Notes from the GDM Pasadena II:
An International Conference on Gestational Diabetes

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DAY 2 - 4/9/10

Epidemiology of Gestational Diabetes and Obesity

Prevalence of Diabetes Mellitus (GDM)

Jean Lawrence, ScD, MPH, MSSA; Research Scientist / Epidemiologist, Dept. of Research And Evaluation, Kaiser Permanente Southern California

Prevalence of GDM increased by 10% to 100 % over the past 20 years
In U.S. - Native Americans, Hispanic and Asians at greatest risk for developing GDM

Pre-gravid Predictors of GDM

Monique Hedderson, PhD; Epidemiologist, Northern California Kaiser Research Center, Oakland, California

Pregravid risk factors for GDM

Non-modifiable	Modifiable	Lifestyle Habits
Race	Increased pregravid BMI	Reduced physical activity
Genetics	Abdominal adiposity	Increased by western diet vs. prudent diet
	Weight at birth (LBW) Weight at adolescence Weight as adult If overweight at all three times at highest risk	Increased fiber intake reduces the chance of DM
	Cardio-metabolic risk factors: Fetuin-A (new marker) CRP (higher in GDM)	5 sugar sweetened colas (beverages) a week increases DM by 20%
		High progestin oral contraceptive increases risk

COMMENT:
Re: DR. HEDDERSON Presentation: I just wanted to point out to you that the comment re: high progestin OCPs being associated with an increased risk of developing GDM from Dr. Hedderson's presentation was not exactly what her article says, since the high-androgenic progestin confidence interval crossed 1. However, low androgenic progestins did seem to protect against GDM, thus another non-contraceptive benefit of contraception highlighted!

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Early Pregnancy Predictors of Gestational Diabetes Mellitus:
Using Biomarkers to Help Elucidate Hypothesized Causal Mechanisms

Michelle Williams, ScD; Professor of Epidemiology, School of Public Health, University of Washington, Seattle

Biological markers:
Altered early pregnancy lipid and lipoprotein profiles
Early chronic systematic inflammation – increased CRP, increased leptin
Vitamin D insufficiency/deficiency
Oxidative stress, antioxidant insufficiency
Decreased adipocytokines (secreted in inverse relationship to obesity)
Small dense LDL more indicative of GDM

Diet	Lifestyle
Reduce GDM risk by half by reducing fat intake from 35% to 20%	Avoid adult weight gain/obesity
Diet rich in fruits vegetables and whole grains reduces the risk of GDM	Participate in regular leisure time physical activity
Vitamin C- an antioxidant	Being active before and during pregnancy reduces the risk of GDM by 60%
Vitamin D – if breastfeeding you need supplementation or will be deficient by 13 weeks	**Sleep disorders** 70 million Americans are at risk for many conditions due to sleep disorders.
	We need 7-8 hours per night. Too much or too little sleep increases the risk for GDM. Short sleepers have greater body mass

Prevention of GDM

Lisa Chasan-Taber, ScD: Associate Professor Epidemiology,
School of Public Health,University of Massachusetts, Amherst, Massachusetts

Lifestyle modification in diet and exercise during pregnancy can prevent GDM and maintained into the postpartum period provide an opportunity to intervene before the development of overt DM

Current recommendations are 30 minutes a day of moderate exercise (brisk walking)
Diet: reduce fat and increase fiber to reduce the glycemic load
Vitamin D recommendations are all over the map from 400 to 4000+ IU/d

Pregnancy Weight Gain in GDM; Implications for the Fetus

Teresa Hillier, MD, MS; Senior Investigator, Center for Health Research, Kaiser Northwest, Portland, Oregon

Two large randomized controlled trials demonstrated improvement in neonatal outcomes with treatment of GDM
Optimal weight gain in pregnancy results in:

- Fewer big babies (macrosomia)
- Fewer Preterm deliveries
- Fewer smaller babies

One abnormality, (>130 mg/dl) on the 50 gm. glucose challenge test or an abnormality on the oral glucose tolerance test (OGTT) increases the risk of childhood obesity.

Hillier TA, PedulaKL, SchmidtMM, MullenJA, CharlesMA, Pettitt DJ. Childhood obesity and metabolic
imprinting: the ongoing effects of maternal hyperglycemia. Diabetes Care 2007;30:2287–92.
3. Hillier TA, Pedula KL, Vesco KK, Schmidt MM, Mullen JA, LeBlanc ES, Pettitt DJ. Excess gestational
weight gain: Modifying fetal macrosomia risk association with maternal glucose. Obstet Gynecol
2008; 112(5):1007-14.

Gestational Diabetes and Birth Defects

Adolfo Correa, MD, PhD: Division of Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA

During the past two decades, there have been several epidemiologic studies on possible associations of gestational diabetes with birth defects. Although findings from these studies have been inconsistent, reports of increasing prevalence of GDM highlight the need to assess the basis for such reports. This presentation will review findings from studies of associations of GDM with birth defects and of the variation of such associations with maternal pre-pregnancy body mass index and with fasting serum glucose during pregnancy, suggesting that the observed associations may be limited to offspring of with undiagnosed pre-existing diabetes. Possible implications for further research, prevention, and monitoring will be highlighted.

Fasting glucose >105 mg/dl at any clinic visit may be pre-diagnostic of GDM
cut points we use may not be the best for risk of fetal malformations
GDM defects were associated with pre-pregnancy obesity.

Independent Contribution of BMI to Outcomes in the HAPO Study

Donald Coustan, MD: Professor of OB/GYN, Division of MFM, Alpert Medical School of Brown University, Women & Infants' Hospital, Providence, Rhode Island

There is a independent direct relationship between increasing
BMI and such adiverse outcomes as fetal macrosomia, primary cesarean section, neonatal hyperinsulinemia (as measured by cord C-peptide), shoulder dystocia/birth trauma and preeclampsia, even when adjusted for maternal fasting plasma glucose.
There was also an inverse relationship between maternal BMI and preterm birth.
Once pregnancy begins, pre-pregnancy BMI is a non-modifiable risk factor
Study of BMI at the time of the 2 hour, 75gram OGTT (fasting and 1 and 2 hours)

Increased Maternal BMI	**Secondary (fetal) outcomes**
Inverse relationship with BMI and preterm birth	+ for admission to the NICU
+ for Shoulder dystocia and birth injury	+ for macrosomia
+ for primary C-section	+ for Neonatal hyperinsulinemia (as measured by cord C-Peptide)
+ for preeclampsia	
Relative contribution of IGT and BMI	

Postpartum DM screen in women with history of GDM

Catherine Kim, MD, MPH: Assistant Professor of Medicine**,** University of Michigan
Ann Arbor, Michigan

Rationale for diabetes screening: Reduction in risk to next offspring, prevention of diabetes and complications in the mother.
HbA1c endorsed by the ADA as a screening test diagnostic of DM (>6.5) is convenient, has a low variability and is associated with perinatal complications both microvascular and macrovascular disease for the pregnant mother.

Testing with HgA1c

Positive	**Negative**
No fasting	Sensitive to red cell turnover –iron deficiency
No glucose challenge	Sensitive to hemoglobin traits
Less variability	Racial and ethnic variability
For Type 1 DM (Jensen study) Predictive of retinopathy (retinopathy increases between A1c 6 and 6.5 & microvascular complications (stroke and heart attack)	Point of care not endorsed

Questions: Is the A1c a good test at 6 weeks PP? How sensitive is it? Doing research to see if A1C can be used PP-problem may be dilutional effect of anemia postpartum

Lactation and Long term disease risk in women with a history of GDM

Erica Gunderson, PhD, RD; Research Scientist II, Division of Research, Kaiser Permanente Northern California, Oakland, California

Benefits of Lactation and post-partum:
Lactation results in favorable cardio metabolic risk factors

- If the mother breastfeeds > 3 months she has better HDL levels
- Lower blood insulin and glucose levels
- Higher insulin sensitivity and B-cell function
- Greater postpartum weight loss
- May protect against new onset of metabolic syndrome

B-cell function and Risk of DM in women with prior GDM

Anny Xiang, PhD; Research Scientist III/Biostatistician, Department of Research & Evaluation, Kaiser Permanente Southern California

Women with prior GDM were more insulin resistant and had reduced b-cell function as compared to normal women.

Reduced B-cell function seems to indicate which GDM women will become diabetic. Causes of B-cell function failure:

- Genetics
- Obesity
- Decreased Adipocytokines
- Increased inflammation (CRP)
- Beta cell overload
- Glucose and lipid toxicity

Where you start correlates with how fast you change. The strongest correlation seems to be:

- Weight gain 40%
- Falling adipocytokine 19%
- Increasing CRP 19%
- All three 70%

The conversion rate to DM is @ 11% per year after GDM, until 12 years out and then it equals about 7.2% per year

Weight gain, additional pregnancy and progestin only contraceptives were additional risks for diabetes development. Diabetes prevention should focus on reducing obesity and its metabolic effects to preserve β-cell function

Diabetes prevention in women with GDM

Assiamira Ferrara, MD, PhD; Senior Scientist, Division of Research, Kaiser Northern California, Oakland, California

For women with GDM, diet exercise and breast feeding started after a diagnosis of GDM and continued post partum were beneficial to reduce the risk for DM by 50% in GDM women.It is time to translate into clinical practice lifestyle intervention programs for diabetes prevention that start during pregnancy, soon after the diagnosis of GDM, or in the early postpartum period.

Risk of obesity/metabolic syndrome in offspring of women with GDM

Tine Dalsgaard Clausen, MD; Department of Obstetrics, University of Copenhagen, Denmark

Diabetes prevention should focus on reducing obesity and its metabolic effects to preserve b-cell function.

Influences include: Intrauterine environment, genetics and post-natal environment

Maternal overweight is an independent predictor of offspring increased BMI but not if the mother is older.
Normalize glucose before the 3rd trimester to reduce the impact of GDM on the offspring
For offspring of women diet-treated GDM there was a 2 x risk of overweight and a 4 x risk of Metabolic syndrome also which is + if

- the mom was overweight,
- the off spring smokes and
- the mother's family had a history of DM

We found that offspring of women with diet-treated GDM
had a two-fold higher risk of overweight and a four-fold higher risk of the metabolic syndrome than offspring from the background population. Maternal overweight was the strongest predictor and maternal 2-h glucose was also an independent predictor, whereas birth weight did not predict offspring outcome. Thus, offspring of women GDM are at risk of overweight and the metabolic syndrome in adulthood and intrauterine hyperglycemia may play a role in the pathogenesis.

Perinatal programming of childhood obesity and type 2 DM

Dana Dabelea, MD, PhD; Associate Professor, Director of Epidemiology, Department of Epidemiology, University of Colorado, Denver, Colorado

By following Pima Indians the strongest risk factor for development of type 2 DM was exposure to diabetes in utero

Those children exposed to DM in utero had increased:

- BMI
- Waist circumference
- Subcutaneous fat
- Central fat

BMI in exposed offspring was more initially but equal to the non-exposed at 27 months.

By age 9 the exposed children's BMI was increased more than those not exposed
There is an accelerated growth trajectory starting at ages 9-13 years.
Breastfeeding < 6 months had increased BMI
Breastfeeding > 6 months had comparable BMI as compared to normal