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Excess pregnancy weight gain in latinas: Impact on infant's adiposity and growth hormones at birth

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ABSTRACT

Excess maternal weight gain during pregnancy has been associated with childhood overweight and obesity both in mothers with and without obesity. Latinx children are at higher risk for earlier obesity compared with other population groups. A cohort of 82 self-identified pregnant Latina women were recruited at the prenatal clinics of Zuckerberg San Francisco General Hospital (ZSFG) prior to delivery during the second and third trimesters of pregnancy in 2011 and 2012. Maternal pre-pregnancy weight and weight prior to delivery were collected by self-report to calculate maternal pre-pregnancy body mass index (BMI) and weight gain in pregnancy. At delivery, anthropometric measurements of infants were obtained and cord blood and maternal finger stick blood samples were collected for hormonal assays. Fifty-three point seven percent of women had excessive weight gain in pregnancy. A high percentage of the cohort was overweight and obese prior to pregnancy (67.1%) with mean pre-pregnancy BMI 27.4 ± 4.5 kg/m^2 and greater pre-pregnancy weight was independently associated with weight gain during pregnancy (OR 1.05, 95%CI 1.002–1.09). Mean infant birthweight was 3377.2 ± 481.5 g and excessive weight gain in pregnancy was independently associated with birthweight percentile (OR 13.46, 95%CI 2.43–34.50). Excessive gestational gain was positively associated with cord blood insulin-like growth factor-1 (IGF-1) and negatively with Peptide YY (PYY) levels. Latina women with pre-pregnancy overweight and obesity have a high rate of excessive gestational gain in pregnancy and could benefit from early counseling about appropriate gain in pregnancy. Excessive gestational weight impacts the intrauterine environment in high-risk infants impacting fetal growth and development.

1. Background

1.1. Excess maternal gestational weight gain and child overweight and obesity

Excess maternal weight gain during pregnancy, defined by the Institute of Medicine (IOM) (2009) and accepted by American College of Obstetrics and Gynecology (ACOG) differs based on pre-pregnancy body mass index status (American College of Obstetrics and Gynecologists, xxxx; Institute of Medicine, 2009). Excessive gestational gain has been associated with childhood and adolescent overweight and obesity both in previously obese and non-obese mothers (Nehring et al., 2013; Starling et al., 2015; Ensenauer et al., 2013; Widen et al., 2015; Leng et al., 2015; Oken et al., 2007, 2008; Guo et al., 2015; Mamun et al., 2014; Van Rossem et al., 2015; Sridhar et al., 2014; Tie et al., 2014; Sparano et al., 2013; Wrotniak et al., 2008; Schack-Nielsen et al., 2009). Excessive maternal weight gain during pregnancy is common, with more than 40% of normal weight and more than 60% of overweight women exceeding the gestational weight gain guidelines (Chu et al., 2009).

1.2. Intrauterine environment, birthweight and childhood overweight

Previous studies have suggested that excessive gestational gain impacts the intrauterine environment and neonatal outcomes at birth including birthweight. (Strauss, 1997; Stotland et al., 2006; Zhang et al., 2015). Given the increasing rate of childhood obesity and overweight and high rates of excess maternal weight gain during pregnancy, it is important to better understand how excessive gain in pregnancy may

Abbreviations: BMI, Body Mass Index; CDC, Centers for Disease Control; CI, Confidence Interval; GDM, Gestational Diabetes Mellitus; IGF-1, Insulin Growth Factor-1; OR, Odds Ratio; PYY, Peptide YY; SFGH, San Francisco General Hospital.

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impact neonatal health from birth. While excessive gestational gain has been associated with increased birthweight, the mechanisms by which excessive gain impacts birthweight have not been fully delineated. Previous studies have found higher birthweight is associated with differences in growth and adiposity hormones but few studies to our knowledge, particularly in high risk populations, have evaluated the relationship between excessive gestational gain and neonatal growth and adiposity hormone levels.

Previous studies have indicated that increased levels of insulin-like growth factor 1 (IGF-1), a hormone that promotes natural tissue and bone growth, are associated with higher birthweight and longer birth length and may serve as a useful marker of increased risk for obesity later in life (Baker et al., 1993; Vatten et al., 2002; Christou et al., 2001; Klauwer et al., 1997; Yang and Yu, 2000; Nam et al., 1997; Ong et al., 2000; Kadakia et al., 2016). However, these studies have not assessed risk factors beyond infant birthweight or maternal pre-pregnancy BMI associated with higher levels of IGF-1 or other infant hormones at birth. Similarly, increased Peptide YY (PYY), a hormone produced by the ileum and colon that reduces appetite, is inversely correlated with birth weight (Siahanidou et al., 2005) yet it is not clear how excessive gestational gain may impact PYY levels at birth. Furthermore, higher neonatal leptin levels, made by adipose tissue that inhibits hunger, have been associated with increasing birth weight and have been shown to predict weight gain not only in infancy but also at 3 years of age. (Ong et al., 1999; Mantzoros et al., 2009; Tsai et al., 2004).

1.3. Excess weight gain in Latina mothers

Latina women are more likely to enter pregnancy overweight or obese compared with non-Hispanic Caucasian women (Dolin et al., 2020). Furthermore, Latina women with overweight and obesity are at greater risk for excessive gain in pregnancy compared with normal weight or underweight women (Walker et al., 2009) and Latina women in general have higher rates of inadequate or excessive pregnancy weight gain outside of the IOM cut-points based on pre-pregnancy weight category (Chasan-Taber et al., 2014). Latinx children are also at higher risk for pediatric obesity at younger ages compared with other racial and ethnic groups suggesting an urgent need to intervene earlier in Latinx families (Liu et al., 2015). As such, a better understanding of the inter-relationship between excessive weight gain in Latina women and pediatric outcomes in this population is necessary including how excessive maternal weight gain may impact cord blood hormone levels at birth.

The purpose of the present study is to investigate maternal factors associated with excessive weight gain in pregnancy in a cohort of low-income Latina women as well as the association between excess maternal gestational weight gain and cord blood levels of adipocyte, growth and appetite-regulating hormones associated with childhood overweight and obesity. To our knowledge, no studies have investigated the relationship between gestational weight gain and hormonal cord blood levels in infants born to high-risk Latina mothers with overweight and obesity to better understand childhood obesity risk in this population group.

2. Methods

2.1. Participants

A cohort of 97 self-identified pregnant Latina women were recruited at the prenatal clinics of Zuckerberg San Francisco General Hospital (ZSFG) during the second and third trimesters of pregnancy in 2011 and 2012 as previously described as the Latinx, Eating and Diabetes cohort (LEAD) study (Wojcicki et al., 2016; Ville et al., 2017). In brief, exclusion criteria included mothers < 18 years of age, mothers who gave birth or anticipated giving birth to infants with special care needs or chronic disease, reported current drug or alcohol abuse (obtained from a screening questionnaire), self-reported history of endocrine disorders such as polycystic ovarian syndrome, pre-existing medication-treated type 2 diabetes mellitus, and eating disorders. Infants who had Apgar scores less than 7 at 5 min were also excluded. The original goals of the LEAD cohort were to evaluate early life exposures including those *in utero* and early childhood obesity (before 5 years of age). As previously described, mothers recruited for LEAD were primarily Spanish-speaking, foreign-born and with less than a high school education (Wojcicki et al., 2016; Ville et al., 2017). Approximately 50% of the mothers self-identified as Mexican origin with the remainder from the countries of Central America.

For this sub-study focused on excessive maternal weight gain in pregnancy and infant blood hormone levels at birth and other infant characteristics at birth, we included all participants who successfully completed the baseline interview and had cord blood collected at delivery as described in detail below. All women who participated in the study signed written informed consents for their participation and that of their children. All aspects of the study were approved by the Committee on Human Research (CHR), the Institutional Review Board (IRB), at the University of California, San Francisco.

2.2. Procedures

Baseline data and socio-demographic information were collected from participants via interview including age, education level, occupation, housheold income, marital status, language use and length of time in the United States. Maternal pre-pregnancy weight and weight prior to delivery were collected by self-report in order to calculate maternal pre-pregnancy body mass index (BMI) and weight gain in pregnancy. As many of our participants presented for prenatal care late in the first or second trimester of pregnancy, the first recorded clinic weight would not necessarily be reflective of weight pre-pregnancy. Pre-pregnancy BMI (kg/m^2) was divided into four categories and defined by CDC guidelines: underweight (<18.5), normal (18.5-<25), overweight (25.0 – <30), and obese (30.0 and above) (Center for Disease Control and Prevention, 2015). Underweight was combined with normal weight woman as we had only one underweight woman in our cohort with a BMI of 18.2. Excess maternal weight gain was defined according to pre-pregnancy BMI as outlined by the IOM and accepted by ACOG for the following weight classes, >18.14 kg for underweight women, >15.8 kg for normal weight, >11.3 kg for overweight and >9.1 kg for obese women (1; 2).

At delivery, infant anthropometric measurements were extracted from the chart including birthweight (standard digital infant scales) as well as infant length (standard tape measurements). Additionally, gestational age at birth and Apgar scores at 1 and 5 min were also obtained from the medical record.

Additionally, at delivery, a 11.5-mL venous blood sample was collected from the distal umbilical cord stump and added to vacutainer collection tubes. Whole blood samples were held for up to 24 h at 4C before spinning in a refrigerated centrifuge. Plasma was stored at −80C until cord blood collection for the study was completed. Maternal blood samples were also collected by finger-stick testing for glucose analysis at delivery. Serum glucose determinations were performed by the Clinical Laboratories at ZSFG and were measured using standard enzymatic kits (Glucose Hexokinase-2) on an Advia Chemistry Analyzer 1800 (Siemens Healthcare, Tarrytown, NY) with a reportable range of 20–1190 mg/dl. Serum insulin, leptin, IGF-1 and PYY determinations were assessed by EMD Millipore (St. Charles, MO). Serum insulin, leptin and PYY assays were performed using the Milliplex MAP Human Metabolic Hormone Magnetic Bead Panel (Millipore, St. Charles, MO) with a sensitivity of 48 pg/ml for insulin, 184 pg/ml for leptin and 26 pg/ml for PYY. Serum IGF-1 determinations were made using the Milliplex MAP Human IGF-1 Single Plex (Linco, St. Charles, MO) with a sensitivity of 60 pg/ml.

2.3. Statistical analysis

Our primary outcome of interest was excess maternal weight gain, dichotomized based on IOM (2009) definitions as described above

(Institute of Medicine, 2009). Chi-squared tests were performed to analyze the relationship between excess maternal weight gain and dichotomous or categorical maternal variables including ethnicity (Mexican or Central American), income (<$25,000/year or ≥$25,000/year), marital status (Single or Divorced/Separated/Widowed versus Single, living with a partner or Married), development of preeclampsia or gestational hypertension (yes or no), and development of gestational diabetes mellitus (GDM) (yes or no) and maternal age (less than or greater than the mean of 28 years and <35 or ≥35 years). Continuous maternal variables such as age and pre-pregnancy weight were examined in relation to excess weight gain using non-parametric Wilcoxon rank sum tests. We assessed the normality of variables such as age, maternal BMI and pre-pregnant weight using the Shapiro Wilk test of normality and concluded that these variables were not normally distributed.

Similar statistical tests were used to evaluate the relationship between neonate characteristics and excessive maternal weight gain. Specifically, we included the following child-specific categorical and dichotomous variables: gender (female or male), Apgar scores at 1 min and at 5 min (<9 or ≥9), weight for length below 5%, birth weight percentile (tertiles), birthweight percentile below 5th, underweight at birth (<2,500 g), preterm birth (<37 weeks), macrosomic at birth (≥4,000 g). Child specific continuous variables included the following: gestational age at birth, birthweight (g), birthweight percentile, birthlength percentile, birthlength (cm), Apgar (1 and 5 min), finger-stick glucose level, and cord blood hormone levels including IGF-1, insulin, leptin and PYY including birthlength (cm), birthweight (g) weight-for-length percentile below 5%, and Apgar scores at 1 and 5 min (continuous). Continuous variables were also not normally distributed and as such, we similarly used the Wilcoxon rank sum non-parametric test to assess associations.

Multivariable models were built to assess maternal- level variables associated with excessive maternal weight gain. Variables with $p \leq 0.05$ in bivariate analysis or that had potential biological plausibility or were possible confounders were included in models. We subsequently assessed possible independent relationships between excessive maternal weight gain and birthweight percentile and cord blood hormone values adjusting for variables that were associated with excessive maternal weight gain. IGF-1 was analyzed in a model separate from PYY given the collinearity between the two variables. Birthweight percentile and birthlength percentile were also similarly not included in the same models due to collinearity; rather, we only included birthweight percentile due to the higher level of statistical significance. The goal of including all variables that were significant in bivariate analysis in a combined multivariable model was to control for potential confounding. A mediation analysis using the *medeff* command in Stata to assess the possible mediation roles of excessive maternal weight gain in the relationship between cord levels of IGF-1 and PYY at birth and birthweight percentile (Hicks and Tingley, 2011). As this was a preliminary and small study, our mediation results were likely underpowered and we only present findings to suggest at the possibility of mediation relationships to guide future studies. All data were analyzed using Stata SE 13.1 software (StataCorp, College Station, TX, USA).

3. Results

3.1. Maternal characteristics and socio-demographics

We enrolled 82 women in this sub-study of which 53.7% reported excessive weight gain in pregnancy (n = 44; Table 1). Of those who did not report excess gain (n = 38), 50% reported inadequate gestational gain for their pre-pregnancy BMI category or 23.1% of the total sample size, with 23.1% reporting appropriate gestational gain. The majority of the participants had an education level no greater than high school (77.8%) and 48.2% of the participants were of self-reported Mexican ethnicity (n = 39) and the other 51.9% were of Central American ethnicity (citing background in El Salvador, Guatemala, Nicaragua, or Honduras; Table 1). The mean maternal age was 28.5 ± 5.3 years and 90.2% were foreign born. Excess weight gain was not significantly associated with maternal education (p = 0.81), ethnicity (p = 0.45), maternal age (p = 0.60), or marital status (p = 0.77; Table 1). Mean pre-pregnancy weight was 66.8 ± 11.8 kg and was predictive of excess weight gain versus non excessive gain during pregnancy (63.6 ± 11.4 kg versus 68.9 ± 11.4 kg for pre-pregnancy weight; p = 0.02; Table 1). Mean BMI was 27.4 ± 4.5 kg/m^2 and was not predictive of excess weight gain during pregnancy (26.7 ± 4.7 versus 28.0 ± 4.2 kg/m^2, p = 0.15, Table 1). Thirty-one point seven percent of women were normal weight, 1.2% were underweight, 42.7% were overweight and 24.4% were obese prior to pregnancy (Table 1). Only 6.1% (n = 6) of the women developed either preeclampsia or gestational hypertension, and the development of these conditions was associated with excess weight gain (0.0% versus 11.4% in those without excess gain versus thos with excess gain; p = 0.03). Gestational diabetes mellitus was not associated with excess weight gain (7.9% versus 4.6%; p = 0.53; Table 1).

Table 1
Maternal characteristics and excess weight gain in pregnancy.

Variable	Population Mean ± Standard Deviation or Percentage (n = 82)	Excess Weight Gain (n = 82)		P Value
		No (n = 38; 46.3%)	Yes (n = 44; 53.7%)	
		Percentiles or Means ± Standard Deviation		
Maternal Age (years)	28.5 ± 5.3	28.9 ± 5.3	28.2 ± 5.2	0.60
Maternal Education				
High school or less	77.8%	79.0	76.7	
At least some college	22.2%	21.2	23.2	0.81
Maternal Ethnicity				
Mexican	48.2%	52.6	55.8	
Central American	51.9%	47.4	44.2	0.45
Marital Status				
Single or Divorced/ Separated/ Widowed	17.1%	15.8	18.2	
Single, living with partner or Married	82.9%	84.2	81.8	0.77
Pre-pregnancy weight (kg)	66.4 ± 11.6	63.6 ± 11.4	68.9 ± 11.4	0.02
Pre-pregnancy BMI (kg/m^2)	27.4 ± 4.5	26.7 ± 4.7	28.0 ± 4.2	0.15
Pre-pregnancy BMI Category				
Underweight	1.2%	2.6%	0.0%	0.34
Normal Weight	31.7%	39.5%	25.0%	
Overweight	42.7%	36.8%	47.7%	
Obese	24.4%	21.1%	27.3%	
Preeclampsia/ Hypertension				
No	93.9%	100.0	88.6	
Yes	6.1%	0.0	11.4	0.03
Glucose at delivery (n = 47)	70.3 ± 20.1	79.1 ± 23.1	64.8 ± 16.1	0.03
Gestational Diabetes Mellitus				
No	93.9%	92.1	95.5	
Yes	6.1%	7.9	4.6	0.53

3.2. Child characteristics

Excess weight gain was not related to infant gestational age (mean ± SD: 39.1 ± 1.3 weeks;39.1 ± 1.4 versus 39.0 ± 11.3 for tertiles; p = 0.50), Apgar scores at 1 or 5 min (p = 0.67 and p = 0.23, respectively; Table 2) or sex (52.5% versus 47.6%; p = 0.07; Table 2). Mean infant birth weight was 3377.2 ± 481.5 g and positively associated with excess

maternal weight gain (322.7 ± 403.5 g versus 3498.5 ± 1510.6 g; p = 0.01) as was birthweight percentile (p < 0.01; Table 2). Infants in the highest tertiles of both birthweight and birthweight percentile represented the majority of infants born to mothers who gained excess pregnancy weight (45.5%, p = 0.03 and 47.7%, p < 0.01, respectively). Mothers who gained excess weight were least likely to have infants born in the lowest birthweight and birthweight percentile tertiles (Table 2). Macrosomic birth neared statistical significant for being associated with excessive weight gain in pregnancy (p = 0.08; Table 2). Cord blood levels of IGF-1 were positively associated with excess maternal weight gain (p < 0.01) while PYY levels were negatively associated (p < 0.01). Cord blood measurements of insulin and leptin were not related to excess maternal weight gain (Table 2).

Table 2
Child characteristics at birth in relation to maternal excess weight gain (n = 82).

Variable	Population Mean ± Standard Deviation or Percentage	Excess Weight Gain		P Value
		No (n = 38)	Yes (n = 44)	
		Percentiles or Means ± Standard Deviation		
Sex				
Female	52.5%	63.1	43.2	
Male	47.6%	36.8	56.8	0.07
Gestational age (weeks)	39.1 ± 1.3	39.1 ± 1.4	39.0 ± 1.3	0.50
Apgar score at 1 min	7.6 ± 1.6			
< 9		68.4	72.7	
≥ 9		31.6	27.3	0.67
Apgar Score at 5 min	8.8 ± 0.6			
< 9		21.1	11.4	
≥ 9		79.1	88.6	0.23
Birth weight (g)	3377.2 ± 481.5	3223.7 ± 403.5	3498.5 ± 510.6	0.01
Birth weight percentile	56.7 ± 25.6	47.7 ± 26.7	64.5 ± 22.1	< 0.01
Birth weight (g) tertiles				
≤ 3180		42.1	22.7	
3181 – 3480		39.5	31.8	
> 3480		18.4	45.5	0.03
Birth weight percentile tertiles				
≤ 43%		45.2	15.9	
44 – 67%		31.0	36.4	
> 67%		23.8	47.7	< 0.01
Birth length percentile	69.2 ± 25.8	63.8 ± 27.8	73.9 ± 23.2	0.10
Weight for length below 5%				
No	86.3%	78.57	93.2	
Yes	13.7%	21.43	6.8	0.05
Macrosomia (Birthweight ≥ 4000 g)				
No	97.4	86.4		
Yes	2.6	13.6		0.08
Low birthweight (<2,500 g)				
No	94.7	97.7		
Yes	5.3	2.3		0.47
Child Hormones				
IGF-1 pg/ml (n = 63)	30760.5 ± 22029.3	21164.0 ± 12341.5	39484.7 ± 25246.5	< 0.01
Insulin pg/ml (n = 59)	976.3 ± 555.6	1030.7 ± 489.7	927.2 ± 612.9	0.06
Leptin pg/ml (n = 56)	21896.6 ± 17672.5	23983.6 ± 22069.9	19953.5 ± 12372.7	0.90
PYY pg/ml (n = 59)	322.9 ± 122.7	375.2 ± 134.3	275.7 ± 89.5	< 0.01

3.3. Multivariable models

Maternal pre-pregnancy weight was associated with excessive gestational weight gain after controlling for maternal age, education level and gestational diabetes (OR 1.05, 95% CI 1.002–1.09; p = 0.038) (Table 3). In a separate multivariable model, excess maternal weight gain in pregnancy was associated with higher birthweight percentile (Coeff 13.46, 95%CI 2.43–24.50; p = 0.02) after adjusting for maternal age and infant sex and pre-pregnancy weight (Table 4). Increasing pre-pregnancy weight was also associated with increasing birthweight percentile (Coeff = 0.61, 0.14–1.08; p = 0.01). In a smaller model evaluating risk factors for higher IGF-1 levels (n = 63), excessive maternal weight gain was independently predictive of higher IGF-1 levels (Coeff 16056.16, 95%CI 5342.18–26770.15; p < 0.01) as was birthweight percentile (Coeff 247.07, 95%CI 42.66–451.49; p = 0.02) (Table 5). In a similar model but evaluating risk factors of PYY cord blood levels, also with a smaller sample size (n = 59), lower levels of PYY were protective against excessive maternal weight gain (Coeff −86.1, 95%CI −149.15-(-)23.04) (results not shown). In mediations models, excessive weight gain mediated 10% and 29% respectively of the relationship between IGF-1 and PPY and birthweight percentile.

4. Discussion

Our study of Latina women with a high prevalence of overweight and obesity pre-pregnancy suggests that gestational weight gain impacts the intrauterine environment via hormone levels potentially impacting fetal growth and development. We found that women with high pre-pregnancy weight, a modifiable risk factor, were more likely to have excessive gain than women with lower weight at the start of pregnancy. Excessive gestational gain was also associated with differences in cord blood hormonal levels at birth, specifically growth and satiety hormones (IGF-1 and PYY). Primary health care providers should be particularly attuned to counseling Latina women with overweight and obesity regarding appropriate gain in pregnancy. In our sample population, 60% of women with overweight and obesity had excessive weight gain in pregnancy, and these same women are at greater risk for having children with future obesity (Heslehurst et al., 2019).

In line with previous studies, we found excess maternal weight gain during pregnancy was positively correlated with birthweight (Li et al., 2013). We additionally found that excessive gestational weight gain impacts the intrauterine environment resulting in higher levels of IGF-1 and lower levels of PYY potentially elucidating the pathway between higher gestational gain and greater infant birthweight. Our study found significant mediation effects (10% and 29%) even though we had a small sample size and were likely underpowered to find any association. Other studies have shown that neonatal adiposity increases with rising IGF-1 cord blood levels, suggesting IGF-1 levels may serve as a useful marker of increased risk of obesity later in life, but these same studies have not investigated the possible association between gestational weight gain and IGF-1 levels at birth (Kadakia et al., 2016). Peptide YY (PYY) also plays an important role in appetite regulation, satiety and obesity, with obese individuals having decreased levels of PYY. PYY deficiency reduces satiety and thus reinforces obesity. Similarly, administration of PYY to normal weight individuals has been shown to reduce food intake (Batterham et al., 2003), and injection of PYY into

Table 3
Maternal Factors Associated with Maternal Excess Weight Gain (n = 81).

Variable	Odds Ratio	95% Confidence Interval	P Value
Maternal age (years)	0.96	0.88–1.05	0.36
Pre-pregnancy weight (kg)	1.05	1.00 – 1.09	0.03
Gestational diabetes	0.54	0.07 – 3.95	0.55
Education level (Any high school versus college and above)	1.10	0.37–3.30	0.86

Table 4
Maternal and Infant Factors including Excessive Maternal Gestational Gain Associated with Birthweight Percentile (n = 82).

Variable	Coeff	95% Confidence Interval	P Value
Excess maternal weight gain (yes)	13.46	2.43–24.50	0.02
Infant sex (Male)	−0.09	−10.76–10.58	0.99
Maternal age (years)	0.03	0.99–1.04	0.96
Pre-pregnancy weight (kg)	0.61	0.14–1.08	0.01

Table 5
Maternal and Child Predictors of IGF-1 levels (pg/ml) at birth (n = 63).

Variable	Coeff	95% Confidence Interval	P Value
Birthweight (percentile)	247.07	42.66–451.49	0.02
Gender (Male)	−8753.64	18828.51–1321.22	0.09
Maternal age (years)	641.36	−286.96–1569.68	0.17
Excessive maternal weight gain (yes)	16056.16	5342.18–26770.15	<0.01
Pre-pregnancy weight (Kg)	70.96	−388.13–530.04	0.76

rats reduces weight gain (Batterham et al., 2002). A study of preterm and full term infants found a negative correlation between body weight and circulating PYY levels (Siahanidou et al., 2005), but again this study did not evaluate the relationship between gestational weight gain and PYY levels at birth.

The only other study to our knowledge that investigated the impact of gestational weight gain on cord blood hormones at birth found that higher gain, only in the second trimester, was associated with higher levels of IGF-1 at birth. This study did not find any association with total gestational gain and IGF-1 levels or excessive gestational gain beyond the IOM (2009) threshold and IGF-1 levels. These findings suggest the need to start interventions early in pregnancy and with women of reproductive age *prior* to pregnancy (Batterham et al., 2002). In contrast, we found that total weight gain in pregnancy above the IOM (2009) threshold was associated with higher levels of IGF-1 and PYY at birth. IGF-1 and PYY mediated the relationship in part between excessive weight gain and birthweight percentile. We did not assess timing of weight gain in pregnancy by trimester and future studies should assess how trimester specific weight gain impacts neonatal hormones at birth. We did find that women entering pregnancy with higher weight were more likely to have excessive gain impacting neonatal weight and hormonal pathways.

4.1. Public health implications

Latina women are at higher risk for excessive or inadequate weight gain compared with non-Hispanic women (Deirelein et al., 2020). Previous studies suggest similar to our own findings that higher risk for excessive weight gain in Latinas is associated with pre-pregnancy overweight or obese status (Dolin et al., 2020). In contrast with other studies of Latina women of Mexican origin, we had a relatively low percentage in our population with inadequate gain (23.2%) compared with the higher percentage with excessive gain (53.7%) (Dolin et al., 2020; Walker et al., 2009). Although, the majority of our cohort was overweight or obese entering pregnancy and as such at higher risk for excessive gain compared with the health characteristics of other studies which may include more normal or underweight women (Walker et al., 2009). Alternatively, we had a high percentage of Latina women who were foreign born (90.2%) which may also account for difference in inadequate versus excessive gain although a previous study with women in New Mexico of Mexican-origin women found that US-born women were at greater risk for inadequate gain (Walker et al., 2009). Our research indicates, similar to other findings, that public health measures need to target Latina women with overweight and obesity prior to pregnancy as a means to stop the cycle of obesity and the ongoing epidemic of pediatric obesity in Latinx children (34; 42).

5. Conclusions and limitations

Excess maternal gestational weight gain may set the stage for future childhood obesity risk through change to the intrauterine environment affecting fetal growth and development. We found that excessive maternal gestational weight gain was associated with increased levels of IGF-1 and decreased levels of PYY in urban neonates born to Latina women ultimately impacting birthweight percentile. This relationship may help explain the pathways by which excess maternal weight gain during pregnancy increases risk of childhood overweight and obesity. Interventions targeting excessive weight gain during pregnancy are needed particularly for Latina women with overweight and obesity as this study and others have indicated (Dolin et al., 2020). Future studies are needed with larger sample sizes to confirm our findings particularly in relation to the mediation analysis of IGF-1 and PYY in the relationship between excessive weight gain and birthweight percentile.

We had a relatively small percentage of our overall sample size that reported gestational gain below the IOM guidelines for adequate weight gain, a risk factor for low birthweight and preterm birth. As such, we did not assess or evaluate risk factors for low gestational weight gain in contrast with other studies with urban Latinas that have found a higher percentage of inadequate gain in their cohorts (Deirelein et al., 2020). Our population was primarily foreign-born (Mexico and Central America) and with less than a high school education level. Other studies that have found higher rates of inadequate gestational gain in Latina women have larger US-born populations and Latinas from Caribbean and South American countries (Dolin et al., 2020). Given the heterogeneity among Latina women in the United States, larger cohorts are needed with more heterogenous populations to better characterize sociodemographic exposures and risk of different levels of gestational gain. We also had low numbers of macrosomic births and low birthweight infants in our cohort and were unable to assess risk factors for these neonatal outcomes in multivariable models. Larger cohorts are necessary to assess these outcomes.

6. Consent for publication

The study was approved by the Committee on Human Research at the University of California, San Francisco (UCSF). All participants provided written consent for participation.

7. Availability of data and material

The principal investigator (JMW) will make all unidentified data available based on specific requests.

8. Authors' contributions

DE and JW designed the study, DE did the analysis and wrote the manuscript, RM and RO assisted with data analysis, RM organized recruitment, all authors approved the final manuscript.

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Ethical statement

The study was approved by the Committee on Human Research at the University of California, San Francisco (UCSF). All participants provided written consent for participation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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References

American College of Obstetrics and Gynecologists. Weight Gain During Pregnancy. Committee Opinion No. 548 [Internet]. American College of Obstetrics and Gynecologists; Available from: https://www.acog.org/-/media/Committee-Opinions/Committee-on-Obstetric-Practice/co548.pdf?dmc=1&ts=20160422T1159569972.

Baker, J., Liu, J.-P., Robertson, E.J., Efstratiadis, A., 1993. Role of insulin-like growth factors in embryonic and postnatal growth. Cell 75 (1), 73–82.

Batterham, R.L., Cowley, M.A., Small, C.J., Herzog, H., Cohen, M.A., Dakin, C.L., et al., 2002. Gut hormone PYY physiologically inhibits food intake. Nature 418 (6898), 650–654.

Batterham, R.L., Cohen, M.A., Ellis, S.M., Le Roux, C.W., Withers, D.J., Frost, G.S., et al., 2003. Inhibition of food intake in obese subjects by peptide YY. N. Engl. J. Med. 349 (10), 941–948.

Center for Disease Control and Prevention. About Adult BMI [Internet]. Centers for Disease Control and Prevention. 2015 [cited 2016 Apr 22]. Available from: http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/.

Chasan-Taber, L., Silverira, M., Lynch, K.E., Pekow, P., Solomon, C.G., Markenson, G., 2014. Physical activity and gestational weight gain in hispanic women. Obesity 22 (3), 909–918.

Christou, H., Connors, J.M., Ziotopoulou, M., Hatzidakis, V., Papathanassoglou, E., Ringer, S.A., et al., 2001. Cord blood leptin and insulin-like growth factor levels are independent predictors of fetal growth. J. Clin. Endocrinol. Metab. 86 (2), 935–938.

Chu, S.Y., Callaghan, W.M., Bish, C.L., D'Angelo, D., 2009. Gestational weight gain by body mass index among US women delivering live births, 2004–2005: fueling future obesity. Am. J. Obstet. Gynecol. 200 (3), 271.e1–271.e7.

Deirelein, A.L., Messito, M.J., Katzow, M., Berube, L.T., Dolin, C.T., Gross, R.S., et al., 2020. Total and trimester-specific gestational weight gain and infant anthropometric outcomes at birth and 6 months in low-income Hispanic families. Pediatric Obesity 15, e12589.

Dolin, S.D., Gross, R.S., Dierelein, A.L., Berube, L.T., Katzow, M., Yaghoubian, Y., Brubaker, S.G., Messito, M.J., 2020. Predictors of gestational weight gain in a low-income hispanic population: sociodemographic characteristics, health behaviors and psychosocial stressors. Int. J. Environ. Res. Public Health 17 (1), 352. https://doi.org/10.3390/ijerph17010352.

Ensenauer, R., Chmitorz, A., Riedel, C., Fenske, N., Hauner, H., Nennstiel-Ratzel, U., et al., 2013. Effects of suboptimal or excessive gestational weight gain on childhood overweight and abdominal adiposity: results from a retrospective cohort study. Int. J. Obes. 37 (4), 505.

Guo, L., Liu, J., Ye, R., Liu, J., Zhuang, Z., Ren, A., 2015. Gestational weight gain and overweight in children aged 3–6 years. J. Epidemiol. Jpn. Epidemiol. Assoc. 25 (8), 536–543.

Heslehurst N, Vieira R, Akhter Z, Bailey H, Slack E, Ngongalah L, et al. The association between maternal body mass index and child obesity; A systematic review and meta-analysis. PLOS One June 11, 2019. https://doi.org/10.1371/journal/pmed.1002817.

Hicks, R., Tingley, D., 2011. Causal mediation analysis. Stata J. 11 (4), 1–15.

Institute of Medicine: National Research Council Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight gain during pregnancy: reexamining the guidelines. National Academies Press, National Academy of Sciences, Washington, DC. 2009.

Kadakia, R., Ma, M., Josefson, J.L., 2016. Neonatal adiposity increases with rising cord blood IGF-1 levels. Clin. Endocrinol. (Oxf). 6.

Klauwer, D., Blum, W.F., Hanitsch, S., Rascher, W., Lee, P.D., Kiess, W.I.G.F.-I., 1997. IGF-II, free IGF-I and IGFBP-1, -2 and -3 levels in venous cord blood: relationship to birthweight, length and gestational age in healthy newborns. Acta Paediatr. Oslo Nor 86 (8), 826–833.

Leng, J., Li, W., Zhang, S., Liu, H., Wang, L., Liu, G., et al., 2015. GDM Women's pre-pregnancy overweight/obesity and gestational weight gain on offspring overweight status. PLoS ONE 10 (6), e0129536.

Li, N., Liu, E., Guo, J., Pan, L., Li, B., Wang, P., et al., 2013. Maternal prepregnancy body mass index and gestational weight gain on pregnancy outcomes. PLoS ONE 8 (12), e82310.

Liu GC, Hannon T, Qi P, Downs SM, DG Marrero. The obesity epidemic in children: Latino children are disproportionately affected at younger ages. International Journal of Pediatrics and Adolescent Medicine March 2015 2(1): 12-18.

Mamun, A.A., Mannan, M., Doi, S.a.R., 2014. Gestational weight gain in relation to offspring obesity over the life course: a systematic review and bias-adjusted meta-analysis. Obes. Rev. Off. J. Int. Assoc. Study Obes. 15 (4), 338–347.

Mantzoros, C.S., Rifas-Shiman, S.L., Williams, C.J., Fargnoli, J.L., Kelesidis, T., Gillman, M.W., 2009. Cord blood leptin and adiponectin as predictors of adiposity in children at 3 years of age: a prospective cohort study. Pediatrics 123 (2), 682–689.

Nam, S.Y., Lee, E.J., Kim, K.R., Cha, B.S., Song, Y.D., Lim, S.K., et al., 1997. Effect of obesity on total and free insulin-like growth factor (IGF)-1, and their relationship to IGF-binding protein (BP)-1, IGFBP-2, IGFBP-3, insulin, and growth hormone. Int. J. Obes. Relat. Metab. Disord. 21 (5), 355–359.

Nehring, I., Chmitorz, A., Reulen, H., von Kries, R., Ensenauer, R., 2013. Gestational diabetes predicts the risk of childhood overweight and abdominal circumference independent of maternal obesity. Diabet. Med. J. Br. Diabet. Assoc. 30 (12), 1449–1456.

Oken, E., Taveras, E.M., Kleinman, K.P., Rich-Edwards, J.W., Gillman, M.W., 2007. Gestational weight gain and child adiposity at age 3 years. Am. J. Obstet. Gynecol. 196 (4), 322.e1–322.e8.

Oken, E., Rifas-Shiman, S.L., Field, A.E., Frazier, A.L., Gillman, M.W., 2008. Maternal gestational weight gain and offspring weight in adolescence. Obstet. Gynecol. 112 (5), 999–1006.

Ong, K.K.L., Ahmed, M.L., Sherriff, A., Woods, K.A., Watts, A., Golding, J., et al., 1999. Cord blood leptin is associated with size at birth and predicts infancy weight gain in humans. J. Clin. Endocrinol. Metab. 84 (3), 1145–1148.

Ong, K., Kratzsch, J., Kiess, W., Costello, M., Scott, C., Dunger, D., 2000. Size at Birth and Cord Blood Levels of Insulin, Insulin-Like Growth Factor I (IGF-I), IGF-II, IGF-Binding Protein-1 (IGFBP-1), IGFBP-3, and the Soluble IGF-II/Mannose-6-phosphate receptor in term human infants. J. Clin. Endocrinol. Metab. 85 (11), 4266–4269.

Schack-Nielsen, L., Michaelsen, K.F., Gamborg, M., Mortensen, E.L., Sørensen, T.I.A., 2009. Gestational weight gain in relation to offspring body mass index and obesity from infancy through adulthood. Int J Obes. 34 (1), 67–74.

Siahanidou, T., Mandyla, H., Vounatsou, M., Anagnostakis, D., Papassotiriou, I., Chrousos, G.P., 2005. Circulating peptide YY concentrations are higher in preterm than full-term infants and correlate negatively with body weight and positively with serum ghrelin concentrations. Clin. Chem. 51 (11), 2131–2137.

Sparano, S., Ahrens, W., De Henauw, S., Marild, S., Molnar, D., Moreno, L.A., et al., 2013. Being macrosomic at birth is an independent predictor of overweight in children: results from the IDEFICS study. Matern. Child Health J. 17 (8), 1373–1381.

Sridhar, S.B., Darbinian, J., Ehrlich, S.F., Markman, M.A., Gunderson, E.P., Ferrara, A., et al., 2014. Maternal gestational weight gain and offspring risk for childhood overweight or obesity. Am. J. Obstet. Gynecol. 211 (3), 259.e1–259.e8.

Starling, A.P., Brinton, J.T., Glueck, D.H., Shapiro, A.L., Harrod, C.S., Lynch, A.M., et al., 2015. Associations of maternal BMI and gestational weight gain with neonatal adiposity in the Healthy Start study. Am. J. Clin. Nutr. 101 (2), 302–309.

Stotland NE, Cheng YW, Hopkins LM, Caughey AB. Gestational Weight Gain and Adverse Neonatal Outcome Among Term Infants: Obstet Gynecol. 2006 Sep;108(3, Part 1): 635–43.

Strauss, R.S., 1997. Effects of the intrauterine environment on childhood growth. Br. Med. Bull. 53 (1), 81–95.

Tie, H.-T., Xia, Y.-Y., Zeng, Y.-S., Zhang, Y., Dai, C.-L., Guo, J.J., et al., 2014. Risk of childhood overweight or obesity associated with excessive weight gain during pregnancy: a meta-analysis. Arch. Gynecol. Obstet. 289 (2), 247–257.

Tsai, P.-J., Yu, C.-H., Hsu, S.-P., Lee, Y.-H., Chiou, C.-H., Hsu, Y.-W., et al., 2004. Cord plasma concentrations of adiponectin and leptin in healthy term neonates: positive correlation with birthweight and neonatal adiposity. Clin. Endocrinol. (Oxf). 61 (1), 88–93.

Van Rossem, L., Wijga, A.H., Gehring, U., Koppelman, G.H., Smit, H.A., 2015. Maternal gestational and postdelivery weight gain and child weight. Pediatrics.

Vatten, L.J., Nilsen, S.T., Odegård, R.A., Romundstad, P.R., Austgulen, R., 2002. Insulin-like growth factor I and leptin in umbilical cord plasma and infant birth size at term. Pediatrics 109 (6), 1131–1135.

Ville, A.P., Heyman, M.B., Medrano, R., Wojcicki, J.M., 2017. Early antibiotic exposure and risk of childhood obesity in latinos. Child Obesity 13 (3), 231–235.

Walker, L.O., Hoke, M.H., Brown, A., 2009. Risk factors for excessive or inadequate gestational weight gain among Hispanic women in a US border state. J. Obstet. Gynecol. Neonatal Nursing 38 (4), 418–429.

Widen, E.M., Whyatt, R.M., Hoepner, L.A., Ramirez-Carvey, J., Oberfield, S.E., Hassoun, A., et al., 2015. Excessive gestational weight gain is associated with long-term body fat and weight retention at 7 y postpartum in African American and Dominican mothers with underweight, normal, and overweight prepregnancy BMI. Am. J. Clin. Nutr.

Wojcicki, J.M., Olveda, R., Heyman, M.B., Elwan, D., Lin, J., Blackburn, E., Epel, E., 2016. Cord blood telomere length in latino infants: relation with maternal education and infant sex. J. Perinaology 36 (3), 235–241.

Wrotniak, B.H., Shults, J., Butts, S., Stettler, N., 2008. Gestational weight gain and risk of overweight in the offspring at age 7 y in a multicenter, multiethnic cohort study. Am. J. Clin. Nutr. 87 (6), 1818–1824.

Yang, S.W., Yu, J.S., 2000. Relationship of insulin-like growth factor-I, insulin-like growth factor binding protein-3, insulin, growth hormone in cord blood and maternal factors with birth height and birthweight. Pediatr. Int. Off. J. Jpn. Pediatr. Soc. 42 (1), 31–36.

Zhang, C.H., Liu, X.Y., Zhan, Y.W., Zhang, L., Huang, Y.J., Zhou, H., 2015. Effects of prepregnancy body mass index and gestational weight gain on pregnancy outcomes. Asia Pac. J. Public Health 27 (6), 620–630.