

Review of Trimester-Specific Gestational Weight Gain and Childhood Adiposity

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Abstract

Childhood obesity is a global epidemic and a major public health challenge. There has been increasing evidence that intrauterine exposures, such as alcohol, smoking, and maternal nutritional status, may affect both the long and short term health consequences of the mother and offspring. Childhood adiposity may be affected by the mother's pre-pregnancy weight and her weight gain during pregnancy. Consequently, interventions may need to start before conception of the child to prevent childhood obesity. In 2009, the Institute of Medicine updated its gestational weight gain recommendations by incorporating rates of gestational weight gain in the second and third trimesters based on the mother's pre-pregnancy Body Mass Index. There is extensive research on the association between total gestational weight gain and short-term offspring adiposity. However, this review focuses on the association between trimester-specific gestational weight gain and childhood adiposity for singleton pregnancies with respect to the Institute of Medicine's newly defined weight gain recommendations as very few studies have examined the association between the gestational weight gain during each trimester and childhood adiposity. Identifying the trimester that is most associated with childhood adiposity may help in the development of targeted interventions, guide physician's nutritional and weight-gain recommendations for child-bearing mothers, and direct future research.

Key words : Childhood overweight and obesity, Offspring's BMI, Gestational weight gain

Introduction

Obesity is a worldwide epidemic across all age groups with little evidence of decline¹. Childhood overweight and obesity are leading causes of early type two diabetes and cardiovascular disease¹. In 2011, more than 40 million children under the age of five were overweight, 30 million of who are living in developing countries². The lack of evidence on the long term efficacy of traditional obesity management emphasizes that prevention should begin early in human development. Researchers have identified numerous modifiable factors in the prenatal and early postnatal periods that may increase the risk of childhood overweight, such as maternal smoking during pregnancy, reduced breastfeeding

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duration, and rapid weight gain during the first few months of life³.

As excessive gestational weight gain (GWG) has been correlated with childhood and later in life overweight and obesity, the importance of appropriate GWG has gained increasing attention in recent times³⁻²⁰. Motivated by recent research on the changing characteristics of the child-bearing population, the Institute of Medicine (IOM) revised GWG guidelines in 2009 to include a specific recommendation for obese women,

and second and third trimester GWG rates based on pre-pregnancy Body Mass Index (Table 1)⁴.

In light of the current IOM recommendations, the primary objective of this review was to examine current knowledge regarding the association between trimester-specific GWG and childhood adiposity. This literature review examines current evidence investigating GWG and childhood adiposity with a focus on trimester-specific GWG and childhood adiposity for singleton pregnancies. As such, the review hopes to provide direction for future research on early predictors of childhood adiposity and for the development of early interventions to prevent obesity.

Methods

Web of Science and Pubmed were used to obtain peer-reviewed studies for the period of January 1990 and March 2013. The search was also limited to journal articles, meta-analyses, randomized controlled trials, reviews, and systematic reviews in the English language. The string of terms that were considered include: gestational weight gain and childhood BMI; gestational weight gain and childhood obesity or offspring adiposity; maternal weight gain during pregnancy and offspring obesity or offspring adiposity; gestational weight gain and adolescent obesity; and trimester-specific gestational weight gain. Both observational studies and review articles were included. The initial search yielded a total of 341 studies. Studies were subsequently screened by abstracting information on study characteristics, study participants, eligibility criteria, interventions, outcome measures, the method of ascertainment, and the outcomes. Opinion and editorial pieces were excluded. Studies that exclusively discussed the biological aspects of gestational weight gain e.g. physiologic mechanisms and those that predominantly focused on exposures other than GWG, such as gestational diabetes, were excluded. 25 studies met the inclusion criteria and were ultimately selected for review.

Results

Maternal Gestational weight gain and Childhood Adiposity

Oken et al.'s study on the Growing Up Today study to identify developmental origins of childhood overweight was one of the first and pioneering studies that examined the relation of gestational weight gain and childhood obesity⁵. GWG was found to be associated with higher child body mass index at 3 years (0.13 units per 5 kg, 95% CI: 0.08, 0.19). A characteristic methodology used in this study was calculating BMI along with, measuring skin fold thickness as a measure of adiposity. Total gestational weight gain was positively associated with both child BMI z-score 0.13 units, 95% CI: 0.08, 0.19 per 5 kg) as well as the sum of subscapular and triceps skinfold thicknesses (0.26 mm, 95% CI: 0.02, 0.51). In addition, compared with inadequate weight gain, women with adequate or excessive weight gain had children with increased relative odds of having children that were overweight (odds ratios=OR=3.77, 95% CI: 1.38, 10.27) and (OR=4.35, 95% CI: 1.69, 11.24). Appreciable change of results was not found upon adjustment to covariates, which were: maternal age and smoking, household income and paternal education, and child race/ethnicity, gestational age, sex, age in 1996, and Tanner stage.

Subsequent cohort studies in the US have resulted in findings consistent to those of Oken et al. Specifically, these studies showed that independent associations exist between maternal GWG and offspring BMI when the child is 3 years⁶, 5 years⁷, 7 years⁸, and in their adolescence⁵. Consistent findings have been found in international studies. A cross-sectional study in Germany by von Kries et al. found, after adjusting for confounders, children of mothers with high GWG were still found to be significantly more likely to be overweight than children of mothers with an average GWG (OR=1.16, 95% CI: 1.02–1.32), which remained unchanged after adjusting for confounders⁹.

Table 1: New Recommendations for Total and Rate of Weight Gain during Pregnancy, by Prepregnancy BMI

| Prepregnancy BMI | BMI (kg/m ²) (WHO) | Total Weight Gain Range (lbs) | Rates of Weight Gain in 2 nd and 3 rd Trimester (Mean Range in lbs/wk) |
|------------------------------|--------------------------------|-------------------------------|--|
| Underweight | <18.5 | 28-40 | 1 (1-1.3) |
| Normal weight | 18.5-24.9 | 25-35 | 1 (0.8-1) |
| Overweight | 25.0-29.9 | 15-25 | 0.6 (0.5-0.7) |
| Obese (includes all classes) | ≥30.0 | 11-20 | 0.5 (0.4-0.6) |

*Calculations assume a 0.5-2.0kg (1.1-4.4 lbs) weight gain in the first trimester

Source: Institute of Medicine 2009⁴

Studies have also been conducted to examine the association between gestational weight gain and offspring's BMI in adulthood. Mamun et al.'s study followed offspring to adulthood (age 21 years) and found offspring BMI was on average 0.3 kg/m² (95% confidence interval, 0.1 to 0.4 kg/m²) higher for each 0.1-kg/wk greater GWG after adjustment for potential confounding factors¹⁰. Similar to Oken et al.'s study, offspring of mothers with excessive weight gain during pregnancy, as defined by the IOM, were more likely to be overweight (OR=1.3, 95% CI: 1.0 to 1.8) and obese (OR=1.5, 95% CI: 1.0 to 2.1) at 21 years of age compared with those with inadequate weight gain. Although there was a positive association with adequate GWG and risk of overweight or obesity at age 21 years, results were insignificant¹¹.

A Danish report on the Copenhagen perinatal cohort that followed-up 1540 offspring to age 42 found that GWG was associated with offspring BMI at all ages: a 2.36 (1.08–5.15)-fold increase in the risk of obesity and a 1.28 (0.89–1.85)-fold increase in the risk of overweight in the highest (≥ 16 kg) versus the lowest (< 6 kg) GWG category¹². Furthermore, there was an increasing risk of obesity at the age of 42 years (OR=1.08, 95% CI: 1.03-1.14 per kg GWG)¹².

Two studies conducted in the United Kingdom have also found similar results. Reynolds et al found GWG, as well as pre-pregnancy BMI and parity, to be independent predictors of percentage body fat of offspring, even after adjustment for confounders¹³. Crozier et al. found that children who were born to mothers with excess GWG had a greater fat mass in the neonatal period (SD: 0.17; 95% CI: 0.02, 0.32), at 4 yr (SD: 0.17; 95% CI: 0.00, 0.34), and at 6 yr (SD: 0.30; 95% CI: 0.11, 0.49) compared to those children who were born to mothers with normal GWG¹⁴.

Trimester of Gestational Weight gain

The association between GWG and offspring BMI has been substantiated with increasing amounts of evidence. Only a few studies are beginning to draw attention to the possible role that "adequate" GWG per trimester, as proposed by the IOM, may have on later-life adiposity¹⁷⁻²². Difficulties in establishing recommendations arise from the importance to strike a balance between a weight gain that is not so reduced as to cause low birth weight, restricted intrauterine growth and prematurity, yet which is not so high as to increase the chances of macrosomia, preeclampsia, caesarean section and gestational diabetes.

Dutch Famine studies and animal models have shown maternal exposure to famine in early pregnancy

is associated with increased adult BMI in women¹⁵. Furthermore, numerous epidemiologic studies have found GWG in the second trimester to be more strongly associated with lower birth weight than the GWG in the first or third trimester¹⁶⁻²⁰. Among these, Hickey et al found that low gain corresponding to IOM recommendations in the first and second, or in the second and third trimesters, were associated with significant decreases in mean birth weight, ranging from 206 to 265g¹⁸. However, low gain in first or third trimester alone was not associated with a significant decrease in mean in birth weight.

Drehmer et al. also found no association between insufficient weight gain in the third trimester and birth weight²¹. In the second trimester, insufficient weight gain was associated with small for gestational age (relative risk= RR 1.72, 95% CI: 1.26–2.33), and excessive weight gain with large for gestational weight gain (RR 1.64, 95% CI: 1.16–2.31)²¹.

Only three studies were found in the literature search to have examined whether trimester-specific GWG associates with offspring adiposity later in life as their primary or secondary objectives, two of them being European cohort studies^{7,22,23}. Fraser et al. examined the importance of IOM guidelines and offspring adiposity directly with Avon Longitudinal Study of Parents and Children (ALSPAC) prospective pregnancy cohort in UK²². The study found that compared with offspring of women gaining recommended levels, those who gained less than recommended levels had lower relative odds of overweight/obesity BMI (OR=0.80, 95% CI: 0.67, 0.96) and of waist-based central obesity (based on waist) of (OR=0.79, 95% CI: 0.69, 0.90), at age 9. Compared with those who met recommended GWG, offspring of mothers who gained more than recommended levels had greater relative odds of being overweight/obesity and central obesity OR=1.73, 95% CI: 1.45, 2.05 and OR=1.36, 95% CI: 1.19, 1.57, respectively, at age 9. In addition, when examining these associations more closely, Fraser et al. found that any weight gain in the first 14 weeks of gestation was incrementally associated with increased offspring adiposity, but between 14 and 36 weeks gestation only GWG above 500g/week was associated with increased offspring adiposity²².

Using data from the Danish National Birth Cohort, Andersen et al. found similar results: that GWG in the first and second (β -coefficient (95% CI): 0.049 z-score/z-score (0.030, 0.067), and 0.059 z-score/z-score (0.041, 0.077), respectively), but not in the last (β -coefficient (95% CI): 0.016 z-score/z-score (-0.002, 0.034)), trimester of pregnancy was positively

associated with offspring BMI at 7 years of age²³. GWG rates were subsequently determined using Life Course Path Analyses based on self-reported prepregnancy weights²³.

Margerison-Zilko et al. examined 3,015 singleton births to women without pregnancy complications in a more heterogeneous population⁷. Based on the US-based Child Health and Development Studies, the study found associations between total as well as trimester-specific GWG and birth weight for gestational age as well as child BMI at age 5, adjusting for maternal age, race/ethnicity, education, marital status, parity, pre-pregnancy body mass index (BMI), and smoking; paternal overweight, gestational age, and infant sex. The study concluded that although all trimesters were associated with birth weight, only first trimester GWG was associated with high child BMI (OR for child overweight = 1.05, 95% CI: 1.02, 1.09) at age 5. A limitation of the study was that it did not control for certain potential confounders: gestational diabetes mellitus, genetic characteristics, nausea, diet, or physical activity. In addition, unlike the Fraser et al., Margerison-Zilko found there to be effect modification by pre-pregnancy BMI⁷.

Discussion

Rates of excessive GWG have been increasing over time and research has shown that greater GWG is associated with increased weight of baby at birth and infancy²⁴⁻²⁷. This raises questions about the long-term adverse effects of higher weight gains in pregnancy. Oken et al.'s investigation of the Growing Up Today Study cohort to identify developmental origins of childhood overweight was one of the first and pioneering studies that examined the relation of gestational weight gain and childhood obesity⁵. A number of studies thereafter have substantiated this association. Furthermore, as only part of the association of GWG with offspring adult BMI is explained only partly by birthweight and BMI up to 14 years of age, this suggests that excessive GWG induces other mediating processes and factors that in turn result in higher offspring adult BMI¹³. Therefore, exploration of mediating variables in the GWG, such as the trimester of pregnancy, could reveal possible points where interventions can be applied.

Much controversy surrounds the accuracy of BMI in measuring childhood fat. The literature review demonstrated that Fraser et al.'s and Oken et al.'s studies are two of the only few studies that have examined childhood adiposity, in relation to GWG, by measures other than BMI^{5,22}. Another pertinent study

is from the Southampton Women's Survey, in which children's body composition was determined using a dual-energy X-ray absorptiometry¹⁴. The Motherwell birth cohort study based in Scotland also examined four-site skinfold thicknesses, waist circumference, and body mass index (BMI) at age 30 yr of offspring¹³.

The literature review identified only three studies that investigated the relationship between trimester-specific GWG and childhood adiposity as a primary or secondary objective^{7,22,23}. All three found GWG in the first trimester to be associated with childhood and later in life childhood adiposity^{6,21,22}. Andersen et al. additionally found that this association to be maintained for the second trimester as well²³. These findings of early pregnancy being most correlated with later in life adiposity are complimented by results from Dutch Famine Studies and biologic evidence of the most rapid growth—thus, the most sensitive period—occurring in the first and second trimesters of pregnancy^{15,18}.

Limitations of the studies included in this review need to be considered when interpreting results. Exposure assessment of trimester-specific GWG has been predominantly based on self-report, introducing possible exposure misclassification due to recall bias or inaccurate recall^{6,21,22}. Additionally, these studies have also been based on European- or USA-based study populations with varied methods of exposure and outcome measurement, contributing to difficulties in valid comparisons between studies. Furthermore, the sample size in Fraser et al.'s study was not large enough to identify a significant association between GWG from 36 weeks onwards as the duration of this period varies largely between pregnancies²².

Conclusion

The publications reviewed in this paper suggest that gestational weight gain in the first and second trimesters of singleton pregnancy may be associated with childhood adiposity. However, further research is needed to better evaluate the possible role of trimester-specific gestational weight gain on childhood adiposity with regard to the Institute of Medicine's recommendations. As the majority of past studies have focused on US and European populations, there is a need to investigate the association in more diverse populations to increase generalizability of findings. More consistent definitions of gestational weight gain and childhood adiposity, as well as a more thorough collection of weight gain data are also needed.

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