Childhood Obesity and Metabolic Imprinting: The Ongoing Effects of Maternal Hyperglycemia

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Running Head: Maternal Hyperglycemia and Future Childhood Obesity
ABSTRACT

OBJECTIVE—To determine how the range of measured maternal glycemia in pregnancy relates to risk of obesity in childhood.

RESEARCH DESIGN AND METHODS—Universal GDM screening (50g glucose-challenge test [GCT]) was performed in 2 regions (Northwest/Hawaii) of a large diverse HMO during 1995-2000, and GDM diagnosed/treated using a 3-hr 100g oral glucose tolerance test (OGTT) and National Diabetes Data Group (NDDG) criteria. Measured weight in offspring (n=9,439) was ascertained 5-7 years later to calculate gender-specific weight-for-age percentiles using USA norms (1963-1994 standard), then classified by maternal positive (+) GCT (1hr>=7.8mmol/l) and OGTT results ([1 or >=2 of the 4 timepoints abnormal; fasting, 1-hr, 2-hr, 3-hr] by Carpenter & Coustan (CC) and NDDG criteria).

RESULTS—There was a positive trend for increasing childhood obesity at age 5-7 years (p<0.0001; 85%ile & 95%ile) across the range of increasing maternal glucose screen values, which remained after adjustment for potential confounders including maternal weight gain, maternal age, parity, ethnicity, and birthweight. The risk of childhood obesity in offspring of mothers with GDM by NDDG criteria (treated) was attenuated compared to the groups with lesser degrees of hyperglycemia (untreated). The relationships were similar among Caucasians and non-Caucasians. Stratification by birthweight also revealed these effects in children of normal birthweight (<=4000g).

CONCLUSIONS—Our results in a multi-ethnic US population suggest that increasing hyperglycemia in pregnancy is associated with an increased risk of childhood obesity. More research is needed to determine if treatment of GDM may be a modifiable risk factor for childhood obesity.
INTRODUCTION
Diabetes in pregnancy is associated with an increased rate of offspring childhood obesity, impaired glucose tolerance, and Type 2 diabetes (1-7). The strongest single risk factor for obesity in Pima Indians children is exposure in utero to maternal diabetes, independent of maternal obesity and birthweight (3,4,8). Pettitt et al found an overall linear association between maternal glucose concentration (2-hour glucose on the 75g OGTT) and obesity in their offspring in the Pimas, with the effect most pronounced for the 2-hr post-OGTT level >=7.8mmol/l (9). Some—but not all—studies in populations other than Pimas report an association of Gestational Diabetes (GDM) with increased offspring obesity (7,10-12).

With normal growth, children’s weight rises in proportion to height at an average age of 6 years. This period, called adiposity rebound (13-15), is thought to be a critical time of risk for adult obesity—obesity in this childhood period strongly predicts adult obesity (16-19).

We sought to determine if increasing hyperglycemia in pregnancy—ranging from normal to GDM—is related to childhood obesity in offspring during the typical period of adiposity rebound in a diverse population. We tested our hypotheses among 9,439 women in a large multi-ethnic US population universally screened for GDM, whose children had weight measured between age 5-7 years. This established universal 2-step GDM screening program (50g Glucose Challenge Test [GCT]; if positive, then a diagnostic OGTT) allows us to evaluate a large number of offspring whose mothers’ glucose intolerance ranged from normal GCT to GDM, diagnosed by old (treated) and current (untreated) criteria during the study period.

RESEARCH DESIGN AND METHODS
Research Setting
The study population was drawn from a combined membership of over 650,000 at two Kaiser regions: Hawaii (KPH) and Northwest (KPNW). Both regions’ memberships are ~20% of the areas’ general populations and reflect their demographic/sociographic characteristics. In Hawaii, low-income individuals enroll under the State Health Insurance Plan for Medicaid, about 10% of the state and KPH population. During the study period, KPNW served ~8% of Medicaid members through the Oregon Health Plan, a population demographically similar to the area population (20). All members in both regions have access to medically necessary services from KP or by referral from their primary care physician.

Both KPH and KPNW maintain administrative and clinical electronic databases on inpatient admissions, pharmacy dispenses, chronic-disease registry, laboratory tests, and outside claims/referrals. All databases are linked through each member’s unique health record number. Both regions also have ongoing validated diabetes registries (21), so women with pre-existing diabetes can be excluded from analyses.

Institutional Review Boards of both KP regions and the State of Hawaii Department of Health approved this study.

Glucose Testing and GDM diagnosis
Both KPH and KPNW universally screen for GDM, initially using a 50g, 1-hour GCT. Women who fail this at a level >11.1mmol/l are assumed to have GDM and not tested further. Those remaining who fail the GCT (≥7.8mmol/l) then receive the 100g, 3-hour OGTT. For women screened more than once during pregnancy, we used the latest test.
Both the National Diabetes Data Group (NDDG) and Carpenter Coustan (C&C) criteria for GDM diagnosis require that 2 or more of the 4 possible timepoints measured with the 100g OGTT are positive, although they have different threshold cut-offs. Relevant to this analysis, during 1995-2000, KP used the NDDG criteria to diagnose and treat GDM, allowing us to also assess potential differences in outcomes with treatment. Therefore, those meeting NDDG’s criteria were likely treated with diet or diet/insulin, but those meeting only C&C’s were likely not treated. We have thus calculated GDM using both criteria sets. The NDDG’s require the 2 or more values to exceed these thresholds (in mmol/l): fasting $\geq 5.8\text{mmol/L}$; 1hr $\geq 10.5\text{mmol/L}$; 2hr $\geq 9.2\text{mmol/L}$; 3hr $\geq 8.0\text{mmol/L}$ (22-23). The more recent C&C criteria have these lower thresholds: Fasting $\geq 5.3\text{mmol/L}$; 1hr $\geq 10\text{mmol/L}$; 2hr $\geq 8.6\text{mmol/L}$; 3hr $\geq 7.8\text{mmol/L}$ (22,24).

**Sample Selection**
We identified 27,560 singleton births at KPH and KPNW during 1995-2000 (KPH=15,002 1995-2000; KPNW=12,558 1995-99). Mothers with pre-existing diabetes (n=261) were excluded from analysis (elevated HbA1c, provider-diagnosed diabetes, or in regional diabetes registry), leaving a pool of 27,229 without pre-existing diabetes. As both regions universally screen for GDM, we had available lab measurements on 26,211 (96% screening rate). Of the 26,211 women, 9,439 children had KP membership at age 5-7 years postpartum and had measured weight data in the electronic medical record (EMR) at age 5-7 years; these 9,439 mother-child pairs are the final included analysis group. Importantly, these 9,439 mother-child pairs did not differ from the excluded mother-child pairs (whose children did not remain members/have measured weight at age 5-7) by category of maternal glucose screening (i.e., percent normal, +GCT with normal OGTT, 1 abnormal value on OGTT, and GDM by C&C and NDDG criteria). They also did not differ by offspring gender or maternal weight gain in pregnancy. Those children who remained members tended to have less macrosomia at birth (12% vs. 13%, p=0.031), were less likely Caucasian (44% vs. 51% Caucasian, p<0.0001), and their mothers were generally older (28.6 vs. 27.4 years, p<0.001) and were less likely nulliparous (43% vs. 44%, p=0.01). Thus, the final sample was reasonably representative of the original sample.

**Classification of Childhood Obesity**
Obesity was classified as age-gender specific percentiles for both BMI and weight, based on US Centers for Disease Control (CDC) criteria (with the normative reference range 1964-1990, when US children were typically more lean) (25), and all outcomes were assessed with both BMI and weight percentiles.

At KPNW, all children with measured weight had a measured height to calculate BMI. However, at KPH a large proportion had only measured weight (2309 of 5841, or 40%) available in the EMR, partly because KPH transitioned to several outpatient EMR systems during our data collection period, and in some cases because a child had a visit for illness where only weight was measured (e.g., to calculate antibiotic dosing). As these children without height measures also represented a large proportion of children whose mothers had GDM with elevated fasting levels on the OGTT (37 of the 117 in Hawaii), we thought the potential bias to analyses would be greater by requiring height to assess obesity with BMI. Therefore, we present weight percentiles as our primary analysis, after confirming results were similar with BMI percentiles with the same CDC normative database (25).
Classification of Ethnicity and Other Covariates
Ethnicity classification was based on the mother’s reported race on the states’ official birth-certificates. As per state algorithms for classifying race, if the mother reported being any part Native Hawaiian, ethnicity is classified as Native Hawaiian. If she did not list Native Hawaiian, but a non-Caucasian race, then we classified the child into that group. Race was classified as Caucasian only if no other race/ethnicity was reported.

Maternal age, baby gender, and birthweight were recorded in the EMRs. State birth-certificate records validated birthweight and also provided mother’s reported parity and pregnancy weight gain.

Statistical Analyses
We conducted all statistical analyses using the SAS Statistical Analysis System® version 6.12 (SAS Institute, Cary, NC).

We assessed the relationship between GCT quartiles and childhood weight, and then stratified maternal glucose screening results into 5 categories: (1) Normal GCT (referent group); (2) +GCT, Normal OGTT; (3) One abnormality on the OGTT by either NDDG or C&C criteria [two or more abnormalities are required to diagnose GDM by either criteria set]; (4) GDM by the lower C&C criteria; (5) GDM by NDDG criteria (during the study period this is the GDM-treated group).

We first conducted all analyses for KPH and KPNW separately, both overall by region and for the Caucasian sub-groups, to confirm results were similar between the two regions. As results were consistent, our final analyses are combined for both regions. We also assessed relationships among varying ethnic sub-groups to confirm results were similar prior to combining into one non-Caucasian category.

We used t-tests, Pearson chi-square test, and Mantel-Haenszel chi-square tests to evaluate univariate relationships with potential confounders and child weight. Excessive pregnancy weight gain is a strong independent predictor of macrosomia (26), and ranged markedly from 0-98 pounds (median 30.0lbs). Therefore, we assessed the relationship between maternal weight gain and childhood weight initially by quartiles. The risk of childhood obesity increased significantly with the highest quartile of maternal weight gain (>40lbs), and thus we dichotomized maternal weight gain (>40lbs) for the multi-variate analyses.

We used Pearson chi-square to test univariate associations and multiple logistic regression to calculate odds ratios and confidence intervals adjusted for other covariates. All the statistical tests that we report are two-sided; the term statistically significant implies a p-value <0.05.

RESULTS
Table 1 presents characteristics of the multi-ethnic 9,439 mother-child pairs.

Childhood Obesity Based on Mother’s GCT and OGTT Results in Pregnancy
Table 2 presents the prevalence and risk of childhood obesity (defined as >85%ile and >95%ile of age-gender adjusted weight to US populations norms 1963-1994) associated with maternal GDM screening results during pregnancy. The highest quartile of hyperglycemia on the GCT was associated with a significantly higher level of childhood obesity compared to the referent lowest quartile (p<0.0001 for trend for both >85%ile and >95%ile, Table 2).

When the range of glycemia, including those requiring a OGTT, was evaluated in categories relative to those with a normal GCT, increasing level of hyperglycemia in
pregnancy was associated with a greater risk of childhood obesity (p<0.0001 for trend for both >85%ile and >95%ile, Table 2). However, only those with an abnormal OGTT significantly differed from the normal GCT group in risk for childhood obesity (Table 2). This significant trend for increasing childhood obesity associated with increasing maternal hyperglycemia remained after multivariate adjustment for maternal age, parity, pregnancy weight gain, ethnicity, macrosomia at birth, and baby gender (Table 2). Importantly, the increased risk of childhood obesity with maternal GDM by NDDG criteria (which was treated) was not significant after multivariate adjustment, whereas the risk of all other levels of hyperglycemia based on one or more abnormal OGTT values remained significant (Table 2).

Increasing maternal glycemic level was associated with greater prevalence of macrosomia (>4,000g, p<0.0001). As some of the effect of increasing maternal hyperglycemia on future childhood obesity could operate through increasing macrosomia, we also assessed models stratified by macrosomia. Interestingly, the relationship of increasing maternal hyperglycemia and associated increased childhood obesity was significant only among children who were not macrosomic at birth (Table 3; see online Appendix). In contrast, the children who were macrosomic at birth had a higher prevalence of childhood obesity irrespective of maternal glycemic level. However, the interaction between maternal glucose levels and birthweight was not significant in the multivariate model. Further, the relationship between maternal glycemia and child weight was not different when birthweight was excluded from the model.

Childhood Obesity Based on Mother’s Fasting Glucose on the OGTT
We did a sub-group analysis in offspring of women who had an abnormal GCT and a subsequent OGTT, stratifying by fasting results on the OGTT (C&C criteria) irrespective of whether at least 2 abnormalities were present on the OGTT (and thus GDM diagnosed). The risk of childhood obesity at age 5-7 years was nearly double in those children whose mother had an elevated fasting glucose of >5.3mmol/l (95 mg/dl) on the OGTT compared to those with normal fasting glucose but other abnormal post-OGTT values (p<0.0001, Figure 1). Results were similar when women with GDM by NDDG criteria (treated) were excluded (data not shown).

CONCLUSIONS
Among 9,439 mother-child pairs in a diverse US population universally screened for gestational diabetes, we found that increasing hyperglycemia level in pregnancy is associated with increased future risk of obesity in their children at age 5-7 years. Importantly, our results suggest this risk is modifiable by treating GDM, as obesity risk was attenuated and no longer significant after multivariate adjustment in the treated GDM group. To our knowledge, this is the first study of a population besides Pimas to evaluate childhood obesity with the complete range of hyperglycemia in pregnancy.

Our results also suggest that “metabolic imprinting” of the future child for obesity occurs with one or more abnormalities on the OGTT, and that fasting hyperglycemia in particular is an important predictor of future childhood obesity. The concept of metabolic imprinting in women and animal models of diabetes has previously been eloquently demonstrated—i.e., the altered metabolic milieu of diabetes in pregnancy increases the offspring’s risk of obesity and Type 2
diabetes greater than would be predicted from genetics alone (2,3,9,27-31). The strongest
single risk factor for obesity in Pima children is maternal diabetes in utero, independent of
maternal obesity and birthweight (3,4,8). Offspring of mothers with diabetes (ODM)
have up to a 10-fold increased risk of becoming obese during childhood and
adolescence and developing impaired glucose tolerance as adolescents (5,7,32). Pettitt et al
found that by age 20-24, 45% of ODM had developed Type 2 diabetes (DM2) in the Pima
population, compared to 8.6% of offspring of pre-diabetic women (mother developed DM2
diabetes post-partum), and only 1.4% of offspring had developed DM2 by age 20-24 if
their mother had not had GDM or later DM2 (1).

Prior literature is less clear on what degree obesity in the offspring occurs among women
with GDM (versus pre-existing Type 1 or 2 diabetes) in other ethnic groups (7,10-12,18).
Among a multi-ethnic population of nearly 10,000 mother-child pairs in which maternal
 glucose was measured as part of a universal screening program, we found that GDM in
pregnancy was associated with increased obesity in their children who were examined
at age 5-7 years.

Macrosomia, is both a recognized short-term obesity complication of diabetes in pregnancy
and an independent risk factor for future childhood obesity (7,33). Treatment of GDM
dramatically reduces the rate of macrosomia (34,35), but it is unclear if treatment might
also reduce the child’s future obesity risk. Our stratified findings based on macrosomia
(<=4,000g vs. >4,000g) revealed a significant relationship with increasing maternal
hyperglycemia and childhood obesity only among those who were normal weight at
birth. Moreover, among this normal group, GDM treatment of (diagnosed by NDDG)
resulted in childhood obesity rates closer to those of mothers with normal glucose
tolerance.

These results suggest that treatment of GDM may reduce childhood obesity rates—and by
metabolic mechanisms other than macrosomia. Our results are consistent with Pettitt et al’s earlier results in which, even among normal birthweight infants, diabetes
during pregnancy increased childhood obesity risk over offspring whose mother did not have
GDM (this effect was also not seen in the macrosomia group) (8). It is also notable that
O’Sullivan’s sentinel randomized controlled trial of GDM treatment over 4 decades ago
found the greatest relative reduction in macrosomia among women who were normal
weight (although the overall prevalence of macrosomia was highest in overweight
mothers) (35).

In addition to our findings that increasing maternal hyperglycemia is associated with
future childhood obesity risk, we found that fasting hyperglycemia in particular is
associated with with future childhood obesity risk. Langer et al assessed perinatal outcomes
in a secondary analysis of a randomized trial of women who need GDM treatment
(glyburide versus insulin) and found that the proportion of large-for-gestational age (LGA)
babies was double among mothers with elevated fasting hyperglycemia on the
screening OGTT irrespective of treatment group (18% LGA in mothers with fasting
<95mg/dl versus 8-9% in both treatment groups with fasting OGTT >95mg./dl) (36).
Together these findings suggest that fasting hyperglycemia is an important risk factor for
immediate and long-term obesity risk in offspring. This needs to be tested further.

Our study has important strengths. The population is a large multi-ethnic US sample
of nearly 10,000 mother-child pairs in which universal GDM screening was measured, and
the children prospectively followed and
assessed for obesity 5-7 years after birth. Measurement of birthweight and other potential confounders such as ethnicity and maternal age and weight gain are also strengths. Additionally, we were able to determine that the relationships observed between hyperglycemia in pregnancy and childhood obesity were consistent among differing ethnic groups as we report in detail for the entire population.

Our study also has limitations. We were limited to evaluating a sub-sample of the birth cohort who remained members to have measured weight at age 5-7 years. However, change in membership would likely be random loss to follow-up and, as detailed in the methods, those children who remained members were remarkably similar to those who did not. Moreover, there were no differences in the distribution of maternal hyperglycemia between the two groups. Thus, a significant bias from losses to follow-up is unlikely. Because the outpatient EMR was just beginning for KPNW during the initial study period and was not in place at KPH, we do not have access to their pre-pregnancy weights. Thus, we cannot determine how prior maternal obesity may have contributed to the hyperglycemia observed in pregnancy or mediated the childhood outcomes. However, we were able to adjust for weight gain in pregnancy (reported on the birth-certificates) and birthweight—both independent predictors of childhood obesity in our analysis—and the relationships we observed were independent of both these weight variables. Moreover, multivariate results were remarkably similar in effect size to the unadjusted results that did not account for weight differences. Finally, our classification of maternal hyperglycemia is based on GDM screening results at one time-point in pregnancy; multiple measures of glycemia are not available on the population.

In summary, among a large multi-ethnic US population we found that increasing hyperglycemia in pregnancy and fasting hyperglycemia, in particular, is associated with an increased risk of childhood obesity. This risk was present in Caucasians as well as other high-risk ethnic groups, and even among children of normal birthweight. These results suggest that metabolic imprinting of the future child for obesity occurs in women with GDM (not only pre-existing diabetes), and thus GDM screening might have long-term benefits to the offspring. They also suggest that GDM treatment may decrease the risk of childhood obesity, and provide an additional reason for screening for GDM in pregnancy. More research is needed to determine if treatment of maternal GDM may be a modifiable risk factor for childhood obesity.

ACKNOWLEDGMENTS
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REFERENCES

32. Centers for Disease Control and Prevention: Diabetes and Women's Health Across the Life Stages: A Public Health Perspective. Atlanta, US Department of Health and Human Services, Centers for Disease control and Prevention, 2001
Table 1. Characteristics of the 9,439 Mother-Child Pairs

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td><strong>Maternal age at screen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18 yrs</td>
<td>260</td>
<td>(2.7)</td>
</tr>
<tr>
<td>18 – 25</td>
<td>2821</td>
<td>(29.9)</td>
</tr>
<tr>
<td>26 – 30</td>
<td>2187</td>
<td>(23.2)</td>
</tr>
<tr>
<td>31- 35</td>
<td>2830</td>
<td>(30.0)</td>
</tr>
<tr>
<td>36+</td>
<td>1341</td>
<td>(14.2)</td>
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<tr>
<td><strong>Parity</strong></td>
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<td>0</td>
<td>4019</td>
<td>(42.6)</td>
</tr>
<tr>
<td>1</td>
<td>3155</td>
<td>(33.4)</td>
</tr>
<tr>
<td>2</td>
<td>1429</td>
<td>(15.1)</td>
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<tr>
<td>3 or more</td>
<td>821</td>
<td>(8.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>15</td>
<td>(0.2)</td>
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<tr>
<td><strong>Maternal Weight Gain (pounds)</strong></td>
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</tr>
<tr>
<td>0 – 24</td>
<td>2014</td>
<td>(21.3)</td>
</tr>
<tr>
<td>25 – 31</td>
<td>2078</td>
<td>(22.0)</td>
</tr>
<tr>
<td>32 – 40</td>
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<td>41 +</td>
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<td>(21.8)</td>
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<td>(6.1)</td>
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<td>Pacific Islander</td>
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<td>(Other than Hawaiian or Samoan)</td>
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<td>(3.7)</td>
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<td>African American</td>
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<tr>
<td>Samoan</td>
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<td>(1.8)</td>
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<tr>
<td>Other*</td>
<td>322</td>
<td>(3.4)</td>
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<tr>
<td><strong>Birthweight &gt; 4000g</strong></td>
<td>1147</td>
<td>(12.2)</td>
</tr>
<tr>
<td><strong>Gender of Baby Female</strong></td>
<td>4618</td>
<td>(48.9)</td>
</tr>
</tbody>
</table>

*Other includes Korean (98), Puerto Rican (58), Native American (54), Vietnamese (39), Other categories (60), and Unknown (13)
Table 2. Prevalence and Risk of Childhood Obesity at age 5-7 years, Stratified by Their Mother’s Glycemia while Pregnant with Them

<table>
<thead>
<tr>
<th>Maternal Glucose Scale with Screening for GDM by GCT and OGTT</th>
<th>Child’s Weight &gt; 85th percentile*</th>
<th>Child’s Weight &gt; 95th percentile*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with Normal GCT (Quartiles)</td>
<td>N</td>
<td>Prevalence (%)†</td>
</tr>
<tr>
<td>43 – 94 mg/dL</td>
<td>1987</td>
<td>21.6</td>
</tr>
<tr>
<td>95 – 108 mg/dL</td>
<td>1953</td>
<td>23.6</td>
</tr>
<tr>
<td>109 – 121 mg/dL</td>
<td>1801</td>
<td>23.3</td>
</tr>
<tr>
<td>122 – 140 mg/dL</td>
<td>1868</td>
<td>25.5</td>
</tr>
<tr>
<td>Women with GCT/OGTT</td>
<td>9,439</td>
<td></td>
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<tr>
<td>Normal GCT</td>
<td>7609</td>
<td>23.5</td>
</tr>
<tr>
<td>+GCT, Normal OGTT</td>
<td>999</td>
<td>23.3</td>
</tr>
<tr>
<td>+GCT, 1 abn C&amp;C or NDDG</td>
<td>288</td>
<td>26.7</td>
</tr>
<tr>
<td>+GCT, GDM-C&amp;C</td>
<td>173</td>
<td>34.7</td>
</tr>
<tr>
<td>+GCT,GDM-NDDG; Treated</td>
<td>370</td>
<td>27.8</td>
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</table>

†p for trend ≈0.0001 in both stratified GCT and GCT/OGTT group analyses.
‡Adjusted for maternal age, weight gain during pregnancy, ethnicity, macrosomia at birth (>4,000 g), and gender of child; significant values are bolded.
§For multivariate analyses only, the final sample sizes were 6,071 total women with Normal GCT and 7,428 women with GCT/OGTT, due to missing self-reported weight gain and parity data; the smallest sub-group for the multi-variate analysis remained women with +GCT; GDM-C&C (n=124).

Abbreviations Used: +GCT= 1 hour 50 gram glucose challenge test >7.7 mmol/l (140 mg/dl); OGTT= 100 gram glucose tolerance test; Gestational Diabetes=GDM (2 or more values exceed the threshold by Carpenter and Coustan (C&C) or National Diabetes Data Group (NDDG) criteria(22))
Figure 1—Relationship of fasting maternal hyperglycemia in pregnancy with childhood obesity at age 5-7 years, among sub-sample with abnormal GCT and complete follow-up OGTT results: (1) Glucose Challenge Test >140 mg/dl (7.7 mmol/l) but follow-up OGTT normal at all 4 timepoints (fasting, 1, 2, and 3 hours post-OGTT) by Carpenter and Coustan (C&C) criteria (22,24) (n=731) (2) Normal fasting glucose (≤ 95 mg/dl [5.3 mmol/l]) but 1 or more C&C post-prandial values equaled or exceeded on OGTT (n=547); (3) Elevated fasting glucose >95 mg/dl (n=184) on OGTT and 0, 1, or 2 C&C post-prandial values equaled or exceeded. Categories 2 and 3 are stratified based on fasting glucose on the OGTT irrespective of whether the woman met criteria for GDM (2 of 4 values exceeded by either C&C or NDDG criteria).