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Excessive gestational weight gain predicts large for gestational age neonates independent of maternal body mass index

Z. M. Ferraro[1,2], N. Barrowman[3], D. Prud'homme[1], M. Walker[4,5], S. W. Wen[4,5], M. Rodger[5,6] & K. B. Adamo[1,2,7]

[1]*Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, Ontario, Canada,* [2]*Healthy Active Living and Obesity Research Group, Children's Hospital of Eastern Ontario Research Institute, Ontario, Canada,* [3]*Clinical Research Unit, Children's Hospital of Eastern Ontario Research Institute, Ontario, Canada,* [4]*Faculty of Medicine, Department of Obstetrics and Gynecology and Division of Maternal-fetal Medicine, University of Ottawa, Ontario, Canada,* [5]*Clinical Epidemiology Program, The Ottawa Hospital Research Institute, Ontario, Canada,* [6]*Faculty of Medicine, Division of Hematology, University of Ottawa, Ontario, Canada, and* [7]*Faculty of Medicine, Department of Pediatrics, University of Ottawa, Ontario, Canada*

***Objective*: To determine the effects of maternal pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) on large-for-gestational-age (LGA) birth weight (≥90th % ile). *Methods*: We examined 4321 mother-infant pairs from the Ottawa and Kingston (OaK) birth cohort. Multivariate logistic regression (controlling for gestational and maternal age, pre-pregnancy weight, parity, smoking) were performed and odds ratios (ORs) calculated. *Results*: Prior to pregnancy, a total of 23.7% of women were overweight and 16.2% obese. Only 29.3% of women met GWG targets recommended by the Institute of Medicine (IOM), whereas 57.7% exceeded the guidelines. Adjusting for smoking, parity, age, maternal height, and achieving the IOM's recommended GWG, overweight (OR 1.99; 95% CI 1.17–3.37) or obese (OR 2.64; 95% CI 1.59–4.39) pre-pregnancy was associated with a higher rate of LGA compared to women with normal BMI. In the same model, exceeding GWG guidelines was associated with higher rates of LGA (OR 2.86; 95% CI 2.09–3.92), as was parity (OR 1.49; 95% CI 1.22–1.82). Smoking (OR 0.53; 95% CI 0.35–0.79) was associated with decreased rates of LGA. The adjusted association with LGA was also estimated for women who exceeded the GWG guidelines and were overweight (OR 3.59; 95% CI 2.60–4.95) or obese (OR 6.71; 95% CI 4.83–9.31). *Conclusion*: Pregravid overweight or obesity and gaining in excess of the IOM 2009 GWG guidelines strongly increase a woman's chance of having a larger baby. Lifestyle interventions that aim to optimize GWG by incorporating healthy eating and exercise strategies during pregnancy should be investigated to determine their effects on LGA neonates and down-stream child obesity.**

Keywords: Gestational weight gain, maternal obesity, macrosomia, pediatric obesity

Introduction

Overweight and obesity affects 50% of women of reproductive age [1] and weight loss and maintenance is difficult for most [2]. This suggests that conceiving at a healthy body weight poses a challenge for the majority of women. Gestational weight gain (GWG) recommendations are often exceeded in those with high pre-pregnancy body mass index (BMI), given the narrow range of acceptable gain for higher BMI categories (Table I) [3,4]. Recent studies have demonstrated that exceeding GWG recommendations may increase the risk of down-stream cardiometabolic complications in children [5]. Li et al. articulated some of the factors that contribute to the intergenerational cycle of obesity noting that maternal overweight, obesity, high birthweight (≥4000 g) and maternal weight gain during pregnancy (≥20.4 kg) are independently associated with the risk of childhood overweight and obesity, even after adjustments for multiple confounders [6]. Overall, given the available evidence we felt it was important to determine which modifiable risk factor (i.e. pre-pregnancy BMI or GWG) was most strongly associated with a neonate being large-for-gestational-age (LGA) in a regional cohort of Canadians.

Several studies [7–21] have examined various relationships between maternal pre-pregnancy weight and GWG on maternal and/or neonatal outcomes. While some suggest that GWG has a greater effect [10,12,14] others note that pre-pregnancy BMI plays a dominant role in the predisposition of being born large [9]. It has been suggested that GWG does not significantly impact infant birth weight in overweight and obese women [16,17,19] and that heavier women may deliver average to large-sized infants in the absence of weight gain or even loss [11,13,17,19]. Furthermore, not all studies have used the most recent GWG guidelines [10,12,14,22] and others have relied on self-reported BMI and weight gain data [14]. There have also been discrepancies when classifying infant birth weight, with some studies using an absolute cut-off for macrosomia (i.e. ≥4000 g) [10,12] and others [14,20] utilizing birth weight percentiles for-gestational-age. Lastly, there is limited evidence [12] specifically addressing the effects of maternal weight gain on infant birth weight from an obesity prevention standpoint. This study aims to determine whether maternal pre-pregnancy BMI or adherence to the 2009 GWG guidelines better predicts neonates born LGA using a cohort from a region of Canada. We hypothesized that being obese pre-pregnancy and exceeding the GWG guidelines would increase the likelihood of giving birth to larger babies.

Correspondence: Kristi B. Adamo MSc, PhD, Research Scientist, Healthy Active Living and Obesity Research Group (HALO), Children's Hospital of Eastern Ontario Research Institute, 401 Smyth Rd. Ottawa, Ontario K1H 8L1, Canada. Tel: 613-737-7600 x4190. Fax: 613-738-4800. E-mail: kadamo@cheo.on.ca. Website: www.cheori.org/halo/

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Material and methods

We performed a secondary analysis of the Ottawa and Kingston (OaK) Birth Cohort which recruited women between 12–20 weeks gestation during their prenatal visit at either the Ottawa Hospital or Kingston General Hospital. The current analysis included subjects from phases I and II of the OaK Birth Cohort, which ran from October 2002–April 2009 and is primarily Caucasian. Demographic and clinical data were collected by structured interview and chart review by the OaK study staff. Pre-pregnancy weight was self-reported and height was measured by the study nurse upon enrolment. Maternal weight at delivery was measured by study staff and GWG was calculated by subtracting pre-pregnancy weight from weight at delivery. Newborn weight was obtained by the study nurse immediately following delivery using a calibrated electronic balance scale and recorded to the nearest gram according to standard operating procedures at participating centres. Gestational age at delivery was determined by last menstrual period (LMP) or estimated date of confinement (EDC) from ultrasound and confirmed using crown-rump length (CRL) by ultrasonography. The Canadian Perinatal Surveillance System birth weight for gestational age classification charts were used as gender-specific population-based reference standards to determine small for gestational age (SGA), AGA and LGA as previously described by Kramer et al. [23] Additional chart review or participant contact was performed if ambiguities or missing data were encountered. Statistical analysis was performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL) and R [R Development Core Team (2009). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org.]. Descriptive statistics and frequencies were used for the pre-pregnancy BMI categories with respect to the outcome variables of interest. To predict the likelihood of giving birth to a LGA neonate, we used multivariate logistic regression to independently assess the contribution of maternal pre-pregnancy BMI and GWG while controlling for maternal age and height, parity, and smoking status. Comparisons were made between those women who fell below, met or exceeded the GWG recommendations in each BMI category. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Two-sided p values less than 0.05 were taken to be statistically significant. This study was approved by the Ottawa Hospital Research Ethics Board.

Table I. Gestational weight gain recommendations, by pre-pregnancy BMI.

	Total weight gain		
Classification	BMI (kg/m^2)	Range (kg)	Range (lb)
Underweight	<18.5	12.5–18	28–40
Normal	18.5–24.9	11.5–16	25–35
Overweight	25–29.9	7–11.5	15–25
Obese	≥30	5–9	11–20

Adapted with permission from weight gain during pregnancy: reexamining the guidelines [3].

Table II. Descriptive characteristics of mothers and infants, $n = 4321$.

	Mean ± SD	Range
Age (years)	30 ± 5.1	16–50
Pre-pregnancy BMI (kg/m^2)	25 ± 5.6	15–61
Pre-pregnancy weight (kg)	68.1 ± 16.0	30–161
Gestational age (weeks from LMP)	39.2 ± 2.0	22–42
Maternal weight at delivery (kg)	84.2 ± 16.3	47–180
Infant birth weight (g)	3449.6 ± 576.8	260–5277

BMI, body mass index; LMP, last menstrual period; SD, standard deviation.

Results

The initial OaK cohort consisted of 7228 cases. We first removed cases that were ineligible: GWG >75 kg or <−25 kg ($n = 18$), gestational age >45 weeks ($n = 3$), gestational age <22 weeks ($n = 72$), multiple birth (i.e. twins) ($n = 105$), and then excluded cases with missing values: maternal weight at delivery ($n = 2609$), pre-pregnancy weight ($n = 72$), BMI ($n = 12$), the number of babies ($n = 8$), maternal age ($n = 2$), GTPAL (Gravida, term, pre-term, abortions, living children) status ($n = 1$), maternal smoking status ($n = 2$), alcohol use ($n = 2$), or neonate gender ($n = 1$). The remaining 4321 cases were included in our analysis. Subject characteristics are presented in Table II and a comparison of the distribution of included and excluded cases, based on eligibility criteria, is noted in Table III. Of the 4321 mother-infant pairs, 56.2% of women had normal pre-pregnancy BMI (18.5–24.9), while 39.9% were overweight or obese (Table IV). With respect to GWG guideline adherence, 78% of overweight and 72% of obese women exceeded the recommendations, compared to 47% and 27% of normal- and underweight women (Figure 1). Obese women gave birth to the greatest percentage of LGA neonates when compared to other pre-pregnancy BMI categories (Table V).

Results from the multivariate logistic regression analyses are summarized in Table VI. Independent of the amount of GWG, being classified as underweight pre-pregnancy and smoking during the index pregnancy were associated with a decreased likelihood of giving birth to a large baby when compared to mothers of normal weight who did not smoke. Conversely, being classified as overweight or obese based on pre-pregnancy BMI significantly increased the rate of LGA neonates. Furthermore, as parity increased so too did the chance of the child being born LGA. When compared to normal weight women who met the IOM guidelines, gaining in excess of the updated GWG recommendations was significantly associated with greater likelihood of birthing a LGA neonate. These effects were compounded when assessing the joint-association of being overweight or obese pre-pregnancy and gaining in excess of the recommendations. When compared to normal weight women who met the IOM guidelines, both overweight and obese women who exceeded the GWG recommendations had over three- (OR 3.59; 95% CI 2.60–4.95) and six-times (OR 6.71; 95% CI 4.83–9.31) the chance of giving birth to a large baby, respectively.

Table III. Comparison of the distribution of included and excluded cases based on study eligibility criteria.

	Mean (standard deviation)		
Variable	Included	Excluded	p Value
Maternal weight at delivery	84.23 (16.35)	91.61 (22.01)	0.001
Pre-pregnancy weight	68.10 (15.96)	67.81 (20.65)	0.541
Gestational weight gain	16.13 (6.76)	16.42 (6.25)	0.808
Age	30.03 (5.07)	30.60 (5.10)	<0.001

Table IV. Pre-pregnancy BMI distribution.

BMI category	n	Percent
Underweight, <18.5	169	3.9
Normal, 18.5–24.9	2428	56.2
Overweight, 25–29.9	1025	23.7
Obese, ≥30	699	16.2
Total	4321	100.0

BMI, body mass index (kg/m^2).

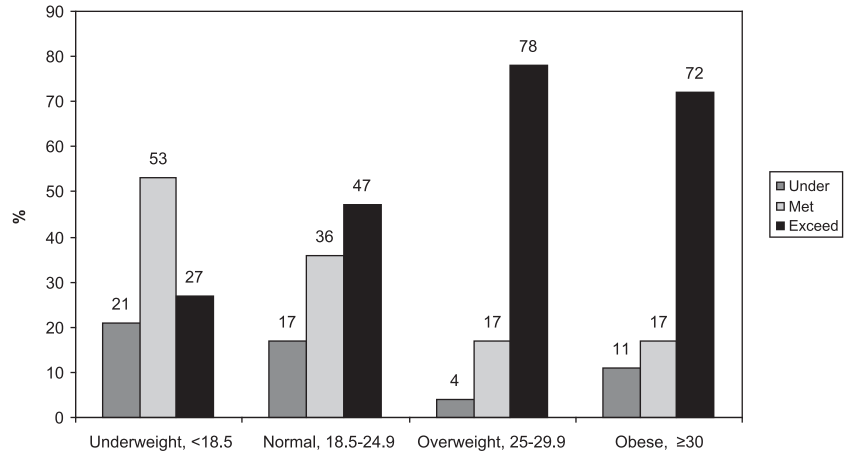

Figure 1. Adherence to gestational weight gain guidelines.

Table V. Percentage of offspring in each category of neonatal size for gestational age by pre-pregnancy BMI category.

	Pre-pregnancy BMI			
Neonatal size for gestational age	Under weight, <18.5	Normal weight, 18.5–24.9	Overweight, 25–29.9	Obese, ≥30
SGA	21	8	7	6
AGA	76	84	79	73
LGA	3	8	14	21

AGA, appropriate for gestational age; BMI, body mass index (kg/m^2); LGA, large for gestational age; SGA, small for gestational age.

Table VI. Logistic regression analyses showing the independent likelihood of having a large baby based on select maternal factors.

	Odds ratio	95% CI	*p*
Underweight, BMI <18.5	0.55	0.17–1.78	0.32
Normal, BMI 18.5–24.9	1	1	1
Overweight, BMI 25–29.9	1.99	1.17–3.37	0.01
Obese, BMI ≥30	2.64	1.59–4.39	<0.001
Parity	1.49	1.22–1.82	<0.001
Age	1.02	1.00–1.04	0.13
Maternal Height	1.54 (per 10 cm)	1.34–1.77	<0.001
Smoking	0.53	0.35–0.79	0.002
Exceed IOM GWG Guidelines	2.86	2.09–3.92	<0.001

BMI, body mass index; CI, confidence interval; GWG, gestational weight gain; IOM, Institute of Medicine.

Discussion

We determined that maternal pre-pregnancy overweight, obesity and gaining in excess of the 2009 GWG guidelines independently increase a woman's chance of having a larger baby. This confirms previous work suggesting that excessive GWG plays a strong and independent role in predisposing women to birthing heavier neonates [12]. By using the most recent IOM evidence-based recommendations for GWG, we were able to assess the validity of the guidelines as a predictive tool for LGA and suggest that these recommendations do offer clinical utility in prenatal care with a focus on obesity prevention for mom and baby. This finding has far-reaching public health implications knowing that pregnancy is a critical period of body weight regulation where natural fluctuations in weight are common and frequently large. To our knowledge, the strength of the joint-association we observed between pre-pregnancy obesity and excessive GWG on LGA births in accordance with the 2009 IOM guidelines has not been reported elsewhere providing a unique contribution in the context of accelerated fetal growth and potentially obesity prevention. We speculate that the strength of our odds ratios differ than those previously published given that it was our *a priori* intent to classify weight-for-gestational age using a validated, population-based Canadian reference for birth weight for gestational age. Using normative data for our outcome of interest (i.e. LGA neonates) coupled with our use of the 2009 IOM GWG guidelines that impose an upper limit of GWG for obese women (i.e. 9 kg) may have contributed to the strength of the joint-association we present in this paper. Thus, our design and analysis plan may have lead to higher odds ratios than previously described.

Using our sample population, we have validated previous findings that found avoidance of higher amounts of GWG, in heavier women, to be advantageous for optimal neonatal birth weights [10,12,14]. Nohr and colleagues assessed the combined association of pre-pregnancy BMI and GWG on both maternal and fetal outcomes and concluded that overweight, obesity and GWG of >16 kg resulted in an increased risk of delivering LGA neonates [14]. While our findings support these results we aligned our GWG categories with those of the IOM guidelines to confirm two potential modifiable determinants of infant size at birth (i.e. pre-pregnancy BMI and GWG). We suggest that the guideline recommendations offer tremendous clinical value for primary care as women and providers can track and monitor weight status throughout pregnancy to reduce the likelihood of a large baby. Specifically, if altering weight pre-pregnancy is not a feasible option, being aware of another modifiable factor, GWG, that may promote down-stream infant health could provide motivation for women to gain weight within the limits. This notion is supported by others [14] who found that the overall contribution of GWG was modest except for infant size at birth and postpartum weight retention. This reinforces the need to optimize GWG for all women as this determinant contributes to postpartum weight retention and infant birth weight; known contributors to the intergenerational obesity cycle.

Furthermore, Ludwig and Currie [12] noted a consistent genetic-independent association between GWG and birth weight using a large within-family comparison, observing a 2.26 (95% CI 2.09–2.44) greater risk of giving birth to an infant weighing >4000 g when gaining more than 24 kg compared to women who gained 8–10 kg. Making a direct comparison with these findings poses a challenge as their reference group for GWG (i.e. 8–10 kg range) falls in between the IOM recommendations for overweight and obese women with their most pronounced effects demonstrated when gains exceeded 24 kg which is above the recommended

GWG for women who are underweight pre-pregnancy. Crane et al. [10] reported similar results for birth weight ≥ 4000 g in that women who gained weight in excess of the 1990 IOM recommendations had an increased odds of birthing a large baby. However, our findings are slightly different than Choi et al. [9] who suggest that pre-pregnancy overweight and obesity has a stronger association with LGA whereas GWG had no effect. In their study, GWG did not have a positive relationship with LGA in overweight and obese women. This difference may be partially explained by ethnic differences in GWG given their predominately Asian cohort as the amount of body fat for a given BMI in these populations tends to be higher when compared to individuals of European decent [24]. While they attempted to correct for differences in weight accretion and distribution by classifying women according to the suggested Asian BMI cut-off points for overweight (≥23) and obesity (≥25) [24], they used the GWG guidelines which have not been validated in Asian cohorts leading us to consider that this may contribute to the observed differences. Others have also noted that GWG had no significant effect on infant birth weight for overweight and obese women [16,17,19]. In a recent review of obesity and pregnancy, Melzer and Schutz [25], conclude that heavier women may deliver average- to large-sized infants with virtually no GWG or even weight loss [11,13,17,19]. This suggests that mechanisms independent of GWG prevail in some women thereby influencing higher birth weights and leads us to speculate that genetic and epigenetic contributions to growth factor and hormone response may mediate this relationship [26,27]. Recently, it was reported that fetal exposure to high maternal glucose in the absence of pre-existing or gestational diabetes, may influence offspring obesity at age 3, independent of maternal pre- pregnancy BMI [28]. Whether obesity presents as a result of a child's unique susceptibility, maternal influence or combination of both, the effects of pre-pregnancy BMI and excessive GWG on infant size at birth cannot be overlooked as both determinants may affect infant birth weight and down-stream health.

Fewer women in our study were overweight or obese at pre-pregnancy when compared to Canadian national averages [29]. We also observed higher rates of LGA neonates with increasing maternal height, a relationship previously described [21]. Finally, we were able to confirm extensive evidence in support of the growth restrictive effects of smoking during pregnancy, a behaviour strongly linked to higher incidence of SGA neonates [30,31].

Our study is not without limitations. We cannot infer that the observed associations are causal in nature, are also aware our primarily Caucasian patient population may not be representative of all ethnic groups, and that our inability to control for socioeconomic status, education level or marital status may have influenced our outcomes. With respect to study outcomes that differed from ours, we suggest that methodological differences between directly measured and self-reported values (e.g. GWG) may have led to the discrepancy. Although we acknowledge that missing data for maternal weight at delivery may increase the propensity for bias within our subsample, given the well documented notion that pregnancy-related complications are more common to maternal obesity than women of normal BMI [32] it is possible that obesity-related complications in these cases precluded documentation. Thus, if mother's struggling with obesity required immediate clinical attention, we speculate that any bias that exists may potentially strengthen our observations. It is well understood that individuals under-report body weight when compared to direct measures [33] although maternal recall of pregnancy-related events tends to be more reproducible and valid [34]. To our credit, we have also considered some of the main pregnancy-related factors tangled in a complex system affecting birth weight, including maternal age and parity. While we acknowledge that mom and baby share similar obesity-related genes and that this may affect the underlying predisposition to macrosomia and excessive GWG, our results are in agreement with recent work that accounted for this using a within-family comparison [12]. In consideration, the present findings reinforce the need to encourage individualized GWG targets that balance the demands of adequate fetal growth and development with the risks of excessive pregnancy weight gain, complicated deliveries (e.g. macrosomia) and excess postpartum weight retention.

Having an awareness of the joint-effects that higher maternal pre-pregnancy BMI and excessive GWG have on the predisposition to giving birth to a LGA baby is of utmost importance for prevention and management of obesity in primary care. Identifying those at greatest risk may facilitate appropriate preventive triage and allow for the introduction of strategies tailored to individual needs (i.e. target therapies based on pre-pregnancy BMI, GWG or both for those struggling with weight in the family planning stages). This may lead to more favourable maternal outcomes postpartum and benefit down-stream child health. Encouraging healthy eating and regular physical activity during pregnancy may optimize fetal size at birth and promote adaptive benefits in the child [35,36]. For care provision during the early years of the child's life, utilizing the information gained from a thorough obstetrical history (i.e. being aware of birth weight and maternal GWG) may promote a more focussed, specialized care and healthful developmental trajectory with virtually no increase in time or resources.

We have shown that the majority of women in our birth cohort population entered pregnancy at an unhealthy weight and gained in excess of recommendations during gestation. At any weight, excessive GWG has a significant effect on the likelihood that their child will be born LGA, and research [6] has demonstrated that size at birth contributes to obesity development down-stream. Knowing that modification of pre-pregnancy BMI may be a challenge for many, focusing on GWG may be advantageous for mothers who aim to limit their weight retention postpartum as well as optimize infant growth trajectory in the early years. Although this hypothesis remains to be tested, the use of the GWG guidelines may have tremendous utility in clinical practice and serve as a monitoring tool for providers and pregnant women. As a result, adherence to the recommendations may attenuate the incidence of LGA births and in turn potentially optimize tracking of excess weight from early childhood into adulthood.

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