Maternal Gestational Diabetes, Birth Weight, and Adolescent Obesity

Matthew W. Gillman, MD*‡; Sheryl Rifas-Shiman, MPH*; Catherine S. Berkey, ScD§; Alison E. Field, ScD|| and Graham A. Colditz, MD, DrPH§

ABSTRACT. Objective. Obesity increases risk of many adverse outcomes, but its early origins are obscure. Gestational diabetes mellitus (GDM) reflects a metabolically altered fetal environment associated with high birth weight, itself associated with later obesity. Previous studies of GDM and offspring obesity, however, have been few and conflicting. The objectives of this study were to examine associations of birth weight and GDM with adolescent body mass index (BMI) and to determine the extent to which the effect of GDM is explained by its influence on birth weight or by maternal adiposity.

Methods. We conducted a survey of 7981 girls and 6900 boys, 9 to 14 years of age, who are participants in the Growing Up Today Study, a US nationwide study of diet, activity, and growth. In 1996, participants reported birth weight, height, weight, and other variables by self-administered mailed questionnaire. We linked these data with information reported by their mothers, participants in the Nurses’ Health Study II, including GDM, height, weight, and child’s birth weight. We excluded births <34 weeks’ gestation and mothers who had pre-existing diabetes. We defined overweight as BMI (kg/m2) >95th percentile, and at risk for overweight as 85th to 95th percentile, for age and gender from US national data.

Results. Mean birth weight was 3.4 kg for girls and 3.6 kg for boys. Among the 465 subjects whose mothers had GDM, 17.1% were at risk for overweight and 9.7% were overweight in early adolescence. In the group without maternal diabetes, these estimates were 14.2% and 6.6%, respectively. In multiple logistic regression analysis, controlling for age, gender, and Tanner stage, the odds ratio for adolescent overweight for each 1-kg increment in birth weight was 1.4 (95% confidence interval: 1.2–1.6). Adjustment for physical activity, television watching, energy intake, breastfeeding duration, mother’s BMI, and other maternal and family variables reduced the estimate to 1.3 (1.1–1.5). For offspring of mothers with GDM versus no diabetes, the odds ratio for adolescent overweight was 1.4 (1.1–2.0), which was unchanged after controlling for energy balance and socioeconomic factors. Adjustment for birth weight slightly attenuated the estimate (1.3; 0.9–1.9); adjustment for maternal BMI reduced the odds ratio to 1.2 (0.8–1.7).

Conclusions. Higher birth weight predicted increased risk of overweight in adolescence. Having been born to a mother with GDM was also associated with increased adolescent overweight. However, the effect of GDM on offspring obesity seemed only partially explained by its influence on birth weight, and adjustment for mother’s own BMI attenuated the GDM associations. Our results only modestly support a causal role of altered maternal-fetal glucose metabolism in the genesis of obesity in the offspring. Alternatively, GDM may program risk for a postnatal insult leading to obesity, or it may merely be a risk marker, not in the causal pathway. Pediatrics 2003;111:e221–e226. URL: http://www.pediatrics.org/cgi/content/full/111/3/e221; birth weight, gestational diabetes, obesity, childhood, adolescence.

ABBREVIATIONS. BMI, body mass index; GDM, gestational diabetes mellitus; OR, odds ratio; CI, confidence interval.

Rates of obesity among children as well as adults in the United States have been rising during the past 4 decades.1–3 Adolescent obesity is strongly associated with adult obesity and predicts both short- and long-term adverse health outcomes.4–11 Research into early-life determinants of obesity could lead to innovative strategies for prevention.

Evidence from animal and human studies indicates that many adult chronic diseases, especially cardiovascular diseases, have their origins in fetal life.12 Less information, however, is available for the early origins of obesity. Several studies have addressed the association between birth weight and body mass index (BMI) in childhood and early adulthood. Most of these studies have found direct associations, ie, that higher birth weight is associated with higher attained BMI.13–30 Many are limited, however, by incomplete data on gestational age, parental adiposity, or socioeconomic factors, which may have independent influences on both birth weight and later weight gain.

Observations that higher birth weight is associated with higher attained BMI have led to the hypothesis that in utero determinants of birth weight may also program the fetus for elevated risk of later obesity. Of primary interest is altered maternal-fetal glucose metabolism. Maternal hyperglycemia leads to excess fetal insulin, itself a growth hormone for the fetus. Thus, offspring of mothers with gestational diabetes mellitus (GDM) have higher birth weights.31 Furthermore, animal studies suggest that fetal hyperinsulinemia can alter expression of hypothalamic neurotransmitters, leading to offspring hyperphagia and increased weight.32
Despite this evidence, few epidemiologic studies have investigated associations of maternal GDM with offspring obesity. These studies have produced mixed results, with some showing evidence of a direct association\(^{3,34}\) and others showing no association.\(^{35}\) Explanations for the lack of consistency could include that some studies have not distinguished between pregestational and gestational diabetes and some included only mild cases of GDM, whereas others took place in areas of endemic diabetes, and some lacked information on covariates such as maternal BMI.

The purposes of this study were to examine the independent associations of birth weight and GDM with adolescent BMI, with adjustment for relevant covariates, and to determine to what extent the effect of maternal GDM is explained by its influence on birth weight. We were also particularly interested in the role of maternal BMI in explaining these associations.

**METHODS**

**Subjects**

The participants in the Growing Up Today Study are sons and daughters of participants in the ongoing Nurses’ Health Study II, a cohort study of \(\geq116,000\) female registered nurses.\(^{36}\) From Nurses’ Health Study II study records, we identified 34,174 participants who had at least 1 child age 9 to 14 years in 1996 and requested permission to contact their children. A total of 18,526 women provided information for 26,765 children, 13,261 girls and 13,504 boys. In the fall of 1996, we sent each of these children a letter inviting them to participate, along with a gender-specific questionnaire, assuring them that we would not convey their individual responses to anyone, including their mothers. Approximately 68% of the girls (\(n = 9,039\)) and 58% of the boys (\(n = 7,843\)) returned completed questionnaires, thereby assenting to participate in the cohort. Human Subjects Committees at the Harvard School of Public Health and Brigham and Women’s Hospital approved the study. In the spring of 1997, we sent a supplemental questionnaire to the participants’ mothers to obtain information on early life factors. Mothers of 16,550 (98%) participants completed this questionnaire.

For this analysis, we excluded 343 participants outside the age range 9 to 14 years on the baseline questionnaire in 1996, 418 whose mothers did not complete the 1997 supplemental questionnaire, 374 who had missing or outlying (\(\geq3\) age- and gender-specific standard deviations) values for BMI on the baseline questionnaire, 46 who had missing or outlying values (\(<0.5\) kg or \(>6.0\) kg) for birth weight, 454 who had missing values for Tanner sexual maturity rating, 71 whose mothers either failed to report their diabetic status during the index pregnancy or had preexisting diabetes, and 167 who had childhood medical conditions that might have interfered with growth. These conditions were diabetes (\(n = 43\)); juvenile rheumatoid arthritis (\(n = 24\)); inflammatory bowel disease (\(n = 18\)); cerebral palsy (\(n = 28\)); Down syndrome (\(n = 6\)); acute lymphocytic leukemia (\(n = 7\)); and 41 other selected infectious, endocrine, metabolic, neurologic, renal, respiratory (not asthma), and orthopedic conditions and congenital anomalies. We also excluded 128 whose mothers reported a gestation of \(<34\) completed weeks. (Excluding subjects born \(<37\) weeks’ gestation gave similar results.) We therefore based our analyses on 14,881 participants, 7,981 girls and 6,900 boys.

**Measurements**

We ascertained all information from mailed self-administered questionnaires. On the 1996 baseline questionnaire, each cohort participant reported age, gender, race/ethnicity, height, weight, pubic hair sexual maturity (Tanner stage) rating using validated pictograms,\(^{37}\) diet and physical activity in the past 12 months using validated frequency questionnaires,\(^{38,39}\) and average time spent watching television.

From the 1997 supplemental questionnaire to mothers, we obtained information about each child’s birth weight and length; gestational age in the categories \(<34\) weeks, 34 to 37 weeks, and \(>37\) weeks; medical illnesses during childhood; and duration of breastfeeding during infancy. From the initial Nurses’ Health Study II questionnaire in 1989, we obtained information about each mother’s diabetes history, including whether she had GDM during the index pregnancy, and about her smoking habits during the early life of the child. From the 1995 Nurses’ Health Study II questionnaire, we ascertained mothers’ other lifestyle habits that may be related to children’s body weight, including single questions representing aspects of dietary restraint (“I eat anything I want, anytime I want”—yes or no), weight fluctuation (“What is the difference between your highest and lowest weight in the last 2 years [excluding pregnancy-related changes]?”), and weight concerns (“I pay a great deal of attention to changes in my figure; yes or no”). When possible or not, we obtained self-reported height and weight from the 1995 Nurses’ Health Study II questionnaire; when not, we obtained this information from the earlier questionnaire closest to 1995.\(^{40}\) Our measure of maternal BMI was thus “current” BMI, ie, the value closest to the 1996 baseline cohort questionnaire.

We explored use of several other estimates for mother’s BMI, including at age 18 or in 1989, or values that we obtained using a parity-adjusted least squares regression model to interpolate her BMI at the time of the child’s conception. Because these estimates were highly correlated with each other and each of these approaches gave similar results, we used “current” maternal BMI in all reported analyses.

To obtain estimates of household income, we mapped each subject’s address to a US Census tract. We used US Census data from 1990 to assign the median household income for that Census tract to the individual subject.

**Exposure Assessment**

Our main exposures of interest were birth weight and maternal gestational diabetes, defined as maternal report of diabetes diagnosed by a doctor during the index pregnancy. The validity of self-report of GDM for this group of women is high: Solomon et al\(^{41}\) found that among a sample of 114 Nurses’ Health Study II participants who self-reported GDM in a singleton pregnancy and whose medical records were available for review, a physician diagnosis of GDM was confirmed in 107 (94%). Among a sample of 100 women who reported a pregnancy not complicated by GDM, 77 (75%) reported having a 1-hour 50-g glucose screening test, and all reported 2 or more urine glucose screens during pregnancy.

**Outcome Ascertainment**

Our outcome variables were overweight, defined as BMI (weight in kilograms divided by the square of height in meters) greater than the age- and gender-specific 95th percentile in a national sample of US children, and at risk for overweight, ie, between the 85th and 95th percentiles.\(^{42}\) For overweight analyses, we defined not overweight (a “noncase”) as BMI less than the 95th percentile; for at risk for overweight, we defined a noncase as BMI less than the 85th percentile. We computed BMI in early adolescence from the height and weight reported by each Growing Up Today Study participant on the baseline 1996 questionnaire. Although self-reports of these measures are known to be valid in adults, recent data also suggest high validity among children and adolescents. In samples ranging in age from 11 to 16 years, Shannon et al\(^{42}\) and Strauss\(^{43}\) reported correlation coefficients in the range 0.84 to 0.94 for self-reported versus actual weight and 0.62 to 0.91 for height. Recently, Goodman et al\(^{44}\) estimated a correlation of 0.92 between BMI calculated from self-report versus measured height and weight among participants in the National Longitudinal Study of Adolescent Health. Despite the tendency for heavier children to underreport their weight, the obesity status of only 3.8% of youth in that study was misclassified.

**Data Analysis**

To adjust for covariates and to account for correlated values among siblings (\(n = 6,343\)), we used logistic models with estimation by generalized estimating equations.\(^{45}\) We analyzed birth weight as a continuous outcome, and fitted separate models for the 2 outcomes, overweight and at risk for overweight. In our base model, we adjusted for age and Tanner.
stage, because adolescent BMI varies by these 2 variables.46,47 Because we obtained similar results in gender-specific analyses, we analyzed girls and boys together and adjusted for gender. In subsequent models, we adjusted for total physical activity, amount of television watched, and total daily energy intake as proxies for energy balance. In addition, we adjusted for duration of breastfeeding because that variable predicts adolescent overweight in this cohort,40 as well as other maternal and family variables that could be related to GDM, birth weight, and/or adolescent BMI. We then added birth weight and maternal BMI to the models, separately and in combination.

RESULTS

The mean (standard deviation) age of subjects in 1996 was 11.9 (1.6) years, and 93.6% were white. A total of 4.9% of girls and 8.8% of boys were overweight. Participants who were overweight reported less total physical activity than the nonoverweight (14.9 vs 16.0 hours/wk), watched more television (2.7 vs 2.2 hours/d), and had slightly lower energy intake (2115 vs 2179 kcal/d). These 3 factors—physical activity, television watching, and energy intake—are associated with BMI change in this cohort.46

Birth weights and current maternal BMI were higher among offspring of mothers who experienced GDM than those who did not (Table 1). Among the 465 participants whose mothers had GDM, 17.1% were at risk for overweight and 9.7% were overweight. In the group without maternal diabetes, these estimates were 14.2% and 6.6%, respectively. In both groups, estimates of both overweight and at risk for overweight were higher for boys than for girls. Among both boys and girls, mean adolescent BMI as well as proportions for overweight and at risk for overweight rose across increasing birth weight category (Table 2).

In multivariate models, we found that for each 1-kg increment in birth weight, the odds ratio (OR) for overweight in adolescence was 1.4 (95% confidence interval [CI]: 1.2–1.6; Table 3). Adjustment for multiple covariates representing energy balance and socioeconomic factors did not materially affect the estimates, but adjustment for maternal BMI attenuated the OR to 1.3 (95% CI: 1.1–1.5). ORs for “at risk for overweight” were slightly lower but showed the same response to covariate adjustment (Table 3).

In similar models examining GDM instead of birth weight as the predictor of interest, we found that maternal GDM was associated with an OR of 1.4 (95% CI: 1.0–1.9) for overweight in adolescence, before adjusting for birth weight or maternal BMI (Table 4). Adjustment for birth weight slightly attenuated the estimates, and additional adjustment for maternal BMI attenuated them further, to a fully adjusted OR of 1.2 (95% CI: 0.8–1.7). The fully adjusted model suggested no association between maternal GDM and “at risk for overweight” (OR: 1.0; 95% CI: 0.7–1.3). In analyses stratified by maternal GDM status, we found no substantial difference in the association of birth weight with later overweight status. In adolescents whose mothers had had GDM, the adjusted OR for overweight was 1.1 (95% CI: 0.5–2.3) for a 1-kg increment in birth weight. In participants without a maternal history of GDM, the OR was 1.3 (95% CI: 1.1–1.5). In an alternative analysis, we addressed this issue by inserting an interaction term into the multivariate model. The P value for that term was .77, again suggesting no meaningful interaction between GDM and birth weight.

DISCUSSION

Because maternal GDM is associated with birth weight and birth weight is directly associated with later BMI, it makes sense to investigate the role of maternal GDM in the genesis of obesity. In this study, we documented a robust direct relationship between birth weight and BMI measured 9 to 14 years later. BMI increases with increasing birth weight, and maternal GDM was associated with an OR of 1.4 (95% CI: 1.0–1.9) in these analyses. The association was slightly lower but showed the same pattern when “at risk for overweight” was used as the outcome measure. This association remained after adjustment for multiple variables that could be related to GDM, birth weight, and/or maternal BMI, including birth weight and maternal BMI. Birth weight, however, was directly associated with BMI measured 9 to 14 years later as well. These results suggest that maternal GDM predicts adolescent BMI, and this relation is independent of both birth weight and maternal BMI.

**TABLE 1.** Mean Maternal BMI and Birth Weight and Number (%) of Participants Who Were Overweight (>95th Percentile*) and at Risk for Overweight (85th–95th Percentiles*), by Gender and Maternal GDM Status

<table>
<thead>
<tr>
<th>Birth Weight Category (kg)</th>
<th>n</th>
<th>Mean (SD) Maternal BMI (kg/m²)</th>
<th>Mean (SD) Birth Weight (kg)</th>
<th>No. (%) at Risk for Overweight</th>
<th>No. (%) Overweight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal GDM</td>
<td>246</td>
<td>27.2 (6.4)</td>
<td>3.55 (0.56)</td>
<td>35 (15.2)</td>
<td>16 (6.5)</td>
</tr>
<tr>
<td>No maternal diabetes</td>
<td>7735</td>
<td>25.0 (5.2)</td>
<td>3.44 (0.48)</td>
<td>966 (13.1)</td>
<td>377 (4.9)</td>
</tr>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal GDM</td>
<td>219</td>
<td>26.8 (6.6)</td>
<td>3.68 (0.61)</td>
<td>37 (19.5)</td>
<td>29 (13.2)</td>
</tr>
<tr>
<td>No maternal diabetes</td>
<td>6681</td>
<td>24.9 (5.2)</td>
<td>3.58 (0.51)</td>
<td>951 (15.6)</td>
<td>581 (8.7)</td>
</tr>
</tbody>
</table>

* From age- and gender-specific US national data.41

**TABLE 2.** Mean BMI and Number (%) of Participants Who Were Overweight (>95th Percentile*) and at Risk for Overweight (85th–95th Percentiles*) at Age 9 to 14 Years, by Gender and Birth Weight Category

<table>
<thead>
<tr>
<th>Birth Weight Category (kg)</th>
<th>n</th>
<th>Mean (SD) BMI (kg/m²)</th>
<th>No. (%) at Risk of Overweight</th>
<th>No. (%) Overweight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5–&lt; 2.5</td>
<td>255</td>
<td>18.6 (3.2)</td>
<td>28 (11.3)</td>
<td>8 (3.1)</td>
</tr>
<tr>
<td>2.5–&lt; 3.0</td>
<td>1006</td>
<td>18.6 (3.3)</td>
<td>116 (12.0)</td>
<td>43 (4.3)</td>
</tr>
<tr>
<td>3.0–&lt; 3.5</td>
<td>3146</td>
<td>18.8 (3.2)</td>
<td>370 (12.3)</td>
<td>128 (4.1)</td>
</tr>
<tr>
<td>3.5–&lt; 4.0</td>
<td>2638</td>
<td>19.2 (3.3)</td>
<td>340 (13.7)</td>
<td>148 (5.6)</td>
</tr>
<tr>
<td>4.0–&lt; 4.5</td>
<td>806</td>
<td>19.4 (3.4)</td>
<td>125 (16.7)</td>
<td>56 (6.9)</td>
</tr>
<tr>
<td>4.5–&lt; 6</td>
<td>130</td>
<td>19.9 (3.7)</td>
<td>22 (18.3)</td>
<td>10 (7.7)</td>
</tr>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5–&lt; 2.5</td>
<td>178</td>
<td>18.7 (3.5)</td>
<td>20 (12.3)</td>
<td>15 (8.4)</td>
</tr>
<tr>
<td>2.5–&lt; 3.0</td>
<td>626</td>
<td>19.0 (3.5)</td>
<td>78 (13.6)</td>
<td>53 (8.5)</td>
</tr>
<tr>
<td>3.0–&lt; 3.5</td>
<td>2182</td>
<td>18.9 (3.3)</td>
<td>290 (14.4)</td>
<td>170 (7.8)</td>
</tr>
<tr>
<td>3.5–&lt; 4.0</td>
<td>2998</td>
<td>19.1 (3.4)</td>
<td>388 (16.3)</td>
<td>224 (8.6)</td>
</tr>
<tr>
<td>4.0–&lt; 4.5</td>
<td>1062</td>
<td>19.6 (3.4)</td>
<td>168 (17.6)</td>
<td>109 (10.3)</td>
</tr>
<tr>
<td>4.5–&lt; 6</td>
<td>254</td>
<td>20.0 (3.5)</td>
<td>44 (20.5)</td>
<td>39 (15.4)</td>
</tr>
</tbody>
</table>

* From age- and gender-specific US national data.41
Each 1-kg increment of birth weight was associated with approximately a 30% increase in the prevalence of overweight, even after adjusting for maternal BMI and other relevant covariates.

In addition, we found that maternal GDM was associated with an OR of 1.4 for adolescent overweight, before controlling for birth weight and maternal BMI. This estimate was slightly attenuated by addition of birth weight to the model, suggesting that the association of GDM with later obesity could partially be explained by its influence on birth weight.

Maternal BMI played a confounding role in these analyses; adding it to the multivariate models resulted in a blunted association of maternal GDM with offspring overweight. Maternal BMI is clearly a risk factor for GDM, but its relation with offspring obesity could be through several pathways. First, preexisting maternal obesity could cause GDM, which in turn could cause offspring obesity. Given the observed confounding effect of maternal BMI, this pathway is unlikely to be the only explanation for our findings. Additional explanations include that offspring of obese mothers could take on similar adverse dietary and physical activity behaviors, and mothers and their children could share genes that cause obesity in both of them.

To some extent, then, GDM may be only a risk marker for offspring obesity, not in the causal pathway. Such an interpretation would be consistent with the null findings of Whitaker et al.\textsuperscript{35} Like the managed care study population of Whitaker et al.\textsuperscript{35} GDM in a cohort of nurses such as ours may not be severe enough to observe a life-long effect of its presence. It is also possible that effective treatment of GDM in this group of health care professionals could have blunted any long-term consequences, but the long-term effects of GDM treatment on the offspring are not known.\textsuperscript{49} In contrast, among the Pima Indians, in which diabetes, including gestational diabetes, is endemic, GDM is more clearly associated with offspring obesity. Dabelea et al.\textsuperscript{33} examined BMI among Pima siblings, aged 9 to 24, whose fetal lives were discordant for the presence of maternal diabetes. Offspring who were exposed to diabetes in utero had higher BMI than their unexposed siblings. That study is important because it mitigates the roles of both shared genes and postnatal environment, likely similar within a sibling set, thus emphasizing the potential role of the fetal environment.

Although our results do not implicate GDM as a sufficient cause of offspring obesity, they may be consistent with GDM’s programming the fetus for later, postnatal influences that lead to obesity. This interpretation is consistent with the findings of Silverman et al.\textsuperscript{34} who reported that at age 14 to 17 years, offspring of mothers with GDM had a mean BMI of 26.0 kg/m\textsuperscript{2}, compared with 20.9 kg/m\textsuperscript{2} in control subjects. In addition, amniotic fluid insulin levels, which reflect fetal pancreatic insulin production, correlated with obesity during adolescence. Notably, the increased BMI was apparent at birth and

<p>| TABLE 3. Adjusted ORs for Overweight (&gt;95th Percentile) and at Risk for Overweight (85th–95th Percentiles) for a 1-kg Increment in Birth Weight Among 14,881 9- to 14-Year-Old Participants in the Growing Up Today Study |</p>
<table>
<thead>
<tr>
<th>Model Covariates</th>
<th>At Risk for Overweight (n = 1989)</th>
<th>Overweight (n = 1003)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>1. Age, gender, Tanner stage</td>
<td>1.3 (1.2–1.4)</td>
<td>1.4 (1.2–1.6)</td>
</tr>
<tr>
<td>2. Model 1 + television watching, physical activity, energy intake</td>
<td>1.3 (1.2–1.5)</td>
<td>1.5 (1.3–1.7)</td>
</tr>
<tr>
<td>3. Model 2 + breastfeeding duration; birth order; household income; and mother’s smoking, dietary restraint, weight cycling, and weight concerns</td>
<td>1.3 (1.2–1.5)</td>
<td>1.4 (1.2–1.7)</td>
</tr>
<tr>
<td>4. Model 3 + mother’s current BMI</td>
<td>1.2 (1.1–1.4)</td>
<td>1.3 (1.1–1.5)</td>
</tr>
</tbody>
</table>

\*From age- and gender-specific US national data.\textsuperscript{41}

<p>| TABLE 4. Adjusted ORs for Overweight (&gt;95th Percentile) and at Risk for Overweight (85th–95th Percentiles) for Maternal GDM Versus No Maternal Diabetes Among 14,881 9- to 14-Year-Old Participants in the Growing Up Today Study |</p>
<table>
<thead>
<tr>
<th>Model Covariates</th>
<th>At Risk for Overweight (n = 1989)</th>
<th>Overweight (n = 1003)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>1. Age, gender, Tanner stage</td>
<td>1.2 (0.9–1.5)</td>
<td>1.4 (1.1–2.0)</td>
</tr>
<tr>
<td>2. Model 1 + television watching, physical activity, energy intake</td>
<td>1.2 (0.9–1.6)</td>
<td>1.4 (1.0–2.0)</td>
</tr>
<tr>
<td>3. Model 2 + breastfeeding duration; birth order; household income; and mother’s smoking, dietary restraint, weight cycling, and weight concerns</td>
<td>1.0 (0.8–1.4)</td>
<td>1.4 (1.0–1.9)</td>
</tr>
<tr>
<td>4. Model 3 + birth weight</td>
<td>1.0 (0.8–1.4)</td>
<td>1.3 (0.9–1.9)</td>
</tr>
<tr>
<td>5. Model 3 + mother’s current BMI</td>
<td>1.0 (0.7–1.3)</td>
<td>1.2 (0.8–1.7)</td>
</tr>
<tr>
<td>6. Model 3 + mother’s current BMI and birth weight</td>
<td>1.0 (0.7–1.3)</td>
<td>1.2 (0.8–1.7)</td>
</tr>
</tbody>
</table>

\*From age- and gender-specific US national data.\textsuperscript{41}
progressively after the age of 4 years but not at ages 1 to 3 years, suggesting a delayed influence of GDM or the necessity of a "second hit" in childhood to produce the adolescent obesity.³¹ It is possible that the effect of GDM on overweight in the participants in our study would be more evident later in adolescence.

Although the participants in this study lived in all 50 states and several US territories, they compose a largely homogeneous population in terms of race/ethnicity. This limitation, however, is more likely to affect generalizability than internal validity. Despite a large sample size, GDM is uncommon enough that CIs were relatively wide. For example, our OR estimate of 1.2 for the maternal BMI-adjusted association of GDM with offspring overweight was consistent (with 95% confidence) with estimates ranging from 0.8 to 1.7. Although a 20% increase in odds could be important from a public health viewpoint, we could not distinguish this estimate very well from larger or smaller, including null, effects.

Because we did not obtain data during the preschool- and school-age periods for each child, we were unable to examine growth trajectories over time. Residual and unmeasured confounding is always of concern in an observational study, but we were able to control for several relevant covariates not available in many previous studies. Another strength is that in contrast to some previous studies, we excluded mothers with pregestational diabetes, because long-standing diabetes can cause severe placental dysfunction and growth-retarded, rather than macroscopic, newborns.

CONCLUSION

In this study of US adolescents who were born no earlier than 34 weeks' gestation, we found that birth weight was directly related to risk of overweight 9 to 14 years later. GDM, itself a determinant of higher birth weight, was also associated with increased risk of adolescent overweight, but much of this association was explained by the confounding influence of maternal BMI, perhaps owing to a combination of pre- and postnatal environmental factors as well as genetic inheritance. Thus, GDM is a risk marker for offspring obesity, but to what extent it exerts a causal influence remains the subject of additional research. Such research is vital, because rising rates of obesity in youth portend an increase in GDM, potentially resulting in a vicious cycle of increasing obesity for generations to come.

ACKNOWLEDGMENTS

This study was supported by grants from the National Institutes of Health (R01 DK 46834, K24 HL 68041), by Harvard Medical School and the Harvard Pilgrim Health Care Foundation, and by the Boston Obesity/Nutrition Research Center (DK 46200).

We thank the staff and participants of the Growing Up Today Study and the Nurses' Health Study II, and we thank Julia C. L. Wong for contributions to the manuscript.

REFERENCES


34. Parsons TJ, Powers C, Manor O. Fetal and early life growth and body

Maternal Gestational Diabetes, Birth Weight, and Adolescent Obesity
Matthew W. Gillman, Sheryl Rifas-Shiman, Catherine S. Berkey, Alison E. Field and Graham A. Colditz
Pediatrics 2003;111:e221
DOI: 10.1542/peds.111.3.e221

Updated Information & Services
including high resolution figures, can be found at:
/content/111/3/e221.full.html

References
This article cites 45 articles, 13 of which can be accessed free at:
/content/111/3/e221.full.html#ref-list-1

Citations
This article has been cited by 45 HighWire-hosted articles:
/content/111/3/e221.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Endocrinology
/cgi/collection/endocrinology_sub
Obesity
/cgi/collection/obesity_new_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Maternal Gestational Diabetes, Birth Weight, and Adolescent Obesity

Matthew W. Gillman, Sheryl Rifas-Shiman, Catherine S. Berkey, Alison E. Field and Graham A. Colditz

*Pediatrics* 2003;111:e221

DOI: 10.1542/peds.111.3.e221

The online version of this article, along with updated information and services, is located on the World Wide Web at:

/content/111/3/e221.full.html