Published in final edited form as:

J Pediatr. 2013 April ; 162(4): 741–745. doi:10.1016/j.jpeds.2012.10.001.

The impact of gestational diabetes mellitus on pubertal changes in adiposity and metabolic profiles in Latino offspring

Jaimie N. Davis, PhD¹, Erica P. Gunderson, PhD², Lauren E. Gyllenhammer³, and Michael I. Goran, PhD^{3,4}

¹Department of Nutritional Sciences, University of Texas at Austin, Austin Texas, USA

²Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA

³Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

⁴Department of Physiology and Biophysics, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Abstract

Objective—To examine the impact of maternal gestational diabetes mellitus (GDM) status on longitudinal changes in adiposity and metabolic variables in overweight Latino offspring (from age 8–20 years) across puberty.

Study design—This is a longitudinal cohort of 210 overweight Latino children who were measured annually for 3 ± 1 years for: Tanner stage via physical examination, adiposity via dual-energy X-ray absorptiometry and magnetic resonance imaging, lipids, glucose and insulin action via oral glucose tolerance test and frequently sampled intravenous glucose tolerance test. Linear mixed-effects modeling estimated the impact of maternal GDM status on baseline and changes in adiposity and metabolic variables across puberty.

Results—Twenty-two percent of offspring were from GDM pregnancies. At baseline, GDM offspring were heavier at birth, had more family history of type 2 diabetes, and were less likely to have been breastfed (any duration). GDM offspring compared with non-GDM offspring had greater increases in total body fat (+6.5% vs +4.5%; $p=0.03$) and steeper declines in acute insulin response (−39% vs. −17%; $p<0.001$) and disposition index (−57% vs. −35%; $p<0.001$) across Tanner stages, independent of ethnicity, sex, breastfeeding status, family history of diabetes, and baseline and changes in body composition.

Conclusion—These findings confirm the elevated risk for excess adiposity and type 2 diabetes in GDM offspring, and further highlight the need for interventions targeting Latino GDM and their offspring.

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Correspondence and Reprint Requests to: Jaimie Davis, PhD, RD 1400 Barbara Jordan Blvd Austin, TX 78723-3092
Jaimie.davis@austin.utexas.edu Telephone: (512) 495-4705; Fax: (512) 495-4948.

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The authors declare no conflicts of interest.

Keywords

Longitudinal study; Hispanics; overweight and obesity; Gestational diabetes; type 2 diabetes risk; puberty

In the past 3 decades, more research has shown intrauterine exposure to gestational diabetes mellitus (GDM) can place offspring at increased risk for long-term health problems, such as obesity, altered glucose metabolism and insulin action, and type 2 diabetes^{6,7,8}. Observational studies have shown that diabetes during pregnancy is associated with higher prevalence of overweight and obesity in the offspring^{13,14}. Gillman et al found that offspring of GDM mothers had a 30% increased risk of being overweight, after controlling for energy balance, socioeconomic status and birth weight². Few studies have examined the effect of GDM on adiposity and fat distribution, beyond BMI. GDM has also been linked to increased risk of type 2 diabetes in the offspring. Most notably are the studies conducted on the Pima Indians⁶ and the birth cohort from the Diabetes Pregnancy Study (DPS)⁸. In the Pima Indian cohorts, 45% of offspring from mothers with GDM (20 to 24 years of age) developed diabetes compared with 9% of offspring from mothers who became diabetic after pregnancy⁷, and 1.4% of offspring from mothers who had not had GDM or later type 2 diabetes. Data from the DPS showed that offspring of diabetic mothers had a higher prevalence of impaired glucose tolerance than age- and sex-matched controls⁸.

Few studies have examined the intrauterine exposure to elevated glucose concentrations on insulin secretion and sensitivity in the offspring, beyond fasting levels. One recent study by Bush et al¹⁵ on 21 mother-child pairs, with prepubertal children (5 to 10 years of age) showed that maternal gestational glucose was associated with lower insulin sensitivity and greater static beta-cell response in prepubertal children, independent of their body composition. However, maternal GDM was not significantly associated with children's disposition index (DI), which is considered the global estimate of beta-cell response to glucose.

Given that puberty is a period in life marked by insulin resistance and subsequent compensatory insulin secretion¹⁶, it is important to examine the role of maternal GDM on insulin action in the offspring across this key life transition. Therefore, this study examines how maternal GDM status affects longitudinal changes in adiposity, lipid profiles, and glucose and insulin action in overweight Latino offspring (ages 8 to 20 years) as they traverse puberty. We hypothesize that GDM offspring compared with non-GDM offspring will have greater adiposity and exhibit metabolic disorders at baseline and across puberty transition.

METHODS

Participants were recruited to participate in the Study of Latino Adolescents at Risk (SOLAR) diabetes project at the University of Southern California (USC), which began in the year 2000, and has been described in detail elsewhere.¹¹ This study is an ongoing longitudinal study investigating potential risk factors for the development of type diabetes in Hispanic children. At study entry, children were required to meet the following inclusion criteria: (1) 8–13 years of age; (2) BMI ≥85th percentile based on the Centers for Disease Control and Prevention guidelines; (3) Hispanic ancestry (all four grandparents of Hispanic origin as determined by parental self-report); and (4) family history of type 2 diabetes in at least one parent, sibling, or grandparent determined by parental self-report. Subjects were ineligible if they were taking medications known to affect body composition, had diseases known to affect body composition or fat distribution, or had any major illness since birth.

The Institutional Review Board at USC, Health Sciences Campus, approved this study. Informed written consent and assent were obtained from both parents and child before testing commenced.

A licensed pediatric health care provider conducted a detailed medical history exam and determined Tanner staging based on breast development in girls and pubic hair stage in boys. Parents reported if the mothers had GDM with this child, whether or not she breastfed and for how long, and the birth weight for the child enrolled in this study.

Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, using a beam medical scale and wall-mounted stadiometer. BMI and BMI percentiles were determined (CDC, 2001). Whole body fat and soft lean tissue were measured by DXA using a Hologic QDR 4500W (Hologic, Bedford, MA). Subcutaneous abdominal adipose tissue (SAAT) and visceral adipose tissue (VAT) were determined by Magnetic Resonance Imaging (MRI), which was performed at the USC Imaging Science Center. A single-slice axial TR 400/16 view of the abdomen at the level of the umbilicus was analyzed for cross-sectional area of adipose tissue. A General Electric 1.5 Signa LX-Echospeed device with a General Electric 1.5-Tesla magnet was used (Waukesha, WI).

After an overnight fast, a 2-hour oral glucose tolerance test (OGTT) was conducted using a dose of 1.75 g glucose/kg body weight (maximum of 75 g). Blood was sampled and assayed for glucose and insulin at −5 min (fasting state) and 120 min relative to glucose ingestion. Fasting and 2-hr glucose levels were used to diagnose type 2 diabetes as defined by the American Diabetes Association.

Within 1 month after the OGTT visit, non-diabetic children were asked to come back to the GCRC for an overnight visit where a frequently sampled intravenous glucose tolerance test (FSIVGTT) was performed. At time 0, glucose (25% dextrose, 0.3 g/kg body wt) was administered intravenously and insulin (0.02 units/kg body wt, Humulin R [regular insulin for human injection]; Eli Lilly, Indianapolis, IN) was injected intravenously at 20 min. A total of 13 blood samples were collected. Plasma collected during the FSIVGTT was analyzed for glucose and insulin, and values were entered into the MINMOD Millenium 2003 computer program (version 5.16, Bergman, USC) to determine insulin sensitivity (SI), acute insulin response (AIR), and disposition index (DI, an index of β -cell function).

Blood samples during the OGTT and FSIVGTT were centrifuged immediately for 10 min at 2500 RPM and 8–10°C to obtain plasma, and aliquots were frozen at −70° C until assayed. Fasting and 2-hour glucose from the OGTT was analyzed on a Dimension Clinical Chemistry system using an *in vitro* Hexokinase method (Dade Behring, Deerfield, IL). Glucose from the FSIVGTT was assayed in duplicate on a Yellow Springs Instrument 2700 Analyzer (Yellow Springs Instrument, Yellow Springs, OH) using the glucose oxidase method. Insulin was assayed in duplicate using a specific human insulin ELISA kit from Linco (St. Charles, MO). Fasting lipids from the OGTT were assessed using Vitros Chemistry DT Slides (Johnson and Johnson Clinical Diagnostic, Inc., Rochester, NY).

Statistical Analyses

Variables not normally distributed including, insulin sensitivity (SI), acute insulin response (AIR), disposition index (DI) and visceral adipose tissue (VAT), were log-transformed. Linear mixed-effects modeling was used to assess the impact of GDM on baseline and longitudinal changes in adiposity and glucose and insulin action over Tanner stages. In all models, the following covariates were included: sex, birth weight, family history of T2D, breastfeeding status (any duration), and SI (when AIR was the dependent variable). We also included body composition as a covariate when glucose/insulin action were dependent

variables When using linear mixed-effects modeling, results included an intercept level (i.e., Tanner stage 1) of the dependent variable, a rate of change over Tanner stages in the dependent variable, and an interaction effect of Tanner stage and GDM on the dependent variable. Data were analyzed with SPSS version 19.0 (SPSS Inc, Chicago, Illinois) with significance level set at $P < 0.05$.

RESULTS

There were 210 overweight Latino children who were measured annually for 3 ± 1 years; 22% of participants ($n=48$) were GDM offspring and 57.3% were male. Physical, adiposity and metabolic characteristics of the children, broken down by the GDM groups at baseline are shown in the Table. There was a significant main effect of GDM on birth weight, with GDM offspring being an average of 0.2 kg heavier at birth compared with non-GDM offspring ($p=0.014$). GDM offspring had a higher percentage of mothers who developed T2D after birth (59% vs. 24%; $p<0.001$). There was a significant main effect of GDM on breastfeeding status (any duration), with GDM offspring being less likely to have been breastfed compared with non-GDM (44.6% vs. 63.8%; $p=0.02$).

The following sample sizes were available at each of Tanner (T) stage, for GDM offspring: T1 ($n=22$), T2 ($n=17$), T3 ($n=17$), T4 ($n=20$), and T5 ($n=24$); and for non-GDM offspring: T1 ($n=64$), T2 ($n=79$), T3 ($n=49$), T4 ($n=76$), T5 ($n=89$). There was a significant effect of GDM status on changes in total body fat across Tanner stages, with GDM offspring having an 6.5% increase in total body fat across Tanner stages compared with a 4.3% increase in non-GDM offspring ($\beta=0.46$ vs. $\beta=0.22$; $p=0.03$), independent of sex, birth weight, breastfeeding status, total lean mass, and family history of T2D. Changes in total fat mass (expressed as kg) between GDM and non-GDM offspring across puberty are shown in Figure 1. There were no significant differences between GDM and non-GDM offspring on changes in any other adiposity measures.

Changes in SI, AIR, and DI between GDM groups are shown in Figure 2. There was a significant effect of GDM status on the slope of AIR, with GDM offspring having a 39.0% decline in AIR across Tanner compared with a 17% decline in non-GDM offspring ($\beta=-0.14$ vs. $\beta=-0.10$; $p<0.001$), independent of sex, birth weight, breastfeeding status, and family history of T2D. There was also a significant effect of GDM on slope of disposition index (DI; a measure of β -cell function), with GDM offspring having a 50.7% decline in DI across Tanner stages compared with a 35.2% decline in non-GDM offspring ($\beta=-0.01$ vs. $\beta=-0.10$; $p<0.001$), independent of sex, birth weight, breastfeeding status, and family history of T2D. These significant main effects of GDM on DI and AIR remained after controlling for baseline and changes in total body fat. There were no significant main effect of GDM on SI or any other metabolic variables.

DISCUSSION

As hypothesized, GDM offspring had greater increases in total but not regional adiposity and steeper declines in acute insulin secretion and beta-cell function across pubertal transition. Contrary to our hypothesis there were no differences at baseline (primarily early Tanner stages) in any adiposity or metabolic measures between GDM and non-GDM offspring. There were also no significant differences in insulin sensitivity or visceral adipose tissue at baseline or across puberty between GDM groups.

Previous studies have shown that GDM offspring are more obese. A large multi-ethnic cross-sectional study of 9,439 mother-child pairs found increasing hyperglycemia levels in pregnancy were associated with increased risk of obesity in their children at age 5 to 7 years.

The strongest risk factor for obesity in Pima Indian children was maternal diabetes, independent of maternal obesity and birth weight¹⁷. In a multi-ethnic retrospective cohort study of 461 children (6 to 13 years of age), maternal GDM was associated with higher BMI, larger waist circumference, higher body fat, as measured by skinfold thickness, and more subcutaneous abdominal fat, as measured by MRI, in the children¹⁸. In a smaller study of 27, primarily African American, mother-child pairs, maternal glucose concentration was positively associated with children's lean mass and fat mass, as measured by DXA, independent of children's resting energy expenditure, physical activity and energy intake¹⁹.

Few studies have examined how GDM impacts type 2 diabetes risk factors in offspring. The Diabetes in Pregnancy Study (DPS) included plasma glucose and insulin after a glucose load annually from age 1.5 years to age 16 in offspring of diabetic mothers and one time in control children (ages 10 to 16 years). This study found that offspring of diabetic mothers had a significantly higher prevalence of impaired glucose tolerance than the age- and sex-matched control group⁸. A longitudinal case-control study with 189 mother-daughter pairs, primarily Caucasian, found that GDM offspring at 15 years had a 2-fold increase in prevalence of overweight, a 40% greater risk of central adiposity, as measured by waist circumference, had higher fasting insulin and insulin resistance, as measured by HOMA-IR, and lower HDL-cholesterol²⁰. Another longitudinal cohort study in Finland on over 4,000 Caucasian adolescents, found that GDM offspring (n=95) compared with non-GDM offspring (n=3,909) were more obese, had higher waist circumferences, higher fasting insulin and were more insulin resistant at age 16. The metabolic results were attenuated after adjusting for BMI, but remained statistically significant²¹. Although the above studies were longitudinal, they all compared adiposity and metabolic variables between GDM and non-GDM offspring in a cross-sectional manner. The current study is the first to assess how GDM impacts changes in adiposity and metabolic variables across puberty, accounting for the intra- and inter-individual correlations in the adiposity and metabolic measurements over time.

Several animal studies have shown that hyperglycemia in the mother during pregnancy leads to impaired glucose tolerance and decreased insulin action and beta-cell function in the adult offspring^{26,27}. Some human studies that directly measure insulin sensitivity and secretion have shown an insulin secretory defect in adult GDM offspring^{28,29}. However, studies examining the impact of GDM on insulin action in children are limited. The cross-sectional study by Bush et al¹⁵ with 21 children (5 to 10 years of age) found that maternal glucose concentration was inversely associated with insulin sensitivity, as measured with a liquid meal tolerance test, and these effects were independent of adiposity. Maternal gestational glucose was positively associated with static beta cell, which is the beta-cell response to average above basal glucose concentrations, but not significantly associated with DI¹⁵. In contrast, in the current study, GDM status did not affect insulin sensitivity in the offspring, but was associated with steeper declines in AIR and DI function across puberty. The above results suggest that GDM initially causes declines in SI and subsequent increases in the compensatory response of beta-cells in prepubertal children, as seen in the study by Bush et al. However, as children traverse puberty, the GDM offspring appear to have increasing beta-cell deterioration and are unable to compensate appropriately in the face of increasing insulin resistance. All of the above results suggest that exposure to hyperglycemia during pregnancy may “program” the developing pancreas in a way that leads to subsequent impaired pancreatic beta-cell function.

There are several limitations of the current study to consider. GDM status was self-reported and was not confirmed with medical records. Thus, our study could not ascertain GDM severity or treatment modality (i.e., insulin versus diet only), or whether women were screened for diabetes after pregnancy. The study sample included only overweight Latino

children with a family history of type 2 diabetes and the results are not generalizable to normal weight Hispanic children and other ethnic populations. We also did not assess maternal or paternal BMI, parity, gestational weight gain, type of delivery mode, or determine the newborn size for gestational age for this study, all of which play a role in subsequent obesity and metabolic disease risk in the offspring. The sample size for GDM offspring is rather small ($n=47$); however, each subject had a minimum of two annual visits, and the average was 3 ± 1 annual visits. Other limitations are that BF was assessed retrospectively up to 13 years later and little information on breastfeeding was collected, i.e. breastfeeding status (yes/no) and duration of breastfeeding, thus exclusive BF could not be assessed.

Future research is still needed to determine if the declines in beta-cell function in this population actually leads to the progression of type 2 diabetes. Further research is also needed to determine the impact of GDM on adiposity and insulin action in offspring of normal weight Hispanic children and other ethnic groups. These results highlight the need for more interventions and public health messages to work with mothers on how to achieve better glucose control throughout pregnancy.

Acknowledgments

We would like to thank project managers Christina Ayala, MPH, and Quintilia Avila, MPA, and the SOLAR team for the facilitation of the study visits as well as the nursing staff at the GCRC. In addition, we are grateful for our study participants and their families for their involvement.

Supported by the National Institutes of Health (RO1 DK 59211) and General Clinical Research Center, National Center for Research Resources (MO1 RR 00043).

REFERENCES

1. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. *Diabetes Care*. 1998; 21(Suppl 2):B161–167. [PubMed: 9704245]
2. Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA. Maternal gestational diabetes, birth weight, and adolescent obesity. *Pediatrics*. 2003; 111(3):e221–226. [PubMed: 12612275]
3. Dabelea D, Snell-Bergeon JK, Hartsfield CL, Bischoff KJ, Hamman RF, McDuffie RS. Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort: Kaiser Permanente of Colorado GDM Screening Program. *Diabetes Care*. 2005; 28(3):579–584. [PubMed: 15735191]
4. Berkowitz GS, Lapinski RH, Wein R, Lee D. Race/ethnicity and other risk factors for gestational diabetes. *Am J Epidemiol*. 1992; 135(9):965–973. [PubMed: 1595695]
5. Ferrara A. Increasing prevalence of gestational diabetes mellitus: a public health perspective. *Diabetes Care*. 2007; 30(Suppl 2):S141–146. [PubMed: 17596462]
6. Pettitt DJ, Bennett PH, Knowler WC, Baird HR, Aleck KA. Gestational diabetes mellitus and impaired glucose tolerance during pregnancy. Long-term effects on obesity and glucose tolerance in the offspring. *Diabetes*. 1985; 34(Suppl 2):119–122. [PubMed: 3996763]
7. Pettitt DJ, Aleck KA, Baird HR, Carraher MJ, Bennett PH, Knowler WC. Congenital susceptibility to NIDDM. Role of intrauterine environment. *Diabetes*. 1988; 37(5):622–628. [PubMed: 3360218]
8. Silverman BL, Metzger BE, Cho NH, Loeb CA. Impaired glucose tolerance in adolescent offspring of diabetic mothers. Relationship to fetal hyperinsulinism. *Diabetes Care*. 1995; 18(5):611–617. [PubMed: 8585997]
9. Cruz ML, Weigensberg MJ, Huang T, Ball GDC, Shaibi GQ, Goran MI. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *J Clin Endocrinol Metab*. 2004; 89:108–113. [PubMed: 14715836]

10. Goran MI, Bergman RN, Cruz ML, Watanabe R. Insulin resistance and associated compensatory responses in African-American and Hispanic children. *Diabetes Care*. 2002; 25(12):2184–2190. [PubMed: 12453958]
11. Goran MI, Bergman RN, Avilla Q, et al. Impaired glucose tolerance and reduced beta-cell function in overweight Latino children with a positive family history of type 2 diabetes. *J Clin Endocrinol Metab*. 2004; 89(1):207–212. [PubMed: 14715851]
12. Toledo-Corral C, Ventura EE, Lane C, et al. Persistence of the metabolic syndrome and its influence on carotid intima media thickness (CIMT) in overweight Latino children. *Atherosclerosis*. 2009; 206:594–598. [PubMed: 19446812]
13. Silverman BL, Rizzo T, Green OC, et al. Long-term prospective evaluation of offspring of diabetic mothers. *Diabetes*. 1991; 40(Suppl 2):121–125. [PubMed: 1748240]
14. Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care*. 2007; 30(9):2287–2292. [PubMed: 17519427]
15. Bush NC, Chandler-Laney PC, Rouse DJ, Granger WM, Oster RA, Gower BA. Higher maternal gestational glucose concentration is associated with lower offspring insulin sensitivity and altered beta-cell function. *J Clin Endocrinol Metab*. 96(5):E803–809. [PubMed: 21346075]
16. Kelly LA, Lane CJ, Weigensberg MJ, Toledo-Corral CM, Goran MI. Pubertal changes of insulin sensitivity, acute insulin response, and beta-cell function in overweight Latino youth. *J Pediatr*. 2011; 158(3):442–446. [PubMed: 20888012]
17. Pettitt DJ, Baird HR, Aleck KA, Bennett PH, Knowler WC. Excessive obesity in offspring of Pima Indian women with diabetes during pregnancy. *N Engl J Med*. 1983; 308(5):242–245. [PubMed: 6848933]
18. Crume TL, Ogden L, West NA, et al. Association of exposure to diabetes in utero with adiposity and fat distribution in a multiethnic population of youth: the Exploring Perinatal Outcomes among Children (EPOCH) Study. *Diabetologia*. 54(1):87–92. [PubMed: 20953862]
19. Chandler-Laney PC, Bush NC, Rouse DJ, Mancuso MS, Gower BA. Maternal glucose concentration during pregnancy predicts fat and lean mass of prepubertal offspring. *Diabetes Care*. 34(3):741–745. [PubMed: 21266649]
20. Egeland GM, Meltzer SJ. Following in mother's footsteps? Mother-daughter risks for insulin resistance and cardiovascular disease 15 years after gestational diabetes. *Diabet Med*. 27(3):257–265. [PubMed: 20536487]
21. Vaarasmaki M, Pouta A, Elliot P, et al. Adolescent manifestations of metabolic syndrome among children born to women with gestational diabetes in a general-population birth cohort. *Am J Epidemiol*. 2009; 169(10):1209–1215. [PubMed: 19363101]
22. Van Assche FA, Holemans K, Aerts L. Long-term consequences for offspring of diabetes during pregnancy. *British Medical Bulletin*. 2001; 60:173–182. [PubMed: 11809625]
23. Odeleye OE, de Courten M, Pettitt DJ, Ravussin E. Fasting hyperinsulinemia is a predictor of increased body weight gain and obesity in Pima Indian children. *Diabetes*. 1997; 46(8):1341–1345. [PubMed: 9231660]
24. Jaquet D, Leger J, Levy-Marchal C, Oury JF, Czernichow P. Ontogeny of leptin in human fetuses and newborns: effect of intrauterine growth retardation on serum leptin concentrations. *J Clin Endocrinol Metab*. 1998; 83(4):1243–1246. [PubMed: 9543149]
25. Wolf HJ, Ebenbichler CF, Huter O, et al. Fetal leptin and insulin levels only correlate in large-for-gestational age infants. *Eur J Endocrinol*. 2000; 142(6):623–629. [PubMed: 10822226]
26. Gauguier D, Bihoreau MT, Ktorza A, Berthault MF, Picon L. Inheritance of diabetes mellitus as consequence of gestational hyperglycemia in rats. *Diabetes*. 1990; 39(6):734–739. [PubMed: 2189765]
27. Aerts L, Sodoyez-Goffaux F, Sodoyez JC, Malaisse WJ, Van Assche FA. The diabetic intrauterine milieu has a long-lasting effect on insulin secretion by B cells and on insulin uptake by target tissues. *Am J Obstet Gynecol*. 1988; 159(5):1287–1292. [PubMed: 3056011]
28. Gautier JF, Wilson C, Weyer C, et al. Low acute insulin secretory responses in adult offspring of people with early onset type 2 diabetes. *Diabetes*. 2001; 50(8):1828–1833. [PubMed: 11473045]

29. Sobngwi E, Boudou P, Mauvais-Jarvis F, et al. Effect of a diabetic environment in utero on predisposition to type 2 diabetes. *Lancet*. 2003; 361(9372):1861–1865. [PubMed: 12788573]

Figure 1.

Changes in total body fat mass (kg) for GDM offspring (n=47) and non-GDM offspring (n=163) across puberty. Data are presented as adjusted mean $\pm$ SEM of total body fat at each Tanner stage. There was a significant effect of GDM status on changes in total body fat across Tanner, with GDM offspring having an 6.5% increase in total body fat across Tanner compare with a 4.3% increase in non-GDM offspring across Tanner ($\beta=0.46$ vs. $\beta=0.22$; $p=0.03$).

Figures 2.

Changes in insulin sensitivity (SI), acute insulin response (AIR) and disposition index (DI) for GDM offspring (n=47) and non-GDM offspring (n=163) across puberty. Data are presented as adjusted mean $\pm$ SEM of insulin action at each Tanner stage. There was a significant effect of GDM status on the slope of AIR, with GDM offspring having a 39.0% decline in AIR across Tanner compared with a 17% decline in non-GDM offspring ($\beta = -0.14$ vs. $\beta = -0.10$; $p < 0.001$), independent of sex, birth weight, breastfeeding status, and family history of T2D. There was a significant effect of GDM status on the slope of disposition index (DI; a measure of β -cell function), with GDM offspring having a 50.7% decline in DI across Tanner compared with a 35.2% decline in non-GDM offspring ($\beta = -0.01$ vs. $\beta = -0.10$; $p < 0.001$), independent of sex, birth weight, breastfeeding status, and family history of T2D. There were no significant differences between GDM and non-GDM offspring on changes in SI.

Table 1Physical and metabolic characteristics at baseline (visit 1) between GDM categories^a

	GDM (n=47)	Non-GDM (n=163)	P-value
Male (n (%))	24 (51%)	96 (58%)	NS
Age (y)	10.9 (1.7)	11.2 (1.7)	NS
Birth weight (kg)	3.9 (0.8)	3.7 (0.6)	0.014
Family history of type 2 diabetes (%)			<0.001
Mother	58.7	24.3	
Father	6.7	2.6	
Both mother and father	10.9	20.8	
Grandparent	27.2	52.4	
Tanner			NS
1	22	64	
2	12	50	
3	3	17	
4	5	20	
5	5	15	
Breastfed (any duration (%))	44.6	63.8	0.02
Duration of breastfeeding (months)	4.7 (6.9)	5.8 (7.9)	NS
Weight (kg)	65.9 (23.1)	65.8 (18.9)	NS
Height (cm)	149.2 (12.2)	149.7 (10.9)	NS
BMI	28.8 (6.0)	28.7 (5.5)	NS
BMI percentile	97.3 (3.0)	97.3 (3.4)	NS
BMI z-score	2.2 (0.4)	2.1 (0.4)	NS
Total Fat (kg)	26.2 (12.0)	25.4 (10.1)	NS
Total Lean (kg)	37.3 (11.8)	37.4 (9.7)	NS
VAT (cm ³)	49.0 (22.0)	48.9 (22.0)	NS
SAAT (cm ³)	350.5 (151.6)	344.4 (150.3)	NS
Fasting Glucose (mg/dl)	89.9 (6.8)	89.0 (6.2)	NS
2-hour Glucose (mg/dl)	129.5 (17.2)	126.5 (18.3)	NS
Fasting Insulin (μU/ml)	15.9 (8.8)	17.2 (10.2)	NS
SI (X10 ⁻⁴ min ⁻¹ /μU/ml)	2.3 (1.4)	2.1 (1.5)	NS
AIR (μU/ml X 10 min)	1469.2 (1107.3)	1828.5 (1302.3)	NS
DI (X10 ⁻⁴ min ⁻¹)	2509.8 (1159.5)	2612.1 (1187.2)	NS

^aData are unadjusted mean (SD).