Parental History and Risk of Type 2 Diabetes in Overweight Latino Adolescents

A longitudinal analysis

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OBJECTIVE — The purpose of this article was to examine metabolic risk factors for type 2 diabetes in children and adolescents as a function of maternal versus paternal family history of type 2 diabetes and to examine whether differences in these risk factors emerge during adolescent growth.

RESEARCH DESIGN AND METHODS — A total of 247 overweight Latino children (baseline age = 11.1 ± 1.7 years) with a parental history of type 2 diabetes were followed annually for 5 years (2.2 ± 1.2 observations/child) with measures of insulin sensitivity, acute insulin response to glucose, and disposition index. Longitudinal linear mixed-effects modeling was used to evaluate the influence of maternal versus paternal family history of type 2 diabetes on changes in diabetes risk factors over age.

RESULTS — Insulin sensitivity and the disposition index decreased over age ($\beta = -0.052$ and $\beta = -0.033$, $P < 0$ 0.01). Acute insulin response to glucose and fasting and 2-h glucose increased ($\beta = 0.019$, $\beta = 0.002$, and $\beta = 0.003$, $P < 0.01$). Declines in insulin sensitivity were significantly greater in participants whose maternal grandmothers had a history of type 2 diabetes ($\beta = -0.03$, $P = 0.03$). Declines in the disposition index ($\beta = -0.02$, $P = 0.04$) and increases in fasting glucose were significantly influenced by a maternal history of type 2 diabetes ($\beta = 0.60$, $P < 0.05$).

CONCLUSIONS — Maternal but not paternal family history for diabetes may have a significant impact on insulin dynamics, becoming more pronounced during growth in overweight Latino adolescents. Further research is clearly warranted.

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The recent epidemic of obesity has been accompanied by an increase in the incidence of type 2 diabetes (1). Recent data show a dramatic increase in the incidence of type 2 diabetes in children and adolescents (2). Despite the abundance of knowledge concerning the epidemiology, pathophysiology, and medical management of type 2 diabetes in adults, little is known about the pathogenesis of the disease in adolescence or the impact of maternal versus paternal family history on future diabetes risk in children.

It is generally agreed that decreased insulin sensitivity and impaired pancreatic function are the two key components in the pathogenesis of type 2 diabetes. In children, greater adiposity and insulin resistance may be exacerbated by transient pubertal insulin resistance. We have previously shown that insulin sensitivity is lower in overweight Latino adolescents than in Caucasian children independent of adiposity (3) and that disposition index is significantly lower in Latino children with impaired glucose tolerance than in children with normal glucose tolerance (4). Impaired fasting glucose is significantly associated with impaired β-cell function in overweight Latino adolescents with a family history of type 2 diabetes (5). More recently we have shown that a decline in insulin sensitivity over time is unrelated to changes in body fat or maturation (6).

Although genetics is an important factor in the pathogenesis of type 2 diabetes, increases cannot be attributed to genetics alone. However, people with certain genetic backgrounds are particularly predisposed to type 2 diabetes, especially when they are exposed to a precipitating lifestyle.

Prior studies in adults have suggested a strong hereditary component in risk for type 2 diabetes (7–9). A family history of type 2 diabetes increases the risk of developing the disease. Moreover, the high concordance of type 2 diabetes in identical twins (10) and the aggregation of type 2 diabetes in families support the existence of genetic determinants for type 2 diabetes in families (11). The risk for developing type 2 diabetes increases when one or both parents are affected (12,13). Some studies have suggested that adult offspring whose mothers have diabetes are more likely to develop the disease themselves than are offspring whose fathers have diabetes (4,13). Recent data have shown that insulin sensitivity and the acute insulin response to glucose exhibit familial clustering, suggesting that these are inherited traits (14). Although this association has been widely explored in adults, there is a paucity of data in at-

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Abbreviations: FSIVGTT, frequently sampled intravenous glucose tolerance test; mtDNA, mitochondrial DNA; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

risk children and adolescents. Previous cross-sectional studies have not shown any evidence of an effect of family history of diabetes on insulin sensitivity in adolescents (15,16). In contrast, cross-sectional studies in adults show a significant relationship between family history and risk for type 2 diabetes.

Collectively, the aforementioned studies suggest that the increased risk of diabetes due to parental and/or family history emerges at some point during growth and development, but this concept has never been tested directly. In the present study, we used a longitudinal design to examine this hypothesis by investigating the influence of a positive parental history of type 2 diabetes on changes in risk factors during growth in overweight Latino adolescents. The aims of the present study were, therefore, to determine *1*) whether glucose/insulin dynamics linked to the pathophysiology of type 2 diabetes are different in participants with a maternal versus a paternal family history of type 2 diabetes and *2*) whether the significance of these risk factors emerged during growth. We hypothesized that insulin sensitivity and β-cell function will be lower and the prevalence of impaired glucose tolerance will be higher in those participants with a stronger maternal versus paternal family history of type 2 diabetes and that the deterioration in insulin sensitivity and β-cell function would become apparent with age.

RESEARCH DESIGN AND METHODS

Participants were recruited to participate in the Study of Latino Adolescents at Risk (SOLAR) diabetes project at the University of Southern California. This study is an ongoing longitudinal study investigating potential risk factors for the development of type 2 diabetes in at-risk youth. Data are collected for each participant annually. Findings from this cohort have been published previously (17).

Data were analyzed from 247 overweight Latino children (142 male and 105 female) recruited through clinics, word of mouth, and local newspaper and radio advertisements. Children were required to meet the following study entry inclusion criteria: *1*) age 8–13 years; *2*) BMI ≥85th percentile for age and sex according to the Centers for Disease Control and Prevention (18); *3*) Latino ancestry (all four grandparents Latino as determined by parental self-report); and *4*) absence of type 1 or type 2 diabetes using established guidelines (19). Participants were characterized as having a family history of type 2 diabetes if the parent (s) and/or grandparent (s) self-reported having the disease at baseline testing. Participants were excluded if they were taking medications known to affect body composition, had any syndromes known to affect body composition or fat distribution, or had had any major illness since birth. Written informed consent was obtained from both parents and children. The institutional review board of the University of Southern California approved this study.

Study protocol

Outpatient visit. On an annual basis, children were admitted to the General Clinical Research Centre at ~7:30 A.M. after an overnight fast. A licensed pediatric health care provider determined Tanner staging using established guidelines (20). A detailed medical history was obtained, including a parental interview detailing the family history of diabetes and gestational diabetes mellitus. A 2-h oral glucose tolerance test (OGTT) was performed using a dose of 1.75 g glucose/kg body weight (to a maximum of 75 g). Blood was sampled and assayed for glucose and insulin at −5 min (fasting state) and 120 min (2-h) relative to glucose ingestion. Blood samples taken during the OGTT were separated for plasma and immediately transported on ice to the Los Angeles County–USC Medical Center Core Laboratory where glucose was analyzed on a Dimension Clinical Chemistry system using an in vitro hexokinase method (Dade Behring, Deerfield, IL). The OGTT results were used to determine fasting and 2-h glucose levels and also as a clinical test to determine normal glucose tolerance (2-h glucose <140 mg/dl) or impaired glucose tolerance (2-h glucose ≥140 and <200 mg/dl).

Inpatient visit. Children were admitted to the General Clinical Research Center in the afternoon within ~2 weeks of completing the OGTT. Total body fat mass and total soft lean tissue mass were determined by dual-energy X-ray absorptiometry (Hologic QDR 4500W; Hologic, Bedford, MA). Children fasted overnight, with only water permitted after 10:00 P.M. An insulin-modified frequently sampled intravenous glucose tolerance test (FSIVGTT) commenced the following morning, as described previously (18). At time 0, glucose (25% dextrose, 0.3 g/kg body wt) was administered intravenously. Blood samples were collected at time points −15, −5, 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min. Insulin (0.02 unit/kg body wt, Humulin R [regular insulin for human injection]; Eli Lilly, Indianapolis, IN) was injected intravenously at 20 min. 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) to determine insulin sensitivity, acute insulin response (i.e., insulin area under the curve above basal for the first 8 min of the FSIVGTT), and disposition index (i.e., the product of insulin sensitivity × acute insulin response, an index of pancreatic β-cell function).

Blood samples from the FSIVGTT were centrifuged immediately for 10 min at 2,500 rpm and 8–10°C to obtain plasma, and aliquots were frozen at −70°C until assayed. Glucose was assayed in duplicate on a Yellow Springs Instrument 2700 analyzer (YSI, Yellow Springs, OH) using the glucose oxidase method. Insulin was assayed in duplicate using a specific human insulin ELISA kit from Linco Research (St. Charles, MO) (intra-assay coefficient of variation 4.7–7.0%, interassay coefficient of variation 9.1–11.4%, and cross-reaction with human proinsulin 0%).

Anthropometry and body composition

Height and weight were measured using a beam medical scale and wall-mounted stadiometer to the nearest 0.1 kg and 0.1 cm, respectively. BMI and BMI percentiles for age and sex were determined using EpiInfo 2000 (version 1.1; Centers for Disease Control and Prevention, Atlanta, GA). Whole body fat and soft lean tissue were measured as described above.

Statistical analysis

Variables not normally distributed (insulin sensitivity, disposition index, acute insulin response, fasting glucose, and 2-h glucose) were log-transformed before statistical analyses were performed. Linear mixed effects modeling was used to evaluate the impact of parental and or family history on longitudinal changes in glucose- and insulin-related variables over age. By modeling over age, we tested the hypothesis that there is a dynamic relationship between family history and diabetes risk factors as children progress through adolescence. The following covariates were entered into all models: Tanner stage, sex, gestational diabetes mellitus, total fat and lean tissue mass,

Table 1—*Characteristics of participants at study entry*

Characteristics	Total
n	247
Age (years)	11.1 ± 1.7
Height (m)	1.49 ± 0.1
Weight (kg)	64.3 ± 20.2
BMI (kg/m^2)	28.3 ± 5.7
BMI percentile	97.2 ± 3.0
Total body fat (kg)	25.0 ± 10.5
Total lean body mass (kg)	36.8 ± 10.2
Tanner stage (%)	
1	42
2	29
3	8
4	12
5	9
Maternal gestational diabetes	53 (22)
Family history of type 2 diabetes (%)	
Mother	40
Father	48
Maternal grandmother	49
Maternal grandfather	29
Paternal grandmother	30
Paternal grandfather	22
Insulin dynamics	
S_I ($\times 10^{-4}$ min^{-1}/[μU/ml])	1.5 (0.8–2.9)
AIR (μU/ml)	1,438.8 (745.1–2,778.4)
DI ($\times 10^{-4}$ min^{-1})	2,213.1 (1,386.1–3,533.5)
Fasting glucose (mg/dl)	92.0 (85.8–98.6)
2-h glucose (mg/dl)	124.3 (106.9–144.5)

Data are means ± SD, *n* (%), or geometric means (upper and lower limit SD). AIR, acute insulin response to glucose; DI, disposition index.

and family member's diabetes status. When using linear mixed-effects modeling, results include an intercept level (i.e., age at baseline) of the dependent variable, a rate of change over age in the dependent variable, and a measure of variation around this rate of change between insulin/glucose variables. For all models, age was centered at a mean baseline age (11.1 ± 1.7 years) for ease of interpretation of the intercept, because a zero age intercept would not be meaningful. Data were analyzed by using SPSS software (version 11.0; SPSS, Chicago, IL). For all models $\alpha = 0.05$.

RESULTS

Baseline characteristics of participants

Characteristics of the cohort at baseline are shown in Table 1. The average age at baseline was 11.1 ± 1.7 years, and our analysis included an average of 2.2 annual visits per participant and a total of 724 visits. At baseline, boys and girls were similar in all physical and insulin- and glucose-related variables, except that girls were significantly more developed in maturation than boys ($P < 0.01$).

Insulin sensitivity

The insulin sensitivity of the cohort at baseline is shown in Fig. 1*A* of the online appendix (available at http://dx.doi.org/10.2337/dc07-0050). In the covariate model, the significant covariates that predicted initial levels of insulin sensitivity were Tanner stage ($\beta = 02.56E^{-02}$; $P = 0.02$), gestational diabetes mellitus ($\beta = 6.35E^{-02}$; $P = 0.05$), fat mass ($\beta = -1.33E^{-05}$; $P < 0.001$), and lean tissue mass ($\beta = -6.80E^{-06}$; $P = 0.002$). The difference between the baseline and covariate model was significant ($\chi^2_{10} = 165.93$, $P < 0.001$) and accounted for 14.6% of the individual difference in insulin sensitivity. When family history of type 2 diabetes was entered into the model, initial levels of insulin sensitivity were predicted by a history of gestational diabetes mellitus ($P = 0.04$), total fat mass ($P < 0.01$), total lean tissue mass ($P = 0.01$), and a history of type 2 diabetes in paternal grandmothers ($P = 0.02$; lower insulin sensitivity in those with a paternal grandmother with type 2 diabetes). Paternal history of type 2 diabetes was not significant ($P > 0.05$) (Table 2 of the online appendix). The decline in insulin sensitivity over age was greater in those with a history of type 2 diabetes in maternal grandmothers ($P = 0.03$) (Table 2 and Fig. 2*A* of the online appendix). The addition of family history in the full family history model did not significantly increase the strength of the covariate model ($\chi^2_{12} = 5.29$; $P > 0.05$) and accounted for an additional 2.6% of the individual difference in insulin sensitivity. When only significant predictors were included (maternal grandmother and mother), the model ($\chi^2_4 = 6.25$; $P > 0.05$) was not a significant improvement over the covariate model and accounted for 14.4% of the individual difference in insulin sensitivity.

Acute insulin response

The acute insulin response of the cohort at baseline is shown in Fig. 1*B* of the online appendix. In the covariate model for log acute insulin response, Tanner stage ($\beta = -4.100E^{-02}$; $P < 0.001$) and log insulin sensitivity ($\beta = -0.692$; $P < 0.001$) significantly predicted initial levels of acute insulin response. The increase in log acute insulin response over age was steeper in girls ($\beta = 2.484E^{-03}$; $P = 0.04$) and increased with total lean tissue mass ($\beta = 1.716E^{-06}$; $P = 0.02$) and log insulin sensitivity ($\beta = 6.683E^{-02}$; $P < 0.01$). The covariate model was a significant improvement over the baseline model ($\chi^2_{10} = 349.8$; $P < 0.001$) and accounted for 43.2% of the individual difference in acute insulin response. When family history variables were entered into the model, initial levels of log acute insulin response were predicted by Tanner stage ($P < 0.01$), log insulin sensitivity ($P < 0.01$), and total lean tissue mass ($P < 0.01$) (Table 3 of the online appendix). The increase in log acute insulin response over age was steeper in girls ($P = 0.02$), increased with total lean tissue mass ($P = 0.01$), and decreased with log insulin sensitivity ($P < 0.01$) and a maternal history of type 2 diabetes ($P = 0.05$), suggesting that the increase over age in log acute insulin response is stronger in those whose mothers have diabetes (Fig. 1b of the online appendix). A paternal history of type 2 diabetes was not a significant predicator

of an increase in log acute insulin response over age ($P = 0.472$). The difference between the covariate model and the full family history model was not significant ($\chi^2_{12} = 13.98$; $P > 0.05$) and accounted for an additional 1.3% of the individual difference in acute insulin response. When the only significant predictor was included (mother), the model ($\chi^2_2 = 5.2$; $P > 0.05$) was not a significant improvement over the covariate model and accounted for an additional 0.3% of the individual difference in acute insulin response.

Disposition index

The disposition index of the cohort at baseline is shown in Fig. 1*C* of the online appendix. In the covariate model for log disposition index, Tanner stage ($\beta = -4.155E^{-02}$; $P < 0.001$) and total fat mass ($\beta = -5.153E^{-06}$; $P < 0.002$) significantly predicted initial levels of log disposition index. The decline in log disposition index over age was steeper in girls ($\beta = 2.324E^{-02}$; $P = 0.04$), smaller with total lean tissue mass ($\beta = 1.542E^{-06}$; $P = 0.05$), and larger with total fat mass ($\beta = -1.347E^{-06}$; $P = 0.05$). The covariate model for log disposition index was significant compared with the baseline model ($\chi^2_{10} = 46.1$, $P < 0.001$) and accounted for 12.2% of the individual differences in the disposition index. When family members were entered into the family model, initial levels of log disposition index were significantly predicted by Tanner stage ($P < 0.01$) and total mass ($P < 0.01$) (Table 4 of the online appendix). The decline in log disposition index over age was steeper in girls ($P = 0.03$), larger with total fat mass ($P = 0.02$), smaller with total lean tissue mass ($P = 0.02$), and larger with maternal history of type 2 diabetes ($P = 0.05$), suggesting that the decline over age in log disposition index is stronger in those whose mothers have diabetes (Table 4 and Fig. 2*C* of the online appendix). Paternal history of type 2 diabetes was not a significant predicator of fall in log disposition index over age ($P = 0.638$). The family history model was not a significant improvement over the covariate model ($\chi^2_{12} = 13.63$, $P = >0.05$) and accounted for an additional 2.2% of the individual differences in the disposition index. When the only significant predictor was included (mother), the model ($\chi^2_2 = 5.3$, $P > 0.05$) was not a significant improvement over the covariate model and accounted for an additional 0.5% of the individual differences in the disposition index.

Fasting glucose

The fasting glucose concentration of the cohort at baseline is shown in Fig. 1*D* of the online appendix). In the covariate model for log fasting glucose, sex ($\beta = -1.778E^{-02}$; $P < 0.001$) was the only covariate to significantly predict initial levels of log fasting glucose. The increase is fasting glucose over age was significantly higher in girls ($\beta = -5.277E^{-03}$; $P = 0.003$) and larger with higher total fat mass ($\beta = 2.727E^{-07}$; $P = 0.004$). The covariate model for fasting glucose was significant compared with the baseline model ($\chi^2_{10} = 95.3$; $P < 0.001$) and accounted for 1.0% of the individual differences in the fasting glucose. When family members were entered into the model, initial levels of fasting glucose were predicted by sex ($P < 0.001$) (Table 5 of the online appendix). The increase in fasting glucose over age was smaller in girls ($P < 0.01$), increased with total fat mass ($P = 0.002$), and was larger with maternal history of type 2 diabetes ($P = 0.05$), suggesting that the increase over age in fasting glucose was stronger in those whose mothers have diabetes (Table 5 and Fig. 2*D* of the online appendix). Paternal history of type 2 diabetes was not a significant predicator of the increase in fasting glucose over age ($P = 0.304$). The family history model was not a significant improvement compared with the covariate model ($\chi^2_{12} = 9.9$, $P > 0.05$) and accounted for an additional 1.8% of the individual differences in the fasting glucose. When only the significant predictor was included (mother), the model ($\chi^2_2 = 3.4$, $P > 0.05$) was not a significant model compared with the covariate model and accounted for an additional 1.7% of the individual differences in the fasting glucose.

2-h glucose

The 2-h fasting glucose of the cohort at baseline is shown in Fig. 1*E* of the online appendix). Although no individual covariate had statistically significant fixed effects, the covariate model for 2-h glucose was significant compared with the baseline model ($\chi^2_{10} = 62.0$, $P < 0.001$) and accounted for 1.2% of the individual differences in the 2-h glucose. When family members were entered into the family history model, 2-h glucose over age increased with a maternal grandfather's history of type 2 diabetes ($P = 0.03$), suggesting that the increase over age in 2-h glucose is stronger in those whose maternal grandfathers have diabetes (Table 6 and Fig. 2*E* of the online appendix). Maternal and paternal history of type 2 diabetes did not significantly predict increases in 2-h glucose over age ($P = 0.960$ and 0.319, respectively). The family history model was not a significant model compared with the covariate model ($\chi^2_{12} = 8.4$, $P > 0.05$) and accounted for 1.9% of the individual differences in the 2-h glucose. When the only significant predictor was included (maternal grandfather), the model ($\chi^2_2 = 3.3$, $P > 0.05$) was not a significant improvement over the covariate model and accounted for an additional 1.8% of the individual differences in the 2-h glucose.

CONCLUSIONS — In adults, a strong hereditary component in risk for type 2 diabetes is well known (7–9). The impact of family history of diabetes on insulin dynamics has been confirmed in cross-sectional studies in adults (12,21) but not in younger children (15,16), suggesting that the emergence of risk occurs at some point during growth and development. It is not clear whether there is any differential risk in the transmission of type 2 diabetes between mothers or fathers with a positive family history of diabetes. To address these issues, we used a longitudinal dataset to investigate the influence of family history of diabetes on insulin dynamics in overweight Latino adolescents. Our major observations included a decline in insulin sensitivity and β-cell function during pubertal growth, which was influenced by a maternal family history of type 2 diabetes, and these effects became stronger as children got older.

In contrast with cross-sectional studies examining the impact of family history of type 2 diabetes (15,16), the key finding of the present longitudinal study is that a decline in insulin sensitivity (maternal grandmother) and β-cell function (mother) during early adolescence in overweight Latino youth is influenced specifically by a family history of type 2 diabetes on the maternal side. Thus, the declines in insulin sensitivity and β-cell function and the increase in fasting and 2-h glucose levels were independent of body composition or gestational diabetes mellitus and were more pronounced in those subjects with a maternal family history of type 2 diabetes. Although the relationship between maternal family

history and acute insulin response is opposite to that of insulin sensitivity and disposition index; i.e., with a positive maternal family history, we see an increase in acute insulin response. The fact that disposition index continues to deteriorate indicates that this acute insulin response is likely to be inadequate for the degree of ongoing deterioration in insulin sensitivity. This inadequacy would lead to a decrease in disposition index relative to insulin sensitivity conveyed by maternal family history. In adults, the progression of insulin resistance and the subsequent inability of the β-cell to adequately compensate through an increase in secretion (22) is the basis for the development of type 2 diabetes. In children, this pathogenesis is likely to be similar but is exacerbated by transient insulin resistance that occurs during puberty (23,24) and may further contribute to β-cell demand. Our results suggest that maternal history of type 2 diabetes may hold further pathophysiological relevance in the offspring. This suggestion is further supported by the finding of increasing fasting glucose levels over time in children with a positive maternal history of diabetes.

The findings of the present study are consistent with adult studies of transmission of type 2 diabetes. Evidence is increasing that offspring whose mothers had diabetes are more likely to develop diabetes themselves compared with offspring whose fathers had diabetes (12,21). Several adult studies have examined the role of parental transmission of type 2 diabetes and have consistently shown an effect of maternal diabetes (23). These findings are limited by the fact that many of the fathers may have undetected diabetes because of reduced screening rates and poor health care provision and utilization or may develop type 2 diabetes at an older age than mothers (25). It may be possible that the reported association between maternal history and insulin/glucose dynamics in their offspring may be attributed to the environment in which the child has been raised. We were unable to compare our findings that a history of type 2 diabetes in maternal grandmothers predicts a fall in insulin sensitivity over age as, to our knowledge, no other longitudinal study has investigated this possible relationship. However, these findings do offer further evidence of maternal transmission of type 2 diabetes. Furthermore, in line with prior evidence suggesting that prenatal exposure to a diabetic intrauterine environment leads to an increased risk of development of diabetes in later life (26), our study shows initial levels of insulin sensitivity to be lower in offspring with a maternal history of gestational diabetes mellitus.

Assuming that maternal influences are important in the transmission of type 2 diabetes, several possible genetic mechanisms have been suggested. These include the role of mitochondrial DNA (mtDNA) (27), gene imprinting, and the effect of maternally determined environments (e.g., intrauterine influences). Although several mutations have been implicated, the strongest evidence suggests a point substitution at nucleotide position 3,243 (A to G) in the mitochondrial tRNA $^{leu(UUR)}$ gene (27). Apart from severe, pathogenic mtDNA mutations, common polymorphisms in mtDNA may contribute to variations of insulin secretory capacity in normal individuals. Although mitochondrial diabetes may account for <1% of all diabetes, the exact mechanism whereby a mother's history of type 2 diabetes imparts increase risk of β-cell dysfunction and diabetes risk in her offspring remains to be determined.

Compared with earlier studies (12,21,23), the present study is unique in several aspects, thereby significantly expanding knowledge of the effects of family history on the development of type 2 diabetes. First, the longitudinal design of the present study allows us to examine the dynamic influence of family history on glucose and insulin variables over age. Second, the minimal model method is applied to the FSIVGTT, which is recognized as a gold standard technique to assess peripheral insulin resistance as a measure of insulin dynamics (28).

A study limitations is the use of parental self-report for diabetes status of the parents and grandparents, thus including those with potentially undiagnosed conditions. Negative parental history may be underestimated, as many parents may not recognize that they have diabetes or they may be still too young to manifest the disease clinically. However, this situation would most likely result in an underestimation of the strength of the association between parental diabetes and risk variables in the offspring during adolescence and adulthood. This underestimation is most likely on the paternal side, as women are more likely to seek medical care and have their diabetes diagnosed. In addition, because mothers most often completed the family history of diabetes form, they may not know the status of their in-laws, again creating a bias toward underreporting and an underestimation of paternal effects. Furthermore, dietary and physical activity data that may have provided more insight into the environment in which these at-risk children are being raised are lacking. The cumulative exposure time to a sedentary lifestyle and hypercaloric diets may have an impact on these at risk for type 2 diabetes children.

In summary, this longitudinal study provides new evidence that a positive maternal family history in a cohort of overweight Latino adolescents may be related to the deterioration of insulin sensitivity, β-cell function, and levels of glycemia in a cohort of overweight Latino adolescents and, therefore, might be considered as a risk factor for the future development of the type 2 diabetes over time. Further research is clearly warranted to elucidate the mechanisms underlying the transmission of type 2 diabetes risks in this and other at-risk populations.

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