Maternal Obesity, Gestational Weight Gain, and Offspring Adiposity: The Exploring Perinatal Outcomes among Children Study

Jill L. Kaar, PhD[1], Tessa Crume, PhD[2], John T. Brinton, PhD[3], Kimberly J. Bischoff, MSHA[4], Robert McDuffie, MD[5], and Dana Dabelea, MD, PhD[2]

Objective To determine whether adequate vs excessive gestational weight gain (GWG) attenuated the association between maternal obesity and offspring outcomes.

Study design Data from 313 mother-child pairs participating in the Exploring Perinatal Outcomes among Children study were used to test this hypothesis. Maternal prepregnancy body mass index (BMI) and weight measures throughout pregnancy were abstracted from electronic medical records. GWG was categorized according to the 2009 Institute of Medicine criteria as adequate or excessive. Offspring outcomes were obtained at a research visit (average age 10.4 years) and included BMI, waist circumference (WC), subcutaneous adipose tissue (SAT) and visceral adipose tissue, high-density lipoprotein cholesterol, and triglyceride levels.

Results More overweight/obese mothers exceeded the Institute of Medicine GWG recommendations (68%) compared with normal-weight women (50%) ($P < .01$). Maternal prepregnancy BMI was associated with worse childhood outcomes, particularly among offspring of mothers with excessive GWG (increased BMI [20.34 vs 17.80 kg/m^2], WC [69.23 vs 62.83 cm], SAT [149.30 vs 90.47 cm^2], visceral adipose tissue [24.11 vs 17.55 cm^2], and homeostatic model assessment [52.52 vs 36.69], all $P < .001$). The effect of maternal prepregnancy BMI on several childhood outcomes was attenuated for offspring of mothers with adequate vs excessive GWG ($P < .05$ for the interaction between maternal BMI and GWG status on childhood BMI, WC, SAT, and high-density lipoprotein cholesterol).

Conclusion Our findings lend support for pregnancy interventions aiming at controlling GWG to prevent childhood obesity. *(J Pediatr 2014;165:509-15)*.

The prevalence of obesity has been increasing dramatically in the US, including among women of reproductive age.[1] Maternal obesity is a major risk factor for gestational diabetes mellitus (GDM) and future type 2 diabetes.[2] Moreover, observational studies suggest an independent association of maternal obesity with excessive fetal growth[3,4] and childhood obesity.[5] Alarmingly, increasing obesity trends are now observed early in life, even among young infants,[6] pointing toward harmful changes in the environment in which contemporary children are born and raised.[7] These and other observations lead to the hypothesis that maternal obesity during pregnancy is associated with lifelong consequences in the offspring[8] and, possibly, over successive generations.[9] It has been suggested that a transgenerational "vicious cycle" results, explaining at least in part, the increases in obesity, GDM, and type 2 diabetes seen over the past several decades.[10] In addition, obese children tend to become obese adults and, once present, obesity and its consequences are expensive and difficult to treat. This makes pregnancy a crucial window of opportunity for obesity prevention in this and the next generation.

The role of gestational weight gain (GWG) on childhood adiposity outcomes is less clear and incompletely studied. Some, but not all,[11,12] epidemiologic studies have found that greater GWG is associated with greater body mass index (BMI) in childhood[13-17] and adolescence[5] and with increased fat mass and poorer metabolic and vascular traits at age 9 years.[18] Some studies have suggested that the association of greater maternal weight gain and offspring obesity persists into adulthood.[12] Maternal prepregnancy BMI and excessive GWG have been linked independently to increased adiposity in the offspring.[11,16,17,19-21] In a group of preschool children, the odds of being categorized as overweight by age 4-5 years was increased by 57% in children exposed to both a maternal prepregnancy BMI greater ≥25 kg/m^2 and excessive weight gain during pregnancy.[16] It remains unclear however, whether the effect of maternal prepregnancy BMI on childhood adiposity outcomes is mitigated by adequate weight gain during pregnancy.

BMI	Body mass index	IOM	Institute of Medicine
EPOCH	Exploring Perinatal Outcomes among Children	KPCO	Kaiser Permanente of Colorado Health Plan
GDM	Gestational diabetes mellitus	SAT	Subcutaneous adipose tissue
GWG	Gestational weight gain	TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol	VAT	Visceral adipose tissue
HOMA-IR	Homeostatic model assessment	WC	Waist circumference

From the [1]Department of Pediatrics, Colorado School of Medicine, Departments of [2]Epidemiology and [3]Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Denver; [4]Institute for Health Research, and [5]Department of Perinatology, Kaiser Permanente of Colorado, Denver, CO

Supported by the National Institutes of Health (RO1 DK068001). The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2014.05.050

The answer to this question is important because it would provide support to the notion that healthier weight-gain patterns during pregnancy may improve the short- and long-term effects on offspring who have been exposed to maternal obesity. To address this question, we used data from the Exploring Perinatal Outcomes among Children (EPOCH) study in Colorado.

Methods

The EPOCH study is an observational historical prospective cohort comprising children born between 1992 and 2002 at a single hospital in Colorado, whose biological mothers were members of the Kaiser Permanente of Colorado Health Plan (KPCO) and who were offspring of singleton pregnancies. All children exposed to maternal GDM were eligible, together with a random sample of children not exposed to GDM. Children were invited to attend an in person-research visit when they were on average age 10.5 years (range, 6-13 years), and approximately 68% agreed to participate.

Included in this analysis were 313 mother-child pairs (141 non-Hispanic white, 145 Hispanic, 27 non-Hispanic African American) who were part of the EPOCH study and had complete data on maternal prepregnancy BMI, GWG, and offspring adiposity outcomes. Children and their mothers completed a research visit between January 2006 and October 2009. Because the EPOCH study was specifically designed to explore the long-term effects of maternal GDM on offspring, the cohort is enriched in offspring of GDM mothers. Because we were exploring specific hypotheses regarding the role of excessive GWG as effect modifier, the small number of offspring of mothers who gained insufficient gestational weight during pregnancy was excluded. The study was approved by the local Institutional Review Board, and all participants provided written informed consent and youth provided written assent.

Maternal Measures

Maternal pregnancy measures (weight, GDM) and offspring birth weight were obtained from the KPCO perinatal database, a linkage of the maternal and perinatal medical record containing prenatal and delivery events for each woman. Maternal prepregnancy weight was measured before the last menstrual cycle preceding pregnancy. Maternal height was collected at the in-person research visit and used to calculate prepregnancy BMI (kg/m^2). BMI was categorized as normal weight (18.5-25 kg/m^2) and overweight/obese ($\geq$25 kg/m^2). Multiple weight measures during pregnancy (on average 4 per participant) were used to model GWG using a longitudinal mixed effects model that included fixed effects for time, time squared, prepregnant BMI, maternal age, gravidity, and a time by prepregnant BMI interaction. The model included subject-specific intercept and slope terms. GWG was estimated using the absolute predicted weight gain for a full-term pregnancy (model predicted weight at term minus model predicted weight at conception). Women were categorized as either exceeding or meeting the 2009 recommended Institute of Medicine (IOM) GWG guidelines (adequate total GWG for normal BMI prepregnancy 11.4-15.9 kg and overweight/obese BMI prepregnancy 5-11.4 kg).[22] Women who gained inadequate weight during pregnancy were excluded from this analysis, according to our a priori hypothesis.

Physician-diagnosed GDM was coded as present if diagnosed through the standard KPCO screening protocol and absent if screening was negative. Since the 1990s, KPCO has routinely screened for GDM in all nondiabetic pregnancies using a 2-step standard protocol and criteria based on the National Diabetes Data Group recommendations.[23]

Childhood Measures

All children were invited to an in-person research visit, which included anthropometric measures, questionnaires, a magnetic resonance imaging exam of the abdominal region and a fasting blood sample. Race/ethnicity was self-reported using 2000 US census-based questions and categorized as Hispanic (any race), non-Hispanic white, or non-Hispanic African American. Pubertal development was assessed by child self-report with a diagrammatic representation of Tanner staging adapted from Marshall and Tanner.[24] Youth were categorized as Tanner <2 (prepubertal) and $\geq$2 (pubertal). Total energy intake (kilocalories per day) was assessed using the Block Kid's Food Questionnaire.[25] Self-reported key activities, both sedentary and nonsedentary, performed during the previous 3 days were measured using a 3-day Physical Activity Recall questionnaire.[26] Each 30-minute block of activity was assigned a metabolic equivalent variable to accommodate the energy expenditure. Results were reported as the average number of 30-minute blocks of moderate-to-vigorous activity per day. Current height and weight were measured in light clothing and without shoes. Weight was measured to the nearest 0.1 kg using a portable electronic SECA scale (SECA, Chino, California). Height was measured to the nearest 0.1 cm using a portable SECA stadiometer. Height and weight were measured and recorded twice, and an average was taken. Scales and stadiometers were calibrated every 2 months using standard weights for scales and an aluminum measuring rod for the stadiometer. BMI was calculated as kg/m^2. Waist circumference (WC) was measured to the nearest 1 mm at the midpoint between the lower ribs and the pelvic bone with a metal or fiberglass nonspring-loaded tape measure.

Magnetic resonance imaging of the abdominal region was used to quantify visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) with a 3T HDx imager (General Electric, Waukashau, Wisconsin) by a trained technician. Each participant was placed supine and a series of T1-weighted coronal images were taken to locate the L4/L5 plane. One axial, 10-mm, T1-weighted images at the umbilicus or L4/L5 vertebra was analyzed to determine SAT and VAT content. The analysis technique used was a modification of the technique of Engelson,[27] where adipose tissue regions were differentiated by their signal intensity and location. Images were analyzed by a single reader.

Cholesterol, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) were obtained while the patient