weight gain may improve pregnancy outcomes among obese GDM women and could have significant public health impact.

Odds of macrosomia by IOM recommendations and BMI category

		Gained less than IOM guidelines (n=142)		Gained more than IOM guidelines (n=202)	
	macrosomia n /sample n	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Normal	10/110	.24 (.03, 1.87)	.34 (.04, 2.76)	1.50 (.27, 8.41)	1.71 (.29, 9.97)
Overweight	27/167	1.35 (.38,4.74)	1.24 (.34, 4.55)	2.77 (.94, 8.17)	2.82 (.91, 8.75)
Obese	52/189	.60 (.18, 2.06)	.70 (.20, 2.44)	2.07 (.86, 5.01)	2.51 (1.01, 6.26)

Reference group, IOM weight gain guidelines met (n=104); normal (BMI 18.5-24.9), overweight (BMI 25.0-29.9), obese (>30.0).

255 Can a threshold third trimester hemoglobin A1C be used to predict maternal and neonatal pathology?

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OBJECTIVE: To determine a threshold, third trimester hemoglobin A1C (HbA1C) that predicts adverse maternal and neonatal outcomes.

STUDY DESIGN: This was a retrospective cohort study of 157 women who delivered 169 singleton infants at Vidant Medical Center between 2007 and 2012 who had either gestational (48%) or pre-existing diabetes (52%). The primary outcome was whether or not the infant was discharged home with mother. Secondary outcomes included macrosomia/ large for gestational age infants, intrauterine fetal demise, neonatal intensive care admission, intravenous treatment of hypoglycemia (<40 mg%), hyperbilirubinemia (>12mg%), and shoulder dystocia. Maternal primary outcomes included preeclampsia and unintended cesarean section. A ROC analysis was performed to determine the threshold HbA1C that would predict a composite adverse neonatal outcome including any one of the latter outcomes.

RESULTS: Our population was typically obese (Table), African-American or hispanic (68%), and indigent. 74% of the term patients went home with their neonates and 22% of term neonates were admitted to the NICU. Our ROC analysis identified a threshold of HbA1C of 5.3 %. There were no significant differences in age, parity, or DM class among the low and high HbA1C classes. The Table depicts the differences in outcomes above and below a third trimester HbA1C of 5.3%. We found a significant difference in the HbA1C between those that had any secondary outcome present compared to those where all adverse outcomes were absent.

CONCLUSION: A HbA1C >5.3 % appears to predict poor pregnancy outcomes for mother and neonate and might be used as a management goal.

Outcomes by high and low HbA1C

Parameter	HbA1C < 5.3	HbA1C >5.3
BMI (STD)	35.1(4.4)	39.7(8.8)
Initial HbA1C (STD)	6.27(1.4)	7.43(1.8)
Max.Units Insulin	94	107
Third Trimester HbA1C (STD	5.07(0.2)	6.35(0.85)
C/S*	20%	38%
Preeclampsia	0	12%
IUFD	0	3.4%

*All patients with intended vaginal birth.

256 Sleep apnea in early pregnancy: an independent risk factor for the development of gestational diabetes

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OBJECTIVE: Objective assessments of the association between sleep apnea (SA) and glucose metabolism in pregnancy are limited. The objective of this study was to evaluate the relationship between objectively assessed SA in early pregnancy and the subsequent development of gestational diabetes mellitus (GDM) in a cohort of high risk pregnant women.

STUDY DESIGN: This was a planned subgroup analysis of data from a SA and preeclampsia study. Women with chronic hypertension, obesity, twin gestation and/or a history of preeclampsia (i.e., those at high risk of preeclampsia) who were between 6 and 20 weeks were recruited to participate in an overnight SA evaluation with a validated portable monitor. Women with pregestational diabetes were excluded. SA was defined as an apnea-hypopnea index (AHI) of ≥ 5. The diagnosis of GDM was abstracted from the medical record and confirmed by a review of oral glucose tolerance testing (OGTT) by study personnel blinded to the sleep study results. The relationship between SA and GDM was explored using univariable and multivariable analysis.

RESULTS: AHI and OGTT results were available for 75 of the 80 women recruited. The mean gestational age at the sleep study was 17.1 ± 4.2 weeks. Twenty-six (35%) women had SA and 20 (25%) developed GDM. Women with SA differed from those without SA according to various demographic characteristics (Table). Women with SA were more likely to develop GDM (46.2% vs. 14.3% p=.003). After controlling for possible confounding factors including BMI, maternal age, and a history of chronic hypertension, SA remained independently and positively associated with the development of GDM (OR 3.7, 95% CI=1.1, 13.3).

CONCLUSION: Among high-risk women, SA during the first half of pregnancy is an independent risk factor for the development of GDM. Further research is needed to determine whether screening for and treatment of SA during pregnancy can lessen the frequency of GDM.

Demographic and clinical characteristics

	Women with SA N = 26	Women without SA N = 49	P value
Maternal age	35.8 ± 4.0	33.9 ± 6.8	0.2
White Black Hispanic Other	42% 35% 19% 4%	33% 37% 18% 12%	0.8
Pre-pregnancy BMI	39.3 ± 7.5	32.4 ± 9.6	0.002
Multiparous	73%	82%	0.4
Chronic hypertension	61%	24%	0.002
Prior preeclampsia	31%	27%	0.7
Twins	4%	10%	0.7

257 Comparison of insulin requirements in women with type 1 diabetes managed with continuous subcutaneous insulin infusion versus multiple daily insulin injections

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OBJECTIVE: Type 1 diabetes mellitus (T1DM) may be managed with continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI), however comparisons of insulin profiles between these two modalities have not been well described. Our objective was to characterize and compare the changes in insulin basal and bolus dosing across gestation in patients managed with CSII and MDI.