Brief Epidemiologic Report

Obesity in Spanish Schoolchildren: Relationship with Lipid Profile and Insulin Resistance

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Abstract

GARCÉS, CARMEN, JAVIER GUTIERREZ-GUISADO, MERCEDES BENAVENTE, BEATRIZ CANO, ENRIQUE VITURRO, HENAR ORTEGA, AND MANUEL DE OYA. Obesity in Spanish schoolchildren: relationship with lipid profile and insulin resistance. *Obes Res.* 2005;13:959–963.

This article reports cross-sectional data from a total of 1048 children, 6 to 8 years of age, categorized by presence or absence of obesity, who participated in a voluntary survey of cardiovascular risk factors in Spain over the period of 1998 to 2000, to establish the relationship between obesity and its metabolic consequences at this age. The prevalence of obesity and overweight were 9.4% and 15.7%, respectively, in boys and 10.5% and 18.0%, respectively, in girls. We observed that, in both sexes, obese children had higher triglycerides and lower high-density lipoprotein-cholesterol levels than non-obese children. No differences were found in plasma glucose or low-density lipoprotein-cholesterol levels between normal and obese children. However, we observed that insulin levels and the homeostasis model assessment for insulin resistance were significantly ($p < 0.001$) higher in obese children of both sexes but that free fatty acid levels were lower in obese children than in non-obese children, with a statistical significance in girls (0.72 ± 0.30 vs. 0.61 ± 0.16 mEq/liter). In summary, our survey found some metabolic consequences of obesity similar to those found in adults (elevated triglycerides, insulin, and the homeostasis model assessment for insulin resistance, and lower high-density lipoprotein-cholesterol). However, other features (glucose, total cholesterol, low-density lipoprotein-cholesterol, and free fatty acid levels) were found to behave differently, indicating that the association of obesity with risk factors seems to change as the children age and may depend on the chronology of sexual maturation.

Key words: BMI, glucose, triglycerides, high-density lipoprotein-cholesterol

Introduction

The prevalence of childhood obesity has considerably increased in many regions of the world, including Spain, and has become a major public health problem, because this increase has been associated with an increase in the prevalence of type 2 diabetes in children (1).

In adults, a close relationship has been found between obesity and the onset of insulin resistance, which is responsible for altered glucose metabolism and may lead to the development of dyslipemia, hypertension, and many other disorders that contribute to atherosclerosis and coronary heart disease (2).

In childhood, obesity also seems to lead to the appearance of a number of cardiovascular risk factors, such as altered lipid levels (3) and impaired glucose tolerance (4), which could contribute to atheroma plaque development and lead to the development of coronary heart disease in adult life (5). It is not clear when this association is established. It is important to understand the chronology in the appearance of these risk factors in obese children to better understand the mechanisms that bring them about.

In this study, we analyzed lipid levels, glucose, free fatty acids (FFAs),[1] insulin, and the homeostasis model assessment for insulin resistance (HOMA) index in a large cohort of prepubertal Spanish children categorized by BMI as non-obese or obese to establish the relationship between obesity and its metabolic consequences at this age.

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[1] Nonstandard abbreviations: FFA, free fatty acid; HOMA, homeostasis model assessment for insulin resistance; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 1. Anthropometric and biochemical characteristics in obese and non-obese children

	Boys			Girls		
	Non-obese	Obese	*p*	Non-obese	Obese	*p*
N	475	49		469	55	
Age (years)	6.7 ± 0.7	6.6 ± 0.6	0.66	6.7 ± 0.7	6.7 ± 0.6	0.88
Weight (kg)	25.9 ± 4.2	36.2 ± 5.7	<0.001	25.5 ± 4.4	35.5 ± 4.5	<0.001
Height (cm)	125.6 ± 6.3	127.4 ± 7.2	0.06	124.7 ± 7.0	126.8 ± 6.4	0.03
BMI (kg/m^2)	16.4 ± 1.7	22.1 ± 1.8	<0.001	16.4 ± 1.8	22.0 ± 1.6	<0.001
Glucose (mg/dL)	91.6 ± 8.3	93.8 ± 7.5	0.08	89.5 ± 13.3	90.1 ± 11.3	0.74
TC (mg/dL)	182.9 ± 29.0	182.5 ± 25.5	0.92	184.7 ± 28.9	175.8 ± 27.6	0.03
TGs (mg/dL)	69.9 ± 19.7	88.8 ± 34.2	<0.001	75.1 ± 27.4	83.5 ± 29.2	0.03
HDL-C (mg/dL)	60.1 ± 13.0	52.5 ± 10.7	<0.001	58.5 ± 12.8	54.8 ± 15.7	0.05
LDL-C (mg/dL)	108.8 ± 28.7	112.2 ± 21.4	0.42	111.5 ± 27.5	104.3 ± 25.1	0.07
TC/HDL-C	3.15 ± 0.76	3.58 ± 0.73	<0.001	3.28 ± 0.77	3.36 ± 0.81	0.52
Apo A1 (mg/dL)	138.4 ± 19.3	135.8 ± 17.8	0.37	136.6 ± 19.1	128.8 ± 18.7	0.005
Apo B (mg/dL)	69.4 ± 15.3	72.1 ± 14.1	0.23	72.2 ± 15.3	68.5 ± 11.8	0.088
Insulin (μU/mL)	3.02 ± 1.96	5.32 ± 2.74	<0.001	3.46 ± 2.52	5.33 ± 3.40	<0.001
HOMA	0.69 ± 0.47	1.26 ± 0.69	<0.001	0.76 ± 0.56	1.18 ± 0.77	<0.001
FFAs (mEq/liter)	0.66 ± 0.25	0.64 ± 0.25	0.65	0.72 ± 0.30	0.61 ± 0.16	0.001

Research Methods and Procedures

The study population included 6- to 8-year-old children who participated in a cross-sectional study designed to analyze cardiovascular risk factors in Spanish schoolchildren (6) categorized by the presence or absence of obesity. A representative sample of these children was selected by means of random cluster-sampling in schools and stratified by sex and type of school (i.e., public vs. private). The response rate was 85%, with little variation among location.

The study protocol complied with Helsinki Declaration guidelines and was approved by the Clinical Research Ethics Committee of the Fundación Jiménez Díaz in Madrid. Parents were required to sign a written consent form for participation of their children in the study.

Measurements were taken with the children lightly dressed and barefoot. Height was measured to the nearest millimeter using a portable stadiometer, and weight was recorded to the nearest 0.1 kg using a standardized electronic digital scale. From these measurements, BMI (weight in kilograms divided by height in meters squared) was computed.

Fasting (12 hours) venous blood samples were obtained by venipuncture. Plasma glucose was measured by the glucose oxidase method. Plasma lipid and apolipoprotein levels were determined as previously described (7). The coefficients of variation of the methods were 2.06% for cholesterol determinations and 3.42% for triglyceride (TG) determinations. We calculated the total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) ratio as a marker of atherogenicity. Serum insulin concentrations were measured by radioimmunoassay using a commercial kit (BI-INSULIN IRMA; Bio-Rad, Marnes la Coquette, France). Insulin resistance was estimated using HOMA [fasting insulin (μU/mL) × fasting glucose (mmol/liter)/22.5] (8). We measured FFA levels using the Wako NEFA-C kit (Wako Pure Chemical Industries, Osaka, Japan).

We considered children to be obese or overweight if their BMI exceeded the age- and sex-specific cut-off points proposed for children by Cole et al. (9). A Student's *t* test analysis was used to compare the mean values between groups. Spearman correlation analyses were performed to evaluate the correlations between anthropometric and biochemical variables and insulin and HOMA. Statistical analyses were performed using the SPSS software package, version 9.0.

Results

The sample group was made up of 1048 healthy school children (524 boys and 524 girls), with an average age of 6.7 years (range, 6 to 8 years). The prevalence of obesity in boys and in girls was similar (9.4% vs. 10.5%). The prevalence of overweight was 15.7% in boys and 18.0% in girls.

When comparing the lipid profile between obese and non-obese children, we observed that, in both sexes, obese

Table 2. Spearman correlation coefficients for fasting insulin levels and HOMA with anthropometric and biochemical variables in boys and girls

	BMI	Glucose	TG	HDL-C	APO AI	Insulin	HOMA	FFA
Boys								
Weight	0.810†	0.197†	0.024	−0.031	−0.010	0.360†	0.354†	−0.143†
BMI		0.127†	0.078	−0.044	0.024	0.366†	0.358†	−0.079
Glucose			0.062	−0.019	0.068	0.330†	0.432†	−0.086
TGs				−0.259†	−0.174†	0.261†	0.254†	0.023
HDL-C					0.701†	−0.121*	−0.116*	0.137*
Apo AI						−0.085	−0.069	0.111*
Insulin							0.992†	−0.234†
HOMA								−0.222†
Girls								
Weight	0.820†	0.222†	0.074	−0.052	−0.078	0.382†	0.388†	−0.156†
BMI		0.168†	0.130†	−0.073	−0.040	0.364†	0.359†	−0.136*
Glucose			0.059	0.006	0.092*	0.273†	0.392†	−0.084
TG				−0.215†	−0.103*	0.275†	0.278†	−0.036
HDL-C					0.735†	−0.102*	−0.098*	0.144*
Apo AI						−0.113*	−0.094	0.133*
Insulin							0.987†	−0.256†
HOMA								−0.249†

* $p < 0.05$.
† $p < 0.01$.

children had significantly lower HDL-C and higher TG levels than non-obese children (Table 1). Obese girls also had significantly lower apolipoprotein AI levels. No differences in plasma glucose levels were found between non-obese and obese children of either sex. The TC/HDL-C ratio was significantly higher in obese boys than in non-obese boys.

We observed that insulin levels and HOMA were significantly ($p < 0.001$) higher in obese children of both sexes (Table 1). FFA levels were lower in obese children than in non-obese children, with statistical significance in girls (Table 1). When comparing non-overweight with overweight children, only insulin levels and HOMA values resulted in significant differences. Insulin and HOMA were significantly higher ($p < 0.01$) in overweight boys than in non-overweight boys (insulin: 3.78 ± 2.21 vs. 2.92 ± 1.91 μU/mL; HOMA: 0.85 ± 0.49 vs. 0.67 ± 0.46) and significantly higher ($p < 0.001$) in overweight girls than in non-overweight girls (insulin: 4.43 ± 2.71 vs. 3.18 ± 2.30 μU/mL; HOMA: 0.97 ± 0.59 vs. 0.69 ± 0.51).

In a Spearman correlation analysis, we found that weight and BMI presented positive correlations with glucose, insulin, and HOMA and negative correlations with FFAs. There were significant positive correlations for insulin and HOMA with glucose and TGs and significant negative correlations for insulin and HOMA with HDL-C and FFAs in both sexes (Table 2). The correlations found between HOMA and glucose and HOMA and insulin were not unexpected because HOMA values are derived from insulin and glucose concentrations.

Discussion

This study describes lipid profile, insulin levels, FFA concentration, and HOMA in obese and non-obese individuals in a large cohort of prepubertal Spanish children.

In our population, obesity was associated with an adverse lipid profile. We found significantly higher TG levels and lower HDL-C in obese children. The atherogenic index (TC/HDL-C) was also significantly higher in obese boys. This unfavorable lipid profile parallels previous observations in other cross-sectional surveys in other populations (10,11). We did not find any significant association between obesity and low-density lipoprotein-cholesterol (LDL-C) levels. Although this association has been reported in some studies in older children (3,11), it has not been observed in children at this age (12).

We found higher levels of insulin and a higher HOMA in obese children. However, no differences in glucose levels were found between obese and non-obese children at this age, although we did find a positive correlation between BMI and glucose. Shea et al. (13) reported that obesity in 2- to 3-year-old children was associated with fasting plasma insulin and insulin resistance but did not find this correlation between anthropometric variables and glucose. In both studies, even though fasting insulin levels were higher, glucose levels remained normal, but in our study of 6- to 8-year-old children, a correlation between BMI and glucose was present. Furthermore, in boys 12 to 16 years of age, Chu et al. (11) found different glucose concentrations between obese and non-obese boys. In adults, the temporal sequence in the pattern of onset of glucose intolerance implies that hyperinsulinemia precedes glucose intolerance (14). The data discussed previously seem to indicate that the risk of progression to chronic hyperglycemia depends on age. The sex differences observed in some studies may suggest a hormonal influence.

Plasma FFA levels were not higher in obese boys and were significantly lower in obese girls. This finding is very interesting because, in adults, FFAs are considered to contribute to the link between obesity and insulin resistance (15). We found a significant negative correlation between FFAs and insulin and HOMA. FFAs in 12- to 16-year-old children were not associated with insulin levels and insulin resistance in the Taipei Study (16). Allard et al. (17) did find negative correlations of FFAs with insulin and HOMA in 9-year-old boys and girls and in 13-year-old boys but did not detect any relationship for 13-year-old girls or 16-year-old girls and boys. The negative correlation between FFAs and insulin concentrations seen in younger children is lost with age and depends on sex. In contrast to what happens in adults, the obese prepubertal children of our study, although they had higher levels of insulin and higher HOMA values, had lower FFA levels than non-obese children. This indicates that the antilipolytic effect of insulin is still present, suggesting that the adipose tissue in the obese children remains sensitive to the action of insulin. As suggested by the different situations observed in obese children depending on the sex and age analyzed (11,13), the alterations associated with insulin resistance in obese children may perhaps be influenced by their hormonal status.

In summary, our survey showed that obese 6- to 8-year-old children have, like obese adults, elevated levels of TGs, lower levels of HDL-C, and higher fasting insulin levels and HOMA. However glucose, TC, LDL-C, and FFA levels were not found to be higher in obese vs. non-obese children. These data, in connection with data from the literature, indicate that the association of obesity with risk factors (glucose, insulin, lipid levels, FFAs) seems to change as the children age and may depend on the chronology of sexual maturation. Long-term longitudinal studies are required to establish when and how obesity starts to be related with these alterations.

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