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Longitudinal changes in gestational weight gain and the association with intrauterine fetal growth☆

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ABSTRACT

Objective: Total pregnancy weight gain has been associated with infant birthweight; however, most prior studies lacked repeat ultrasound measurements. Understanding of the longitudinal changes in maternal weight gain and intrauterine changes in fetal anthropometrics is limited.

Study design: Prospective data from 1314 Scandinavian singleton pregnancies at high-risk for delivering small-for-gestational-age (SGA) were analyzed. Women had ≥1 (median 12) antenatal weight measurements. Ultrasounds were targeted at17, 25, 33, and 37 weeks of gestation. Analyses involved a multi-step process. First, trajectories were estimated across gestation for maternal weight gain and fetal biometrics [abdominal circumference (AC, mm), biparietal diameter (BPD, mm), femur length (FL, mm), and estimated fetal weight (EFW, g)] using linear mixed models. Second, the association between maternal weight changes (per 5 kg) and corresponding fetal growth from 0 to 17, 17 to 28, and 28 to 37 weeks was estimated for each fetal parameter adjusting for prepregnancy body mass index, height, parity, chronic diseases, age, smoking, fetal sex, and weight gain up to the respective period as applicable. Third, the probability of fetal SGA, EFW <10th percentile, at the 3rd ultrasound was estimated across the spectrum of maternal weight gain rate by SGA status at the 2nd ultrasound.

Results: From 0 to 17 weeks, changes in maternal weight were most strongly associated with changes in BPD [β = 0.51 per 5 kg (95%CI 0.26, 0.76)] and FL [β = 0.46 per 5 kg (95%CI 0.26, 0.65)]. From 17 to 28 weeks, AC [β = 2.92 per 5 kg (95%CI 1.62, 4.22)] and EFW [β = 58.7 per 5 kg (95%CI 29.5, 88.0)] were more strongly associated with changes in maternal weight. Increased maternal weight gain was significantly associated with a reduced probability of intrauterine SGA; for a normal weight woman with SGA at the 2nd ultrasound, the probability of fetal SGA with a weight gain rate of 0.29 kg/w (10th percentile) was 59%, compared to 38% with a rate of 0.67 kg/w (90th percentile).

Conclusion: Among women at high-risk for SGA, maternal weight gain was associated with fetal growth throughout pregnancy, but had a differential relationship with specific biometrics across gestation. For women with fetal SGA identified mid-pregnancy, increased antenatal weight gain was associated with a decreased probability of fetal SGA approximately 7 weeks later.

Introduction

Gestational weight gain represents the accumulation of maternal, fetal, and placental tissue throughout pregnancy and maternal fluid expansion. The Institute of Medicine (IOM) provides weight gain recommendations with the intention of optimizing maternal and neonatal outcomes [1]. Birthweight, was a primary outcome studied when defining the recommendations, as it is predictive of neonatal and long-term morbidities [1]. Gaining less or greater than recommended increases the risk for neonatal small-for-gestational-age (SGA) or large-for-gestational-age (LGA) birthweight, respectively [2]. There may be advantages of using

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Abbreviations: AC, abdominal circumference; BMI, body mass index; BPD, biparietal diameter; CI, confidence interval; EFW, estimated fetal weight; FL, femur length; IOM, Institute of Medicine; LMP, last menstrual period; MAD, middle abdominal diameter; SGA, small-for-gestational-age.

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intrauterine fetal growth instead of birthweight. Assessing the relationship between maternal weight gain and fetal biometrics, may aid in better understanding the mechanism by which maternal weight impacts growth and in identifying timeframes for interventions. Also, most prior research related to fetal growth was limited to total weight gain [3], which limits detection of critical periods where maternal weight may be more or less important for fetal growth [4–6], and has methodological limitations [7]. Previous longitudinal gestational weight gain and intrauterine fetal growth studies have been limited by small sample sizes [8,9], did not examine the changing dynamics between weight gain and fetal growth across gestation [9], or only examined longitudinal linear growth [7].

Our objective was to characterize the association between maternal weight gain and fetal growth across gestation in a prospective cohort study with longitudinal measures of antenatal weight gain and fetal growth including femur length (FL), abdominal circumference (AC), biparietal diameter (BPD) and estimated fetal weight (EFW). We also assess the importance of maternal weight change for fetal SGA after detection mid-gestation.

Materials and methods

The NICHD Study of Successive Small-for-Gestational-Age Births was a prospective cohort study conducted in Norway and Sweden (1986–1988) [10]. Eligible women were parity 1 or 2, Caucasian, spoke a Scandinavian language, had a singleton gestation, and were <20 weeks of gestation by enrollment ($n = 5722$). The original cohort design included two groups of women. First, a 10% random sample of women were enrolled to be representative of the underlying source population ($n = 561$). Second, women who were identified as having an elevated risk for delivering an SGA neonate based on the following were enrolled: prior low birthweight infant ($n = 462$; 33.4%) or perinatal death ($n = 85$; 6.1%), smoking at conception ($n = 955$; 69.0%), chronic renal disease or hypertension ($n = 39$; 2.8%), and/or a prepregnancy weight <50 kg ($n = 306$; 22.1%) ($n = 1384$). By design of the original protocol, the remaining non-high-risk women were not enrolled in the study. All participants provided signed informed consent and institutional review board approval was obtained.

We limited the current analysis to high-risk women with data on, height, ≥1 antenatal weight measurement, ≥1 fetal ultrasound, and relevant covariates, describe below ($n = 1314$). The women in the final sample were more likely (69.5%) to be primiparous than excluded women (55.9%) ($P = 0.01$). No other meaningful or significant differences were observed in prepregnancy weight, height, age, smoking, chronic diseases, fetal sex or gestational age at delivery between the final and excluded sample ($n = 70$; 5.0%) (data not shown).

Antenatal visits were targeted at 17 (95% ±2), 25 (95% ±1), 33 (95% ±1), and 37 (95% ±1) weeks. Gestational age was calculated based on last menstrual period (LMP) and confirmed ±14 days by second trimester ultrasound. The ultrasound estimate was used if discrepant with LMP or LMP was missing ($n = 260$; 18.8%) [10]. At enrollment, women reported smoking at conception, chronic diseases including renal disease, chronic hypertension, heart disease or diabetes, and their prepregnancy weight and height. Parity was defined as the number of previous births ≥20 weeks. Women were instructed to bring their personal health record to each study visit. This record contained women's weight recorded at each prenatal visit by her regular health care provider and at hospital admission for delivery. Study midwives extracted the weight and date of each measurement (median 11, max 21).

The fetal ultrasound measures obtained at each study visit included BPD (mm), middle abdominal diameter (mm), and FL (mm). The AC (mm) was calculated as 3.1416*(middle abdominal diameter). The Hadlock formula was used to calculate EFW (g) [11]. Intrauterine SGA was defined as EFW < 10th percentile of the random 10% of the study sample ($n = 561$) to be representative of the source population. Fetal sex was reported from the newborn's medical exam.

Longitudinal associations between maternal weight gain and fetal growth (AC, BPD, FL, and EFW) were analyzed using a multi-stage approach. First, individual trajectories across gestation of weight gain and fetal growth were estimated using linear mixed models [12]. This approach allowed for the estimation of overall trajectories and individual's trajectories. Second, we used individual's trajectories to calculate each individual's weight and fetal growth at 17, 28 and 37 weeks, this accounted for the different number of weight measurements and the variation in study visit days between women.

Prepregnancy weight was obtained by extrapolation from the maternal weight linear mixed model in order to correct for potential errors in self-reported weight and account for missing values ($n = 6$). Prepregnancy body mass index (BMI, kg/m^2) was calculated and categorized: underweight (BMI < 18.5), normal weight (18.5–24.9), overweight (25.0–29.9), or obese (≥30.0) [13]. Due to the limited number of obese women ($n = 32$), overweight and obese were combined.

We computed Pearson correlations between changes in maternal weight and fetal size between early- (0–17 weeks), mid- (17–28 weeks), and late-pregnancy (28–37 weeks). We used linear regression to estimate the association between weight gain and fetal growth for each period adjusting for maternal age, prepregnancy BMI, height, parity, chronic diseases, smoking, and fetal sex. Mid- and late-pregnancy models were also adjusted for maternal weight gain up to the start of the respective period. We tested for multiplicative interactions between each of the covariates and maternal weight change.

We assessed the impact of maternal weight gain on fetal SGA, an important clinical endpoint. For this analysis, subjects had to have EFW estimated at both the 2nd and 3rd ultrasound ($n = 972$). Logistic regression was used to estimate the probability of 3rd ultrasound fetal SGA across the spectrum of maternal weight gain rate between ultrasounds and tested for an interaction between 2nd ultrasound fetal SGA and maternal weight gain. Goodness of fit tests and spline analyses confirmed that the logistic regression model with a linear term for weight gain rate fit well.

SAS version 9.4 (Cary, NC, USA) and R version 3.0.2 (Vienna, Austria) were used and P-values <0.05 were considered significant.

Results

Women were on average 29 years of age and all were parous with 30.8% having had two prior births (Table 1). Many women smoked at conception (69%), of which 88% and 81% continued into the 2nd and 3rd trimesters, respectively. Maternal weight gain increased across gestation (Fig. 1) for an average total gain of 15.0 kg (standard deviation [SD] 4.7). The large variations in percentiles reflect in part prepregnancy weight variation. Weight gain differed by prepregnancy BMI ($P < 0.001$) with overweight/obese women gaining the lowest rate during the 2nd and 3rd trimester (0.40 kg/week; SD 0.18); however, there was no difference between underweight (0.45 kg/week; SD 0.14) and normal weight women (0.47 kg/week; SD 0.14) ($P = 0.25$). As expected, fetal growth rate increased with increasing gestation (Fig. 2).