Insulin resistance and impaired glucose tolerance in overweight and obese Costa Rican schoolchildren

Ileana Holst-Schumacher, Hilda Nuñez-Rivas, Rafael Monge-Rojas, and Mauro Barrantes-Santamaría

Abstract

Background. *Worldwide obesity has become an unprecedented public health challenge. In addition, a notable increase in the risk of insulin resistance and type 2 diabetes mellitus has emerged. In Costa Rica, there are no epidemiological data to establish the prevalence of type 2 diabetes in the pediatric population. However, information from the Endocrinology Department of the Children's National Hospital indicates an increased number of cases in the last 2 to 3 years.*

Objective. *To determine the prevalence of insulin resistance and impaired glucose tolerance in overweight and obese schoolchildren.*

Methods. *This cross-sectional study was conducted among 214 healthy 8- to 10-year-old children from urban schools of San José, Costa Rica. Anthropometric measurements and blood determinations of glucose, insulin, proinsulin, glycosylated hemoglobin, C-peptide, and leptin were performed. Indexes were calculated to assess insulin resistance. Information on social and lifestyle variables was obtained from questionnaires, and acanthosis nigricans was certified by a physician. Statistical analysis was performed with SPSS software for Windows, version 10.0.*

Results. *The prevalence of type 2 diabetes mellitus was very low (0.5%) in the studied population. However, hyperinsulinemia and impaired glucose tolerance were present in 20.6% and 6.5% of the subjects, respectively. On the basis of the Fasting Glucose-to-Insulin Resistance Ratio (FGIR), 46.7% of the children showed insulin resistance. Girls and obese children (body mass index ≥ 95th percentile) were more likely to have higher serum insulin levels and insulin resistance than boys and overweight children (BMI ≥ 85th percentile). Compared with the lowest quintile, children in the highest quintile of body-fat tissue had higher insulin resistance but had similar serum concentrations of glucose, C-peptide, and proinsulin. Positive family histories of type 2 diabetes mellitus and sedentarism (73.7% and 40.7%, respectively) were highly prevalent among overweight and obese children.*

Conclusions. *The prevalence of impaired glucose tolerance and insulin resistance in obese children indicates a worrisome trend in the incidence of type 2 diabetes in Costa Rica. Strategies for weight reduction, obesity prevention, and promotion of healthy lifestyles are necessary to prevent the onset of type 2 diabetes during childhood and adolescence.*

Key words: Childhood obesity, diabetes mellitus type 2, FGIR, HOMA-IR, hyperinsulinemia, impaired glucose tolerance, insulin resistance, QUICKI

Introduction

For several developed [1] and underdeveloped [2] countries, obesity represents an unprecedented public health challenge whose magnitude has been underestimated. In addition to the worldwide epidemic of obesity, a notable increase in the risk of insulin resistance and type 2 diabetes has emerged [3].

Type 2 diabetes mellitus, once considered an adult-onset disease, is now a worrisome and significant public health problem among young people. During the past decade, the incidence of type 2 diabetes mellitus in children has increased dramatically in countries such as Japan, New Zealand, Australia, Canada, Libya, Bangladesh, and the United States, among others

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[4-8]. Obesity and other lifestyle risk factors, such as unhealthy eating habits and physical inactivity, have been strongly associated with a higher predisposition for type 2 diabetes mellitus during childhood.

Because glucose homeostasis is maintained by the balance between insulin sensitivity and secretion, decreased insulin sensitivity and impaired pancreatic beta-cell function are considered the two main components in the pathogenesis of type 2 diabetes mellitus [7]. Therefore, the assessment of these physiological parameters is a key element in the evaluation and follow-up of children with obesity and risk factors for type 2 diabetes mellitus.

The diversity of clinical manifestations and the lack of pediatric information available to physicians make it difficult to diagnose type 2 diabetes mellitus in children [9]. However, current evidence shows that fasting insulin and glucose levels could be used to estimate valuable indicators of insulin resistance and pancreatic beta-cell function in nondiabetic children. Indexes such as the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), the Quantitative Insulin Sensitivity Check Index (QUICKI), and the Fasting Glucose-to-Insulin Resistance Ratio (FGIR) have been identified as valid tools for estimating insulin resistance in prepubertal obese children [9-11].

In Costa Rica, there are no epidemiological data to establish the prevalence of type 2 diabetes mellitus in the pediatric population. However, data from the Endocrinology Department of the Children's National Hospital indicate an increased number of cases in the last 2 to 3 years.

Overweight and obesity are highly prevalent in Costa Rican children, with rates of 34.5% and 26.2%, respectively, and according to the Institute for Research and Education on Nutrition and Health (INCIENSA), 29.1% of these obese children are at high risk for central fat distribution [12]. This is particularly important, because some evidence shows that abdominal obesity increases the risk of developing insulin resistance and metabolic syndrome (hyperinsulinemia, dyslipidemia, glucose intolerance, and hypertension), a condition that links obesity with cardiovascular disease [13]. However, the progression from impaired glucose tolerance to diabetes can be delayed or prevented by promoting healthy lifestyles [7]. This study determined the prevalence of insulin resistance and impaired glucose tolerance in 8- to 10-year-old overweight and obese schoolchildren.

Materials and methods

Study sample

The study sample included Hispanic male and female children aged 8 to 10 years of Mestizo background (triethnic heritage resulting from the blending of Spanish, indigenous peoples, and Africans). They were recruited among 2nd-, 3rd-, and 4th- grade students from six urban schools in the city of San José, Costa Rica. The schools were selected with probability proportional to size from a list of urban schools in the study area. A research team member encouraged at least two classes in each grade level to participate in the study. Consent forms were distributed in the classrooms, and children were asked to return them with parental signatures. Of 420 schoolchildren who returned signed consent forms, 214 fulfilled all the inclusion criteria. To be included in the study, boys and girls had to be of Costa Rican nationality, prepubertal, and with a body mass index (BMI) at or above the 85th percentile for age and sex according to the World Health Organization (WHO) guidelines [14].

Anthropometric variables

Anthropometric measurements were performed by professional investigators using the procedures recommended by Lohman et al. [15]. A standard Harpenden stadiometer and a portable Tanita scale were used to measure height, weight, and body composition. Weight was measured to the nearest 0.1 kg with the child not wearing shoes or heavy outer clothing. Height was measured to the nearest 0.1 cm with the child barefoot and standing upright on a platform with eyes on the Frankfort plane. To assess nutritional status, the BMI was calculated as the weight in kilograms divided by the square of the height in meters. Children with BMI at or above the age- and sex-specific 85th percentile were considered overweight, and those with BMI at or above the 95th percentile were considered obese. In the absence of other data specifying optimum cutoff values for BMI in children, the BMI values according to age for US children were used, as recommended by the WHO Expert Committee [14].

Body composition was established with leg-to-leg bioimpedance equipment (model TBF-401, Tanita Corporation). Children were asked to wear the school uniform of cotton shirt and pants only, empty their bladders, remove all metallic objects (rings, necklaces, earrings and coins), and stand barefoot on the machine. Sex and height details were entered manually into the system on a keyboard. The percentage of body fat, estimated by using the standard built-in prediction equations for children, was displayed on the machine and printed out.

Biochemical variables

For the assessment of biochemical variables, each child provided a blood sample after 8 to 12 hours of fasting. Blood was drawn by antecubital venipuncture according to Clinical and Laboratory Standards Institute procedures [16]. Samples were collected both into

plain Vacutainer tubes (Becton-Dickinson) for serum analyses and into EDTA-containing tubes for determination of glycosylated hemoglobin (HbA_{1c}). Serum was obtained by centrifugation at 6,000 rpm for 5 minutes at 25°C, and removal from the red cell pack was done within 30 minutes after venipuncture. The samples were stored at –20°C until biochemical tests were performed. HbA_{1c} analyses were carried out the same day the blood was extracted with a Hitachi automated chemistry analyzer, model 911 (Roche Company, Roche-Diagnostics Division). Glucose was determined by enzymatic colorimetric reactions using the same analyzer (intra-assay coefficient of variation, 1.7%). Insulin was determined by immunoassay methods in a fully automated IM_X System (Abbott Laboratories, Diagnostics Division Dainabot) (intra-assay coefficient of variation, 8%). Proinsulin and C-peptide were determined by enzyme-linked immunoassays (IBL-Hamburg). Human leptin was also quantified with the use of a commercial enzyme-linked immunosorbent kit (Diagnostics Systems Laboratories). The following indexes were calculated to assess insulin resistance: HOMA-IR (fasting insulin [mIU/L] × fasting glucose [mmol/L]/22.5), QUICKI (1/log fasting insulin [mIU/L] + log fasting glucose [mg/dL]), and FGIR (fasting glucose [mg/dL]/fasting insulin [mIU/L]) [11, 17, 18]. Insulin resistance in children was established when FGIR < 7 [11, 19], HOMA-IR > 5.4 [20], and QUICKI < 0.300 [20].

According to the American Diabetes Association guidelines, impaired glucose tolerance was defined as a fasting serum glucose level ≥ 5.55 mmol/L and < 6.99 mmol/L, whereas diabetes mellitus was defined as a fasting serum glucose level ≥ 6.99 mmol/L [21]. Fasting hyperinsulinemia was defined as a serum insulin level > 20 mIU/L [20], and hyperproinsulinemia as a serum proinsulin level ≥ 9.4 pmol/

Social, clinical, and lifestyle variables

The children's parents or guardians were sent a questionnaire that included information about sociodemographic variables: child's age and sex, consumption of services such as cable TV and Internet, and possession of household amenities such as hot water system, microwave oven, washing machine, VHS or DVD, computer, double vertical door refrigerator, and vehicle. Ownership of these goods was used to determine an indicator of socioeconomic status according to the method described by Madrigal [22].

The questionnaire asked if the child's parents, siblings, mother, or father had received a diagnosis of type 2 diabetes from a physician. The answers were used to establish a history of diabetes in the child or the family.

Physical activity was assessed by a validated questionnaire administered by four trained interviewers [23], and a score was obtained based on the child's physical activities at school, at home, and during leisure time. Scores ranged from 0 to 48. Children who scored 30 or less were considered sedentary. The presence of acanthosis nigricans (thickening and increased pigmentation of the skin in areas with increased mechanical exposure) was certified by a physician by direct examination of each child's neck and flexion areas.

Data analysis

The analysis was performed with SPSS Software for Windows, version 10.0. The normality of parameters was assessed by the Kolmogorov–Smirnov test. Those values exceeding the mean by ± 3SD were eliminated as outliers. Data are presented as means ± SD. Differences in means of continuous variables between overweight and obese groups of children were examined by Student's *t*-test for independent samples. Nonparametric statistics were applied to analyze data with a skewed distribution. Because most variables violated the statistical assumption of normality, a Spearman correlation was used. To detect whether mean serum levels of biochemical variables and resistance indexes varied across the quintiles of body fat percentage, parametric tests for unpaired data (one-way ANOVA) were used. A value of $p < .05$ was considered to indicate statistical significance.

Ethical approval

The ethics committees of the University of Costa Rica and INCIENSA approved all procedures followed in the study, and we certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. In order for a child to participate, an informed consent form, which included permission for the children to be screened for acanthosis nigricans and blood extraction, had to be signed by the parents or guardians of the child and a witness. Participation was voluntary, and the informed assent of each child was also required. The children participating in the study were compensated only with a report of their anthropometric and biochemical evaluation.

Results

The study sample consisted of 110 boys and 104 girls with a mean age of 9.14 ± 0.80 years; 38% of the children were overweight, and 62% were obese. **Table 1** shows the demographic, clinical, and anthropometric characteristics of the study population. Overall, obese and overweight children had a similar prevalence of positive family history of type 2 diabetes mellitus and sedentarism (74.4% and 72.5%, respectively). However,

TABLE 1. Demographic, clinical, and anthropometric characteristics of the study population[a]

Characteristic	Overweight children (n = 81)	Obese children (n = 133)	p^b	Total (n = 214)
Age (yr)	9.22 ± 0.79	9.10 ± 0.81	.823	9.14 ± 0.80
Sex (%)				
Male	50.6	51.9	.965	51.4
Female	49.4	48.1	.965	48.6
Socioeconomic status (%)				
Low	22.2	29.3	.327	26.6
Middle	40.7	45.1	.626	43.5
High	37.0	25.6	.107	29.9
Type of school (%)				
Public	70.4	84.2	.026	79.0
Private	29.6	15.8	.026	21.0
Sedentarism (%)	39.5	41.4	.896	40.7
Positive family history of type 2 diabetes (%)	72.5	74.4	.884	73.7
Acanthosis nigricans (%)	6.2	33.1	< .001	22.9
Weight (kg)	38.6 ± 5.2	46.3 ± 8.5	.006	43.4 ± 8.3
Height (m)	1.37 ± 0.07	1.40 ± 0.27	.390	1.39 ± 0.22
Body mass index	20.46 ± 1.07	23.98 ±3.40	< .001	22.65 ± 3.24
Body composition				
Fat (%)	28.7 ± 4.8	36.6 ± 6.7	.093	33.6 ± 7.2
Fat mass (kg)	10.9 ± 2.7	16.8 ± 6.0	< .001	14.6 ± 5.8
Lean mass (kg)	26.6 ± 3.9	28.2 ± 4.2	.006	27.6 ± 4.2

a. Plus–minus values are means ± SD.
b. Student's *t*-test.

a greater proportion of girls were sedentary than boys (59.8% vs. 40.0%, p = .018).

There were no statistically significant differences in the prevalence of acanthosis nigricans by age or sex. The prevalence of acanthosis nigricans was higher in obese children (33.1%) than in overweight children (6.2%). In the overall obese group (boys and girls combined) with acanthosis (n = 44), 38.6% presented with hyperinsulinemia (data not shown).

The mean values of glucose, C-peptide, insulin, glycosylated hemoglobin, leptin, and proinsulin were 4.9 ± 0.5 mmol/L, 0.8 ± 0.4 nmol/L, 86.1 ± 55.5 pmol/L, 5.7 ± 0.4%, 31.8 ± 17.6 pg/L, and 5.5 ± 9.5 pmol/L, respectively (**table 2**).

TABLE 2. Fasting biochemical measurements and insulin resistance indexes in Costa Rican prepubertal overweight and obese schoolchildren

	Overweight children (n = 81)		Obese children (n = 133)			Total (n = 214)	
Variable	Mean ± SD	Range	Mean ± SD	Range	p^a	Mean ± SD	Range
Glucose (mmol/L)	4.81 ± 0.52	3.00–5.94	5.03 ± 0.45	4.00–7.16	.484	4.94 ± 0.49	3.00–7.16
C-peptide (nmol/L)	0.72 ± 0.42	0.03–1.99	0.90 ± 0.48	0.03–1.49	.003	0.79 ± 0.45	0.03–1.99
Insulin (pmol/L)	70.46 ± 43.79	23.40–346.8	95.81 ± 59.79	8.40–462.00	.007	86.08 ± 55.49	8.40–462.00
Glycosylated hemoglobin (%)	5.5 ± 0.3	4.9–6.7	5.8 ± 0.5	4.9–7.2	.006	5.7 ± 0.4	4.9–7.2
Leptin (pg/L)	24.9 ± 10.9	5.2–53.9	34.4 ± 18.8	4.8–108.9	< .001	31.8 ± 17.59	4.8–108.9
Proinsulin (pmol/L)	5.5 ± 10.6	0.1–66.0	5.6 ± 9.1	0.2–66.0	.942	5.5 ± 9.5	0.1–66.0
HOMA-IR	2.5 ± 1.4	0.8–9.3	3.6 ± 2.3	0.3–18.6	.003	3.2 ± 2.1	0.3–18.6
QUICKI	0.341 ± 0.025	0.120–0.170	0.326 ± 0.029	0.110–0.210	< .001	0.332 ± 0.029	0.110–0.210
FGIR	9.2 ± 4.2	1.1–23.9	8.1 ± 7.3	1.3–66.4	.218	8.5 ± 6.3	1.1–66.4

HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; QUICKI, Quantitative Insulin Sensitivity Check Index; FGIR, Fasting Glucose-to-Insulin Resistance Ratio
a. Mann–Whitney test.

TABLE 3. Prevalence (%) of abnormalities in glucose metabolism in Costa Rican prepubertal overweight and obese schoolchildren

Abnormality	Overweight children (n = 81)	Obese children (n = 133)	p^a	Total (n = 214)
Diabetes mellitus	0 (0)	1 (0.5)	< .001	1 (0.5)
Impaired glucose tolerance	3 (1.4)	11 (5.1)	< .001	14 (6.5)
Insulin resistance				
HOMA-IR	4 (1.9)	19 (8.8)	< .001	23 (10.7)
QUICKI	4 (1.9)	21 (9.8)	< .001	25 (11.7)
FGIR	23 (10.8)	77 (35.9)	< .001	100 (46.7)
Hyperinsulinemia	6 (2.8)	38 (17.8)	< .001	44 (20.6)
Hyperproinsulinemia	6 (2.8)	18 (8.4)	< .001	24 (11.2)

HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; QUICKI, Quantitative Insulin Sensitivity Check Index; FGIR, Fasting Glucose-to-Insulin Resistance Ratio
a. Student's *t*-test.

On average, obese children had significantly higher mean serum concentrations of insulin, C-peptide, glycosylated hemoglobin, and leptin than overweight children, but both groups had similar serum proinsulin and glucose levels. Girls were more likely to have high serum insulin levels than boys (96.32 ± 62.71 vs. 76.31 ± 45.80 pmol/L, p = .048). Similarly, insulin resistance as estimated directly by HOMA-IR and inversely by FGIR and QUICKI was higher in girls than in boys: 3.5 ± 2.4 vs. 2.8 ± 1.7 (p = .014) by HOMA-IR, 7.4 ± 4.9 vs. 9.6 ± 7.3 (p = .011) by FGIR, and 0.327 ± 0.027 vs. 0.336 ± 0.029 (p = .020) by QUICKI (data not shown).

Obese children were more likely to present with higher HOMA-IR indexes (3.6 ± 2.3 vs. 2.5 ± 1.4, p = .003) and lower QUICKI values (0.326 ± 0.029 vs. 0.341 ± 0.025, p < .001) than overweight children. FGIR values were similar among overweight and obese children.

On the basis of fasting serum glucose levels, the prevalence of type 2 diabetes mellitus was very low (0.5%) in the studied population (**table 3**). However, 20.6% of the schoolchildren had hyperinsulinemia and 6.5% had impaired glucose tolerance. In addition, on the basis of the FGIR index, 46.7% of the children had insulin resistance.

Overall, the prevalence rates of type 2 diabetes mellitus, impaired glucose tolerance, hyperinsulinemia, hyperproinsulinemia, and insulin resistance assessed by FGIR values were higher in obese than in overweight children (p < .001).

Table 4 shows the mean values of insulin, leptin, glycosylated hemoglobin, and HOMA-IR indexes according to quintile of body fat percentage. The mean HOMA-IR and insulin concentrations among children in the first quintile of body fat percentage are about half those among children in the last quintile ($HOMA\text{-}IR_{Q1}$ = 2.0 ± 0.8, $HOMA\text{-}IR_{Q5}$ = 4.1 ± 2.1; p < .001; $insulin_{Q1}$ = 56.07 ± 22.11, $insulin_{Q5}$ = 108.35 ± 51.69; p < .001); the serum levels of leptin among children in the first quintile of body fat percentage are about one-third of

TABLE 4. Mean ± SD biochemical values and insulin resistance indexes according to quintile of body fat percentage in Costa Rican prepubertal overweight and obese schoolchildren

Variable	Quintile of body fat (%)					p^a
	Q1 (lowest–27.8) (n = 42)	Q2 (27.9–31.8) (n = 45)	Q3 (31.9–34.5) (n = 42)	Q4 (34.6–38.3) (n = 44)	Q5 (38.4–highest) (n = 41)	
Glucose (mmol/L)	4.80 ± 0.43	5.02 ± 0.46	4.89 ± 0.60	4.91 ± 0.39	5.09 ± 0.51	.060
Insulin (pmol/L)	56.07 ± 22.11	79.28 ± 56.00	88.73 ± 39.75	99.03 ± 77.07	108.35 ± 51.69	< .001
C-peptide (nmol/L)	0.90 ± 0.49	0.76 ± 0.43	0.89 ± 0.51	0.69 ± 0.42	0.73 ± 0.39	.131
Proinsulin (pmol/L)	7.50 ± 18.14	4.55 ± 4.89	6.42 ± 12.35	4.05 ± 3.79	6.02 ± 6.14	.579
Leptin (pg/L)	17.01 ± 8.32	24.55 ± 11.12	28.02 ± 9.19	32.37 ± 13.37	49.24 ± 21.64	< .001
Glycosylated hemoglobin (%)	5.44 ± 0.42	5.68 ± 0.44	5.63 ± 0.40	5.71 ± 0.36	5.87 ± 0.46	< .001
HOMA-IR	2.0 ± 0.8	2.9 ± 1.7	3.3 ± 1.6	3.6 ± 3.0	4.1 ± 2.1	< .001
QUICKI	0.349 ± 0.021	0.338 ± 0.036	0.327 ± 0.022	0.326 ± 0.025	0.318 ± 0.024	< .001
FGIR	10.7 ± 4.3	11.0 ± 10.1	7.0 ± 2.8	7.3 ± 3.9	6.5 ± 3.7	.001

HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; QUICKI, Quantitative Insulin Sensitivity Check Index; FGIR, Fasting Glucose-to-Insulin Resistance Ratio
a. One-way ANOVA.

those among children in the last quintile ($leptin_{Q1}$ = 17.01 ± 8.32, $leptin_{Q5}$ = 49.24 ± 21.64; $p < .001$).

The mean values of FGIR and QUICKI decreased significantly as the percentage of body fat increased ($p = .001$). In contrast, the mean serum concentrations of glucose, C-peptide, and proinsulin did not change significantly as the percentage of body fat increased.

Spearman correlations among biochemical and medical variables and body composition show that insulin had a strong positive correlation with HOMA-IR values ($r = 0.982$) and a strong negative correlation with QUICKI ($r = -0.982$) and FGIR ($r = -0.977$) values. Acanthosis nigricans showed a mild correlation with BMI ($r = 0.448$), body fat percentage ($r = 0.411$), and fat mass ($r = 0.412$) and a weak correlation with serum insulin levels ($r = 0.178$). BMI had a mild negative correlation with FGIR values ($r = -0.302$). Strong correlations were observed between serum leptin concentrations and body fat and fat mass ($r = 0.611$ and $r = 0.602$, respectively; data not shown).

Discussion

To our knowledge, this is the first survey to study the prevalence of insulin resistance and impaired glucose tolerance in a group of healthy, prepubertal, overweight and obese Latin American schoolchildren. We found that, compared with other countries such as Japan, New Zealand, Australia, Canada, Libya, Bangladesh, and the United States [4–8], the prevalence of type 2 diabetes mellitus among overweight and obese Costa Rican schoolchildren was quite low (0.5%) and was similar to values reported in several European countries [7, 24-26].

The frequency of insulin resistance reported in this study (46.7%) was slightly lower than that reported for obese American adolescents (52.1%) [27].This finding is worrisome, given the high prevalence of type 2 diabetes among US adults [28]. Insulin resistance precedes an earlier onset of type 2 diabetes. Increased insulin resistance in peripheral tissues has been shown to be an early manifestation in the development of type 2 diabetes mellitus, followed by compensatory hyperinsulinemia [7]. Later, pancreatic beta-cell function collapses, and impaired glucose tolerance finally appears.

Reported cases of type 2 diabetes in children show that puberty is the peak age for diagnosis [29, 30]. For most, the mean age is in early adolescence between 12 and 14 years [30], even though we reported one case of type 2 diabetes in a prepubertal obese child.

Given the high frequency of insulin resistance in the study population, lifestyle modifications are urgent to prevent the development of type 2 diabetes during the pubertal process. The insulin resistance present in prepubertal overweight and obese children, in addition to the temporary increase in insulin resistance that occurs during puberty [31, 32], may considerably elevate the risk of developing type 2 diabetes. Factors that are most likely to contribute to this increase in insulin resistance are the sex steroids produced at puberty [33] and the 25% to 30% reduction in insulin sensitivity that peaks by Tanner maturation stage 3 [29, 31].

The early onset age of type 2 diabetes in children and adolescents may particularly increase the risk of microvascular complications, which are known to be directly related to the duration of diabetes and hyperglycemia [7]. For many children and adolescents, the progression of obesity-related insulin resistance could mean conditions such as hypertension, atherogenic serum lipid profile, premature cardiovascular disease, and emotional and behavioral disorders, particularly depression and eating upsets [34, 35].

The importance of measuring insulin resistance in obese populations has been highlighted recently. Several studies [33, 36], including ours, have shown that serum glucose concentrations do not change significantly as body fat percentage increases. However, some studies [37, 38], but not all [39–41], have linked body fat distribution, specifically abdominal obesity, to a higher risk of insulin resistance in children, whereas others point out that the association between insulin resistance and body fat is related to ethnicity [39–41]. Therefore, further research is needed to investigate the use of body composition as an early indicator of insulin resistance in Costa Rican children.

Simple estimates or indexes of insulin resistance using fasting insulin and glucose levels have been developed as surrogates for the gold standard methods of measuring insulin resistance (isoglycemic glucose clamp and simplified minimal model method). In our study, the highest proportion of children with insulin resistance was identified with the use of the FGIR index (46.7%).

Several validation studies [10, 11, 19, 42, 43], but not all [44], demonstrate that FGIR is a highly specific measure of insulin sensitivity among prepubertal obese children. However, the results of the validation studies of estimates of insulin sensitivity among obese children and adolescents are controversial. Some studies using different mathematical analyses find that QUICKI has a higher discrimination power than HOMA-IR [45], whereas others conclude that HOMA-IR and QUICKI have similar sensitivity and specificity [46]. In contrast, others indicate that HOMA-IR is more reliable than FGIR and QUICKI for the evaluation of insulin resistance in children and adolescents [44], whereas others find that these indexes are not accurate predictors of insulin resistance during adolescence [47].

There is insufficient information regarding the comparison of measured insulin sensitivity with estimates of insulin sensitivity, especially in prepubertal obese children. However, our study suggests that FGIR could be a valuable tool for assessing insulin resistance in prepubertal overweight and obese children of Mestizo

background. Studies in several ethnic groups have demonstrated an association between ethnic differences in insulin resistance and body fat during childhood [39-41]. Therefore, further surveys are needed to assess the predictive value of FGIR in the Costa Rican pediatric population.

Our results are in agreement with previous studies [39–42] that demonstrate that the degree of adiposity is one of the most important risk factors for insulin resistance. Current research shows that insulin resistance, as estimated by HOMA-IR, QUICKI, or FGIR, increases significantly as the percentage of body fat increases, as does leptin concentration. Serum leptin concentration is independently associated with the development of insulin resistance [48].

It is important to point out that several studies have demonstrated that adiposity is a better clinical predictor than acanthosis nigricans of insulin resistance in Hispanic children [7, 49–51]. Moreover, Hirschler et al. [52] recently determined that abdominal obesity is more closely related to cardiovascular risk factors than general obesity. Central adiposity has been associated during puberty with high triglyceride levels, low high-density lipoprotein (HDL) cholesterol concentrations, and insulin resistance [53]. Therefore, waist circumference could be used as a tool to identify overweight and obese children at risk for developing metabolic or cardiovascular complications.

We found acanthosis nigricans in approximately 30% of the obese children; nevertheless, a number of studies have indicated that obese children without acanthosis nigricans should not be presumed to have normal insulin sensitivity [49-51]. Therefore, our findings highlight the need to encourage weight reduction and obesity control in the pediatric population as measures to improve insulin sensitivity and prevent the future burden of type 2 diabetes in Costa Rican children.

The high prevalence of a positive family history of type 2 diabetes evidenced in our study population is particularly troublesome. Several studies show that a family history of type 2 diabetes is associated with approximately 25% less insulin sensitivity and an inadequate compensation in insulin secretion in prepubertal healthy children [4, 7, 32]. Environmental factors, such as obesity and a sedentary lifestyle, added to the familial phenotype of an impaired balance between insulin secretion and insulin resistance may lead to the premature onset of type 2 diabetes. Slinger et al. [48] reported that the influence of a family history of diabetes or insulin resistance is shown as a trend in 7- and 8-year-old children. Moreover, the American Diabetes Association has highlighted the fact that the Hispanic population has a twofold greater risk of acquiring type 2 diabetes than other populations [30].

The high prevalence of insulin resistance in girls is also worrisome, because type 2 diabetes has a sex-related effect. Girls have a higher basal insulin level, which increases with age, and a physiological insulin resistance period occurs during Tanner 3 and 4 puberty maturation stages [54]. Moreover, in most ethnic groups, the female-to-male incidence ratio of type 2 diabetes is 1.7:1 [31]. The National Heart, Lung, and Blood Institute Growth and Health Study [55] recently established that girls who are overweight during childhood are 11 to 30 times more likely to be obese in young adulthood. In addition, the girls in our study had a sedentary lifestyle; thus, increasing physical activity should be a key goal to decrease the risk of type 2 diabetes in this group. Krekoukia et al. [56] recently stated that total and central adiposity are positively associated and physical activity is negatively associated with insulin resistance in children, and that interventions to improve glucose metabolism in youth should target reducing total body and abdominal fat and increasing physical activity. Physical activity improves insulin sensitivity, reduces body weight, modifies body composition, and improves cardiovascular fitness [51, 57–60].

This study had some limitations. First, insulin resistance was estimated because the gold standard for measuring insulin sensitivity is too invasive and expensive. However, validation studies of derived indexes of insulin sensitivity (HOMA-IR, QUICKI, and FGIR) in prepubertal obese children have reported a strong correlation between these indexes and insulin sensitivity measured by euglycemic and hyperglycemic clamps [10, 11, 19, 42, 43]. Second, although studies have demonstrated that waist circumference is associated with abdominal fat and insulin resistance in children [36, 37], we did not include a waist circumference measurement in the study because there are no defined standard categories of waist circumference associated with risk in children, as there are for BMI [61].

In summary, this study indicates that impaired glucose tolerance and insulin resistance in overweight and obese Costa Rican children are far more common than has been believed. Lifestyle interventions focusing on weight management and increasing physical activity should be a public health priority in overweight and obese children and should be promoted in several social environments, such as the family, school, and community, to prevent the future development of type 2 diabetes. Early screening for impaired glucose or insulin resistance in obese children should also be included at the primary levels of health care as a key approach to identify a disturbed glucose metabolism and avoid the progression and consequences of the disease. The use of indexes derived from fasting glucose and insulin samples should also be considered and further studied.

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