OBSTETRICS

Association of trimester-specific gestational weight gain with fetal growth, offspring obesity, and cardiometabolic traits in early childhood

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OBJECTIVE: The purpose of this study was to investigate the association of trimester-specific gestational weight gain with offspring fetal growth, obesity risk, and cardiometabolic health outcomes from birth to 4 years of age.

STUDY DESIGN: We conducted the present study with 977 mother-child pairs of the pregnancy cohort "Rhea" study in Crete, Greece. We measured birthweight, body mass index from 6 months to 4 years of age, waist circumference, skinfold thickness, blood pressure, and blood levels of lipids, C-reactive protein, and adipose tissue hormones at 4 years of age. We used multiple linear and log Poisson regression models to examine the association of exposure with continuous or binary outcomes, respectively.

RESULTS: Greater rate of gestational weight gain in the first trimester of pregnancy (per 200 g/wk) was associated with increased risk of overweight/obesity from 2 years (relative risk [RR], 1.25; 95% confidence interval [CI], 1.09—1.42) to 4 years of age (RR, 1.15; 95% CI, 1.05—1.25), but not with birth size. Each 200 g/wk of weight gain in the first trimester of pregnancy was also associated with greater risk of high waist circumference (RR, 1.13; 95% CI, 1.04—1.23), high sum of skinfold thickness (RR, 1.15; 95% CI, 1.02—1.29), and higher diastolic blood pressure at 4 years of age (β, 0.43 mm Hg; 95% CI, 0.00—0.86). Greater rate of gestational weight gain during the second and third trimesters of pregnancy (per 200 g/wk) was associated with greater risk of large-for-gestational-age neonates (RR, 1.22; 95% CI, 1.02, 1.45) and higher levels of cord blood leptin (ratio of geometric means, 1.08; 95% CI, 1.00—1.17), but not with child anthropometry at later ages.

CONCLUSION: Timing of gestational weight gain may influence childhood cardiometabolic outcomes differentially.

Key words: blood pressure, children, gestational weight gain, obesity, pregnancy cohort

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Gestational diabetes mellitus, maternal obesity, and excessive weight gain during pregnancy, which are each markers of fetal overnutrition, are considered among the most important modifiable early-life risk factors of childhood obesity.[1] From a public health perspective, gestational weight gain (GWG) recently has gained particular

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interest because interventions on GWG could benefit from the fact that they (1) target women for the short duration of pregnancy, (2) can take advantage of the frequent visits of women to their obstetricians, and, if successful, (3) can reduce maternal postpartum weight retention and the risk of maternal obesity that might complicate future pregnancies.[2-4]

Excessive GWG has been associated with poor health outcomes for both mother and child over the short- and long-term.[5,6] Two recent metaanalyses suggested that excessive GWG is associated with higher risk of offspring obesity throughout life[7,8]; more debatable are the results when offspring adiposity is assessed by measures other than body mass index (BMI).[9-14] Some birth cohorts have attempted to disentangle the effect of GWG depending on the timing of the gain and have suggested that early pregnancy weight gain might be critical for the development of offspring obesity later in life.[12,13,15-18] However, we are not aware of any studies that have examined the association of trimester-specific GWG with offspring obesity in the first 4 years of life.

Findings for the association between GWG and other offspring cardiovascular traits such as blood pressure or serum lipid profile have been less consistent, mainly because of confounding by offspring adiposity.[9,13,14,19,20] We are not aware of any studies that have examined the association of trimester-specific GWG with offspring blood pressure, lipid profile, and adipose tissue hormones in children as young as 4 years old in a population of substantial size.

In the present study, we examined the association of GWG (total and trimester-specific) with offspring birthweight, postnatal growth, obesity, and a range of cardiometabolic risk factors at 4 years old (waist circumference, skinfolds, blood pressure, lipids, adiponectin, leptin, and C-reactive protein) in the "Rhea" pregnancy cohort in Crete, Greece.

Materials and methods

We recruited mothers who became pregnant from February 2007 to January 2008 who were residents in the prefecture of Heraklion Crete, Greece.[21] Research assistants invited women to provide blood and urine samples and to participate in a face-to-face interview at enrollment at <15 weeks of gestation. The next contact with the mothers was at 24 weeks of gestation, at birth, at 8-10 weeks after delivery, and for the child's follow-up examination at 9 and 18 months, and at 4 years old. The study was approved by the Ethical Committee of the University Hospital of Heraklion (Crete, Greece), and all participants provided written informed consent.

Of 1363 singleton live births, 977 had complete data on maternal GWG, offspring birthweight, and BMI from 6 months to 4 years. Of these, 451 children had cord leptin measurements; 661 children had waist circumference and skinfold thickness measurements at 4 years; 518 children had blood pressure measurements, and 567 children provided blood samples at the 4-year follow-up examination. Trimester-specific GWG data were available for 595 mother-child pairs. We excluded births at <34 weeks of gestation (n = 20) to limit bias because of the dependence of GWG on gestational age.[22]

GWG

At enrollment, research assistants measured mother's height (centimeters) and weight (kilograms) in light clothing without shoes and obtained information on prepregnancy weight. We calculated first-trimester GWG rate to be the difference between self-reported prepregnancy weight and weight as measured at enrollment and divided it by the corresponding gestational age. We calculated second- and third- trimester GWG rate to be the difference between total and first-trimester GWG. We decided to examine changes in first-trimester and second- and third- trimester GWG per 200 g/wk in an effort to use a common rate of change that would be reasonable for both periods of pregnancy.[23] This weekly rate corresponds to a 2.8-kg more weight gain up to 14 weeks of gestation and to 5.2-kg more weight gain for the remaining period of pregnancy, which is close to the recommended weight gain for the first trimester of pregnancy, and corresponds to one-half of the recommended weight gain for the second and third trimester of pregnancy for normal-weight women.[23] We obtained information on total GWG after delivery (9 ± 2 months), based on a phone-interview with the mother. We examined total GWG as continuous variable (per 2 kg change) and as categoric (inadequate, adequate, or excessive).[23]

Child anthropometry

Weight and length at birth were obtained from the hospital delivery logs and medical records. Large-for-gestational-age (LGA) neonates were defined as live-born infants above the 90th percentile of birthweight for gestational age in a referent population.[24]

At child follow-up visits, trained research assistants measured weight and length (up to 2 years old) or height (from 2-4 years old) using validated scales (Seca 354 baby scale, Seca Bellisima 841; Seca Corporation, Hanover, MD) and stadiometers (Seca 210 measuring mat, Seca 213; Seca Corporation) according to standard operating procedures. Repeated measures of weight and length/height were also abstracted from the children's health cards. We calculated BMI and converted raw values into sex- and age-specific standard deviation scores (SD scores) by using internally generated growth reference curves. Because of variation in children's ages at measurement, we estimated BMI SD scores at exactly 6 months and 1, 2, 3, and 4 years of age with a sex- and age-specific, multilevel (mixed) linear model that was fitted with fractional polynomials and random effects for the child.[25] To minimize the effect of children with implausible growth trajectories, we excluded children whose measurements were ≤5 SD or >5 SD from the mean at any age.

We defined rapid BMI growth the first 6 months of life as a BMI SD score gain >0.67; children with a BMI SD score gain ≤0.67 constituted the reference group.[26] For defining childhood overweight/obesity at 2, 3, and 4 years old, we used the BMI cutoff points for sex and