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Lean adolescents with increased risk for metabolic syndrome

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SUMMARY. The aim of the present study was to determine in adolescents the relationship between insulin levels and body mass index (BMI), body fat distribution, diet, life style and lipid profile. We studied 167 adolescents (68 boys and 99 girls) whose ages ranged from 14 to 17 years. A detailed medical (including pubertal stage) and nutritional record was obtained from each subject. Biochemical measurements included fasting serum insulin, glucose, total cholesterol (TC), triglycerides (Tg), HDL-C, LDL-C and VLDL-C. HOMA insulin resistance (IR) and HOMA β-cell function (β-cell) were calculated. Insulin levels were over 84 pmol/L (cut off normal value in our lab) in 56% of the boys and 43% of the girls. Thirty-seven percent of lean adolescents whose BMI was 21.5 ± 1.9 kg/m^2 presented higher fasting insulin levels, HOMA IR, Tg, systolic (SBP) and diastolic blood pressure (DBP) values when compared to a lean normoinsulinemic group. Insulin levels were correlated (p< 0.01) with body mass index. Both boys and girls in the highest BMI quartile (BMI > 24 kg/m^2) had significantly higher serum insulin, HOMA β-cell, and Tg levels, and the lowest HDL-C levels. A high-energy intake rich in saturated fat and low physical activity were found in this lean but metabolically altered adolescents. We conclude that even with a BMI as low as 21 kg/m^2 an inappropriate diet and low physical activity might be responsible for the high insulin levels and dislipidemias in adolescents.

Key words: Insulin, body mass index, diet, physical activity, insulin resistance, adolescents.

RESUMEN. Adolescentes delgados con alto riesgo de presentar Sindrome Metabólico. El objetivo del presente estudio fue determinar la relación entre los niveles de insulina y el Indice de Masa Corporal (IMC), distribución de grasa corporal, dieta, estilo de vida y perfil lipídico en adolescentes. A cada adolescente se la realizó una historia clínica detallada (incluyendo estadío puberal), además de una encuesta nutricional. Dentro de los parámetros bioquímicos se determinaron en suero los niveles de glicemia e insulina basal, colesterol total (CT), triglicéridos (TG), HDL-C, LDL-C, y VLDL-C. Se calcularon el HOMA-IR, y el HOMA-ß-cell. Se encontró que el 56% de los varones y el 43% de las hembras tenía valores de insulina > 84pmol/L (valor de referencia para nuestro laboratorio). Un 37% de los adolescentes delgados, con un IMC promedio de 21,5 ± 1,9 kg/m^2, presentó niveles elevados de insulina, HOMA-IR, TG, presión arterial sistólica y diastólica comparados con el grupo de adolescentes delgados normoinsulinémicos. Se encontró una correlación positiva y significativa (p< 0,01) entre los niveles de insulina y el IMC. Tanto los varones como las hembras ubicados en los cuartiles más altos de IMC (IMC>24 kg/m^2), tenian niveles significativamente más altos de insulina, HOMA- ßcell y TG, acompañados de niveles más bajos de HDL-C. Una alta ingesta de energía rica en grasa saturadas y una baja actividad física, se encontraron en estos adolescentes delgados pero metabólicamente alterados. En conclusión, niveles tan bajos de IMC como 21 kg/m^2, una dieta inapropiada y una baja actividad física pueden ser responsables de los altos niveles de insulina y dislipidemias en los adolescentes.

Palabras clave: Insulina, índice de masa corporal, dieta, actividad física, insulino resistencia, adolescentes.

INTRODUCTION

The emerging worldwide epidemic of type 2 diabetes and cardiovascular disease establishes as research priorities to analyze risk factors in adolescents. There is an increasing evidence that acquired cellular resistance to insulin leads to impaired glucose tolerance, hyperglycemia, hyperinsulinemia and dyslipidemia. Genetic factors in combination with sedentary life-style, and a high-energy diet lead to obesity. Nearly 20 years ago, it was suggested that individuals exist who are not obese on the basis of height and weight, but who, like people with overt obesity, are hyperinsulinemic, insulin-resistant, and predisposed to type 2 diabetes, hypertriglyceridemia, and premature coronary disease (1). Since then, it has become increasingly clear that such metabolically obese, normal weight individuals are very common in the general population and they probably represent one end of the spectrum of people with insulin resistance syndrome. Metabolic obesity could account for the higher prevalence of type 2 diabetes and other disorders in people with body mass index (BMI) in the 20-27 kg/m^2 range who have gained modest amounts of weight (2–10 kg of adipose mass) in adult life. Such individuals might be characterized by hyperinsulinism and possibly by an increase in fat cell size compared to

patients of similar age, height and weight (1). Bergström et al (2) demonstrated that features typical of the insulin resistance syndrome were already present in Swedish adolescents. In addition, Young and Rosenbloom (3) reported type 2 diabetes in a pediatric population. The measurements of serum insulin concentrations is an accepted way of estimating insulin resistance (4) but there are not reference values (normative data) available in the adolescent age group. Hyperinsulinemia is used as a biochemical marker for insulin resistance as it has itself been implicated in the development and maintenance of excess adiposity (5,6). However, little attention has been paid to the metabolic consequences of *hyperinsulinemia in adolescents*, even though such studies might provide important insights into the natural history of obesity and cardiovascular disease in adult life. The objective of the present study was to determine the relationship between insulin level and body mass index, body fat distribution, diet, life style and lipid profile in adolescents.

METHODS

Subjects

The study was performed on healthy adolescents with similar socioeconomic status, from an urban school in Maracaibo-Venezuela, and were selected in accordance with sex and age. The study involved 167 subjects aged between 14 and 17 y: 68 boys and 99 girls. All volunteers received verbal and written information on the purpose and content of the study, and the participation was voluntary. All subjects were documented to be in good health based on their health history that included height (m), weight (kg), pubertal age (estimated according to Tanner's criteria), collection of data on chronic disease history (diabetes, hypertension, cardiovascular disease and obesity), medication and physical activity (min/week). None of the adolescents received medication.

Anthropometric assessment

Waist circumference was measured at the umbilical level and hip circumference as the largest measure around the hips. Biceps, triceps, subscapular and suprailiac skinfolds were measured with a Lange Skinfold Caliper. Height and weight were measured in the standard fashion, and BMI (kg/m^2) was calculated from these values. We considered lean adolescents when BMI was = 25 kg/m^2 and obese adolescents when BMI was > 25 kg/m^2. These cutoffs' BMI were established according to body mass index curves reported by FUNDACREDESA Venezuela Project 1994 (7).

Blood pressure

Systolic (SBP) and diastolic ([DBP] Korotkoff 4th phase) blood pressures were measured in the right arm in the sitting position using a standard mercury sphygmomanometer. The mean of two blood-pressure measurements obtained five minutes apart was used in the analyses.

Biochemical measurements

After a 12-h fasting blood samples (10 ml) were collected from each subject and transported and processed immediately after collection. Blood glucose was measured by the glucose oxidase method (Glucose liquicolor Human). Total cholesterol (TC), triglycerides (Tg), HDL-C and LDL-C were measured by enzymatic methods (Cholesterol liquicolor, Triglycerides liquicolor and HDL-cholesterol liquicolor test kits from Human, Germany and cholesterol LDL, PVS method from Boehringer); VLDL-C was determined by the formula: VLDL-C = TC – HDL-C – LDL-C. Serum insulin level was measured using a solid-phase ^{125}I radio immunoassay (Coat-A-Count Insulin, Diagnostic Products, USA). Insulin resistance and β-cell function were determined by the Homeostasis Model Assessment [HOMA] (8).

Macronutrient intake

Macronutrient intake was assessed from the subject's daily record of food eaten during 7 days (including breakfast, lunch, dinner and snack). The questionnaires were processed using the Expert System Ceres, a program that converts declared quantities of food into quantities of nutrients on the basis of the food composition table by National Nutrition Institute, Foods Composition Table (Venezuela) (9).

Data analysis

Statistical analysis was performed using the Stat Most Framework for Windows version 3.0 software. For normally distributed data the differences between means were evaluated with the Student's *t*-test. For non-normally distributed data differences between distributions were evaluated with the Mann Whitney U test and correlation analysis with the Pearson's correlation coefficient.

Ethical considerations

The study was approved by Ethics Committee of the Institute of Clinical Investigations, and informed written consent was requested and obtained from parents in the school where the study was performed; all adolescents were freely consenting.

RESULTS

Adolescents data are shown in Table 1. Anthropometric measurements, HOMA IR Index and blood pressures were significantly different between boys and girls. According to the criteria of Tanner both boys and girls were pubertal adolescents (boys 89.7% Tanner IV-V pubic hair and genitals; girls 97.9% Tanner IV-V breast and pubic hair, after the onset of menses). They were normotensive and had fasting

serum insulin levels that were above our reference value (84 pmol/L). In both boys and girls, BMI was positively ($p<0.05$) correlated to central fat distribution, estimated as subscapular/ triceps ratio, and with both circumference and skinfold measurements ($p<0.001$) (Table 2). In boys, anthropometric measurements were correlated positively with serum insulin, HOMA insulin resistance (IR), TC and LDL-C values and negatively with HDL-C (Table 3). In contrast, anthropometric measurements in girls were correlated positively only with systolic and diastolic blood pressures and negatively with HDL-C (Table 3). Both boys and girls in the highest BMI quartile (boys > 23.7 kg/m^2, girls > 24 kg/m^2) had significantly higher serum insulin levels, HOMA β-cell function (β-cell), and Tg values and lower HDL-C values than adolescents in the lowest quartile (boys and girls < 19.6 kg/m^2). Boys also had higher mean HOMA IR, LDL-C and VLDL-C values in the 4th quartile and girls presented higher SBP and DBP values in the 4th quartile (Table 4). In both boys and girls, there were no significant correlations between serum insulin and serum lipid values (data not shown).

As shown in Table 5, among the 167 adolescents studied, we found that 139 subjects had BMI = 25 kg/m^2 (lean) and 28 with BMI >25 kg/m^2 (obese). They were divided in 4 groups (A, B, C and D) according to the cutoff insulin value (84pml/L): Group A that was lean and had insulin values ≤ 84 pmol/l. Group B had a slightly higher BMI and skinfolds values than Group A. Hyperinsulinemia (>84pmol/L) and significantly (p=0.00000) higher HOMA IR and HOMA β-cell index were found in Group B compared with Group A. Also Group B had significantly higher serum triglyceride and a higher systolic and diastolic blood pressure than Group A. The physical activity (min/week) was lower in Group B than in Group A. In addition, waist circumference was higher than the Group A. In summary, insulin resistance and hyperinsulinemia occurred together in these non obese, normoglycemic adolescents. They were metabolically more affected than the Group C.

TABLE 1
Adolescents characteristics

n	Boys 68	Girls 99	p
Age (years)	15.5 ±. 1.0	15.8 ± 0.9	ns
Anthropometry			
Weight (kg)	63.9 ± 12.2	55.5 ± 9.3	0.0000
Height (m)	1.69 ± 0.07	1.58 ± 0.04	0.0000
BMI (Kg/m^2)	22.2 ± 3.4	22.1 ± 3.7	0.4
Waist (cm)	73.6 ± 9.2	67.2 ± 6.9	0.0000
Hip (cm)	91.7 ± 8.3	89.8 ± 7.4	0.06
Waist to hip ratio	0.79 ± 0.04	0.74 ± 0.04	0.0000
Skinfolds (mm)			
Biceps	8.4 ± 5.1	11.8 ± 4.6	0.0000
Triceps	14.6 ± 6.5	20.3 ± 6.0	0.0000
Subscapular	15.2 ± 8.4	19.0 ± 6.9	0.001
Suprailiac	15.5 ± 9.2	17.5 ± 6.4	0.05
Subscapular to Triceps ratio	1.03 ± 0.25	0.94 ± 0.24	0.009
Fasting Glucose (mmol/L)	4.67 ± 0.46	4.49 ± 0.45	0.01
Fasting Insulin (pmol/L)	100.8 ± 49.8	90.6 ± 40.8	0.07
Homa IR Index	3.5 ± 1.8	3.03 ± 1.3	0.02
Homa β-cell Index	337.9 ± 260.3	428.9 ± 491.2	0.08
Blood pressure (mm Hg)			
Systolic	113.8 ± 9.7	105.7 ± 8.6	0.0000
Diastolic	71.0 ± 6.9	68.3 ± 7.4	0.01

Data are means ± Standard Deviation.

TABLE 2
Associations between Body Mass Index, Circumferences and Skinfolds in adolescents

BMI (kg/m^2)	Circunferences (cm)					Skinfolds (mm)	
	Waist	Hip	W/H	Bicipital	Triceps	Subscapular	Subscapular to triceps ratio
Boys	0.85‡	0.85‡	0.30*	0.58‡	0.71‡	0.78‡	0.24*
Girls	0.82‡	0.81‡	0.52‡	0.65‡	0.82‡	0.84‡	0.28

*p ≤0.05; ‡ p ≤0.001

TABLE 3
Associations between anthropometric measurements and serum insulin, serum lipids and blood pressure

	Insulin	HOMA IR	*HOMA* B-cell	TC	Tg	HDL-C	LDL-C	VLDL-C	SBP	DBP
Boys										
BMI (kg/m^2)	0.38 ‡	0.37 ‡	0.23 *	0.40 ‡	0.18	-0.23*	0.37 ‡	0.35 †	0.25 *	0.10
Waist Circumference (cm)	0.36 †	0.36 †	0.22	0.32 †	0.28 †	-0.25 †	0.30 †	0.24 *	0.23	0.08
Waist to hip ratio	0.15	0.15	0.15	0.31 †	0.23 *	-0.21	0.35 †	0.08	0.14	0.02
Subscapular skinfold (mm)	0.34 †	0.34 †	0.14	0.40 ‡	0.21	-0.23 *	0.42 ‡	0.26	0.14	-0.06
Subscapular to triceps ratio	-0.06	-0.16	-0.16	0.11	0.10	-0.36 †	0.20	0.29 †	0.05	0.05
Girls										
BMI (kg/m^2)	0.17	0.14	0.16	-0.04	0.09	-0.28 †	0.09	-0.06	0.34 ‡	0.27 †
Waist Circumference (cm)	0.16	0.17	0.22 *	0.01	0.21 *	-0.29 †	0.16	-0.01	0.37 ‡	0.31 ‡
Waist to hip ratio	-0.01	0.0002	0.07	0.03	0.22 †	-0.18	0.10	0.13	0.19 *	0.25 †
Subscapular skinfold (mm)	0.17	0.15	0.12	0.06	0.14	-0.20 *	0.18	-0.03	0.42 ‡	0.26 †
Subscapular to triceps ratio	0.11	0.06	0.23 *	0.06	0.23 *	-0.18	0.09	0.19 *	0.21 †	-0.05

* p ≤ 0.05; † p ≤ 0.01; ‡ p ≤ 0.001

TABLE 4
Insulin levels, lipid profile and blood pressure values by body mass index quartiles

	BMI Quartiles									
	Boys (n = 68)					Girls (n = 99)				
	1	2	3	4	Variation	1	2	3	4	Variation
Fasting Insulin (pmol/L)	77.4	97.8	90.6	131.4	4>1 †	75.0	89.4	100.2	97.2	4>1 † ; 3>1 *
Homa IR index	2.5	3.5	3.8	4.6	4>1 †	2.6	3.0	3.3	3.2	
Homa β-cell index	367.3	261.3	293.3	455.5	4>2 †	252.2	426.8	432.1	606.8	4>1 † ; 2>1 *
Tg (mmol/L)	0.82	0.72	0.71	1.08	4>2 † ; 4>3 †	0.80	0.84	0.86	0.97	4>1*
CT (mmol/L)	3.11	3.11	3.73	3.71	4>1 †; 4>2 † ; 3>1 †	3.70	3.61	3.84	3.72	
HDL-C (mmol/L)	1.10	1.13	11.5	0.94	4<2 * ; 4<3 *	1.28	1.19	1.26	1.11	4<1 *
LDL-C (mmol/L)	1.8	1.62	2.07	2.31	4>1 * ; 4>2 † ; 3>2 *	2.07	2.04	2.17	2.21	
VLDL-C (mmol/L)	0.21	0.37	0.46	0.46	4>1 ‡ ; 3>1 * ; 2>1 ‡	0.36	0.36	0.36	0.40	
SBP (mm Hg)	110.6	111.6	118.7	117.1	3>1 * ; 3>2 *	102.4	103.8	106.2	110.8	4>1‡ ; 4>2‡ ; 4>3 *
DBP (mm Hg)	68.0	72.6	72.1	70.6	2>1 *	65.8	67.0	68.6	72.0	4>1† ; 4>2 *

* $p \leq 0.05$; † $p \leq 0.01$: ‡ $p \leq 0.001$. Mean values for each variable are shown. BMI Quartiles: Boys: 1) < 19.6; 2) 19.6 – 20.8; 3) 20.9 – 23.7; 4) >23.7. Girls: 1) < 19.6; 2) 19.6 – 21.4; 3) 21.5 – 24; 4) >24. TC: 0.02586 mmol/L is equal to 1 mg/dL. Tg: 0.01129 mmol/L is equal to 1 mg/dL.

TABLE 5
Clinical and metabolic characteristics of adolescents by insulin levels and body mass index

	BMI ≤ 25 kg/m²		BMI > 25 kg/m²		p					
	A. Insulin ≤ 84 pmol/L	B. Insulin > 84 pmol/L	C. Insulin ≤ 84 pmol/L	D. Insulin > 84 pmol—L	A-B	A-C	A-D	B-C	B-D	C-D
n	76	63	10	18						
Age (years)	15.6 ± 2.0	15.5 ± 0.9	15.7 ± 0.9	15.9 ± 1.06						
Physical Activity (min/week)	198.0 ± 176.4	134.5 ± 131.1	190.5 ± 288.1	202.8 ± 229.2	*	ns	ns	ns	*	ns
Anthropometry										
BMI (Kg/m²)	20.4 ± 2.1	21.5 ± 1.9	28.4 ± 3.6	28.3 ± 2.4	**	**	**	**	**	ns
Waist (cm)	66.3 ± 5.4	68.5 ± 5.7	80.1 ± 6.6	83.3 ± 11.0	*	**	**	**	**	ns
Waist / hip	0.75 ± 0.04	0.75 ± 0.04	0.79 ± 0.04	0.8 ± 0.06	ns	*	**	*	**	ns
Skinfolds (mm)										
Biceps	8.5 ± 3.8	10.3 ± 4.6	16.5 ± 5.3	15.5 ± 5.2	*	**	**	**	**	ns
Triceps	15.5 ± 5.6	17.1 ± 4.9	26.3 ± 8.0	26.6 ± 6.0	*	**	**	**	**	ns
Subscapular	14.4 ± 5.3	16.3 ± 5.6	26.5 ± 7.8	29.4 ± 8.2	*	**	**	**	**	ns
Suprailiac	13.9 ± 5.4	15.4 ± 6.1	24.4 ± 8.6	28.6 ± 7.3	ns	**	**	**	**	ns
Bic+Tri+Sub	38.6 ± 13.7	43.6 ± 13.0	69.3 ± 19.6	71.1 ± 18.9	*	**	**	**	**	ns
Sub/Tri	0.95 ± 0.21	0.96 ± 0.27	1.03 ± 0.2	1.12 ± 0.26	ns	ns	*	ns	*	ns
Clinical Chemistries										
Fasting Glucose (mmol/L)	4.54 ± 0.21	4.62 ± 0.48	4.39 ± 0.57	4.6 ± 0.54	ns	ns	ns	ns	ns	ns
Fasting Insulin (pmol/L)	63.6 ± 12	120.6 ± 39	64.2 ± 17.4	147.0 ± 55.2	**	ns	**	**	*	**
Homa IR Index	2.1 ± 0.4	4.1 ± 1.4	2.4 ± 0.7	5.0 ± 2.0	**	ns	**	**	*	**
Homa β-cell Index	246 ± 145	491 ± 480.6	530.6 ± 859.5	563.4 ± 392.1	**	*	**	ns	ns	ns
TC (mmol/L)	3.57 ±0.68	3.59 ± 0.75	3.56 ± 0.68	3.84 ± 0.55	ns	ns	*	ns	ns	ns
Tg (mmol/L)	0.78 ± 0.35	0.90 ± 0.49	0.85 ± 0.40	0.96 ± 0.37	*	ns	*	ns	ns	ns
HDL-C (mmol/L)	1.19 ± 0.28	1.18 ± 0.26	0.9 ± 0.23	1.10 ± 0.29	ns	**	ns	**	ns	*
VLDL-C (mmol/L)	0.35 ± 0.19	0.39 ± 0.21	0.32 ± 0.14	0.43 ± 0.26	ns	ns	ns	ns	ns	ns
LDL-C (mmol/L)	1.98 ± 0.62	2.00 ± 0.68	2.33 ± 0.84	2.31 ± 0.49	ns	*	*	ns	*	ns
Blood Pressure (mmHg)										
Systolic	106.4 ± 9.8	109.8 ± 10.0	114.0 ± 6.9	114.4 ± 7.0	*	*	**	ns	*	ns
Diastolic	67.8 ± 7.4	69.9 ± 6.5	71.0 ± 8.4	73.3 8.0	*	ns	*	ns	*	ns

$p < 0.05$; ** $p < 0.001$

Group C obese adolescents (BMI>25kg/m^2) with normal insulin values (<84 pmol/L), (Table 5) had similar insulin levels and HOMA IR values and higher (p=0.004) HOMA β-cell values compared to Group A. Despite this, higher LDL-C, systolic blood pressure and the lowest HDL-C value were observed. These high levels might be related to an increase in BMI as it was established in Table 2. This group had similar BMI and skinfolds to the obese hyperinsulinemic group (Group D) and the lowest level of HDL-C of all groups (Table 5).

Group D, obese adolescents with insulin levels > 84 pmol/L, had anthropometric measurements, fasting insulin level, HOMA IR, TC, TG LDL-C, systolic and diastolic blood pressure values significantly higher and HDL-C lower than Group A. Central fat distribution (subscapular to triceps ratio) was significantly higher (p=0.003) in these obese adolescents with higher insulin levels compared with in Group A (Table 5), having boys a higher ratio [p<0.0000] (Table 1).

In general, daily intake of energy and nutrients among the adolescents were higher than required (calculated on the basis of age, weight, sex and physical activity). High protein, fat and carbohydrate intake was observed according to the intake to required ratio values. Dietary fat came mainly from saturated fatty acids. Monounsaturated fatty acids intake did not reach 14% of total fat intake and the P/S ratio was less than 2.00 (recommended ratio). Low intake of vegetables, legumes and fruits was observed. Although no statistically significant, Group B had the highest intake of protein and saturated fat and the lowest intake of monounsaturated fat (Table 6).

TABLE 6
Daily intake of energy and nutrients of the adolescents by insulin levels and body mass index

	BMI ≤ 25 kg/m^2		BMI > 25 kg/m^2		p					
Energy or Nutrient	A. Insulin ≤ 84 pmol/L	B. Insulin > 84 pmol/L	C. Insulin ≤ 84 pmol/L	D. Insulin > 84 pmol/L	A-B	A-C	A-D	B-C	B-D	C-D
N	33	37	8	18						
Energy (Kcal)										
Required	2199.1 ± 352.6	2144.2 ± 311.89	2309.3 ± 501.0	2316.6 ± 516.7	ns	ns	ns	ns	ns	ns
Intake	2728.5 ± 972.2	2862.27 ±921.64	2440.2 ± 722.3	2768.6 ±1018.1	ns	ns	ns	ns	ns	ns
I/R x 100	123.7 ± 38.0	131.94 ± 36.48	105.7 ± 35.5	119.8 ± 35.5	ns	ns	ns	*	ns	ns
Protein (g)										
Required	77.12 ± 12.45	75.59 ± 9.63	80.7 ± 17.4	81.3 ± 17.7	ns	ns	ns	ns	ns	ns
Intake	107.8 ± 38.08	112.75 ± 32.82	103.1 ± 35.0	104.3 ± 39.5	ns	ns	ns	ns	ns	ns
I/R x 100	140.81 ± 39.41	150.02 ± 38.97	126.8 ± 27.5	126.8 ± 37.8	ns	ns	ns	*	*	ns
Fat (g)										
Required	73.42 ± 11.7	72.05 ± 9.07	80.5 ± 15.5	77.1 ± 17.0	ns	ns	ns	*	ns	ns
Intake	103.0 ± 50.39	106.91 ± 41.58	101.5 ± 49.2	94.5 ± 46.4	ns	ns	ns	ns	ns	ns
I/R x 100	139.21 ± 52.8	148.59 ± 50.52	129.8 ± 49.1	121.2 ± 39.7	ns	ns	ns	ns	*	ns
Saturated	61.3 ± 43.01	63.37 ± 35.85	51.5 ± 32.8	48.7 ± 25.6	ns	ns	ns	ns	ns	ns
Monounsaturated	2.57 ± 3.0	1.78 ± 2.78	4.7 ± 5.8	3.8 ± 3.7	ns	ns	ns	*	*	ns
Polyunsaturated	25.27 ± 13.9	22.72 ± 9.68	18.8 ± 9.5	17.7 ± 8.2	ns	ns	*	ns	*	ns
Modified fat °	31.12 ± 26.76	34.4 ± 29.59	38.9 ± 26.5	35.6 ± 30.1	ns	ns	ns	ns	ns	ns
P/S ratio	0.25 ± 0.35	0.45 ± 0.32	0.50 ± 0.38	0.47 ± 0.25	ns	ns	ns	ns	ns	ns
Carbohidrate (g)										
Required	307.84 ± 49.34	303.18 ± 39.69	323.2 ± 69.8	324.2 ± 72.2	ns	ns	ns	ns	ns	ns
Intake	335.0 ± 131.1	377.18 ± 129.04	286.2 ± 98.1	393.6 ± 150.6	ns	ns	ns	*	ns	*
I/R x 100	125.5 ± 81.34	126.51 ± 40.49	89.8 ± 26.1	121.6 ± 41.2	ns	ns	ns	*	*	*

* $p \leq 0.05$. Data are means ± SD
° From fried foods, mayonnaise and margarines
I/R: Intake/Required

DISCUSSION

This study found that 37% of the adolescents with BMI 21.5 ± 19 kg/m^2 (Group B) presented higher fasting insulin levels, HOMA IR, Tg, systolic and diastolic blood pressure values when compared to Group A.

The mean insulin values were similar in both boys and girls. Hoffman et al (10) have demonstrated that insulin sensitivity is greater in pubertal and early pubertal boys than girls and is primarily determined by body mass. It has been suggested that individuals exist who are not obese on the basis of height and weight, but who, like people with overt obesity, are hyperinsulinemic, insulin resistant and predisposed to type 2 diabetes, hypertriglyceridemia and premature heart disease (1,11). In addition, central abdominal adiposity, even when estimated crudely by anthropometric measures, predicts the development of type 2 diabetes (12), cardiovascular morbidity and mortality (13) and is now

recognized as part of the metabolic syndrome that includes insulin resistance, dyslipidemia and hypertension (14). Central adiposity is strongly related to insulin resistance, which is considered the precursor of type 2 diabetes (15). The abdominal fat depot may induce deterioration in insulin sensitivity through its characteristic high lypolysis (16) and its rapid turnover of fatty acids (17). Both insulin resistance and central adiposity were present in adolescents in Group B. Arslanian et al (18) demonstrated, that in nonobese normal children, percent adiposity is an important correlate of in vivo insulin sensitivity. However, independent of degree of adiposity, there remains significant relationship between diastolic blood pressure and insulin sensitivity as well as insulin levels in prepuberty, and insulin levels and VLDL in pubertal subject, possibly signaling the initiation of syndrome X in childhood.

Ferrari et al (19) observed that lean offspring (BMI<22.5 kg/m^2) with one hypertensive parent, had significantly higher systolic blood pressure and they were insulin resistant. This situation has also been reported in nonobese, normoglycemic offspring and/or first degree relatives of patients with type 2 diabetes (20). Similarly, our Group B were first or second degree relatives of patients with type 2 diabetes [49 % (31/63)] and/or hypertension [(76% (48/63)]. The family history for diabetes was slightly higher in Group B compared with group A (49% vs 44%). Both had similar percentage for family history of hypertension. According to this result the alteration observed in Group B maybe related to other factors.

Bergström et al (2) reported that during midpuberty serum insulin values in both boys and girls were higher in the younger age group. In this study, the mean age in Group B was not different to that of adolescents with similar or higher BMI. It has been suggested that the peak in serum insulin level in midpuberty results from an increased resistance to insulin (21). In fact, Table 5 shows that Group B, with high fasting insulin levels, had HOMA IR values significantly higher (2 fold) than those of the Group A. Insulin is known to have a growth hormone-like effect, and an increased level may be caused by an increased secretion of insulin related to the pubertal growth spurt. In effect, Group B had significantly higher HOMA β-cell index, indicative of non-impaired insulin secretion. They also had higher triglyceride levels, a good marker for risk of atherosclerosis at an early age (22). Amiel et al (23) suggest that insulin resistance during puberty is restricted to peripheral glucose metabolism. Selective insulin resistance leading to compensatory hyperinsulinemia may serve to amplify insulin's effect on amino acid metabolism, thereby facilitating protein anabolism during this period of rapid growth.

In general, increases in insulin resistance tend to parallel the increases in BMI. This was observed in the adolescents studied (Table 3). However, a small group (Group C) with BMI>25 kg/m^2 had fasting insulin levels as low as Group A. Parameters linked to insulin resistance (high insulin level, high triglyceride levels, low HDL-C and high blood pressure) were found in the subjects of this study and emphasize the importance of increases in BMI in adolescents. Universal definition of obesity related to cutoff in adolescents has not been established. In Venezuela, the 90th and 97th of body mass index for age and sex have been recommended to define overweight and obesity based on FUNDACREDESA Venezuela Project (7). Cole et al (24) proposed cutoff points to define child obesity. These cutoff points are recommended for international comparisons of prevalence of overweight and obesity. According to Cole et al data (24) the Group B, having a BMI=21.5 kg/m^2 (15.5 ± 0.9 years) can be considered lean. Adolescents with BMI>25 kg/m^2 will be obese. The Group B had an increase in adipose tissue mass (measured by skinfolds and waist circumference) compared with normoinsulinemic adolescents in Group A. BMI was positively correlated ($p<0.05$) to central fat distribution estimated as the subscapular to triceps ratio. Also, BMI was significantly correlated with circumferences (waist, hip and waist/hip ratio) and skinfolds (Table 2). Central obesity, like hyperinsulinemia and insulin resistance, not only accompanies but also antedates metabolic disorders such as type 2 diabetes (11,25) and coronary heart disease (26). That it may be a very early event is suggested by the finding of the Bogalusa Heart Study (27,28) that increases in central fat, as reflected by increases in subscapular, suprailiac and subcostal skinfold thickness, correlate closely with increases in plasma insulin, blood pressure, and triglycerides in school-aged (6-18 y) children.

This study also found variations in serum insulin levels, partly caused by variations in daily dietary intake. Daily intake of energy and nutrients were higher than the requirements calculated for gender, ages and physical activity. A recent report suggests that high-protein diets may contribute to the more rapid progression of type 2 diabetes from IGT (29). Kitagawa et al (30) demonstrated that an increased incidence of noninsulin dependent diabetes mellitus among Japanese schoolchildren correlates with an increased intake of animal protein and fat. Intake of animal fat increased the consumption of saturated fatty acids that may increase insulin levels and decrease P/S ratio; these nutritional alterations increase the cardiovascular disease risk.

Another factor present in the Group B was the lowest physical activity in comparison with Group A. These adolescents require neither the high intake of calories nor the larger amount of carbohydrates. Physical activity has a beneficial effect in reducing plasma insulin levels among people with and without type 2 diabetes (31). Moderate amounts of physical activity have a significant role in reducing the burden of hyperinsulinemia and diabetes among

ethnic populations at highest risk for these conditions (32). Daily physical activity is important to decrease risk for insulin resistance. Group B with low physical activity, hyperinsulinemia and insulin resistance have high risk to develop diabetes.

In conclusion, this study shows that adolescents with BMI as low as 21.5 kg/m^2, but exhibiting hyperinsulinemia and insulin resistance, that co-exist with low physical activity and high energy, animal protein and fat intake, are at increased risk for obesity, cardiovascular disease and diabetes.

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REFERENCES

1. Ruderman N,Chisholm D, Pi-Sunyer X, Schneider S. The metabolically obese, normal-weight individual revised. Perspectives in diabetes. Diabetes 1998; 47:699-713
2. Bergström E, Hernell O, Persson LA, Vessby B. Insulin resistance syndrome in adolescents. Metabolism 1996;45:908-914
3. Young RS, Rosenbloom AL. Type 2 (non-insulin dependent) diabetes in minority youth: Conference report. Clin Pediat 1998; 37:63-66
4. Bergman RN, Finegood DT, Ader M. Assessment of insulin sensitivity in vivo. Endocr Rev 1985; 6:45-86
5. Cusin I, Rohner-Jeanrenaud F, Terrettaz J, Jeanrenaud B. Hyperinsulinaemia and its impact on obesity and insulin resistance. Int J Obes 1992; 16:S1-S11
6. Le Stunff C, Bougneres P. Early changes in postprandial insulin secretion, not in insulin sensitivity, characterize juvenile obesity. Diabetes 1994; 43:696-702
7. Landaeta Jimenez M, Lopez-Blanco M, Mendez Catellano H. Body mass index curves for age and sex. FUNDACREDESA-Venezuela Project 1994. In Manual de Crecimiento y Desarrollo. FUNDACREDESA 1997
8. Haffner S, Miettinen H, Stern M. The homeostasis model in the San Antonio Heart study. Diabetes Care 1997; 20:1087-1092
9. National Nutrition Institute, Foods Composition Table Venezuela. 1994
10. Hoffman R, Vicini P, Sivitz W, Cobelli C. Pubertal adolescent male-female differences in insulin sensitivity and glucose effectiveness determined y the one compartment minimal model. Pediatr Res 2000; 48:384-388
11. Hollenbeck CB, Reaven G. Variations in insulin-stimulated glucose uptake in healthy individual with normal glucose tolerance. J Clin Endocrinol Metab 1987; 64:1169-1173
12. Ohlson L-O, Larsson B, Svärdsudd K, Welin L, Eriksson H, Wilhelmsem N, Bjorntord P, Tibblin G. The influence of body fat distribution on the incidence of diabetes mellitus: 13.5 years of follow-up of the participants in the study of men born in 1913. Diabetes 1985; 34:1055-1058
13. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, Hennekens CH, Speizer FE. Body weight and mortality among women. N Engl J Med 1995; 333:677-685
14. Samaras K, Campbell LV. Increasing incidence of type 2 diabetes in the third millennium. Is abdominal fat the central issue? Diabetes Care 2000; 23:441-442
15. Carey DG, Jenkins AB, Campbell LV, Freund J, Chisholm DJ. Abdominal fat and insulin resistance in normal and overweight women: direct measures reveal a strong relationship in subjects at both low and high risk of NIDDM. Diabetes 1996; 45:633-638
16. Rebuffé-Scrivé M, Andersson B, Olbe L, Björntorp P. Metabolism of adipose tissue in intra-abdominal depots of non-obese men and women. Metabolism 1989; 38:453-458
17. Boden G. Role of fatty acids in the pathogenesis of insulin resistance and NIDDM. Diabetes 1997; 45:3-10
18. Arslanian S, Suprasongsin CH. Insulin sensitivity, lipids, and body composition in childhood: "Syndrome X" Present? J Clin Endocrinol Metab 1996; 81:1058-1062
19. Ferrari P, Weidmann P, Show S, Giachino D, Riesen W, Allemann Y, Heynen G. Altered insulin sensitivity, hyperinsulinemia, and dyslipidemia in individuals with hypertensive parent. Am J Med 1991; 91: 589-596
20. Laws AM, Stefanick ML, Reaven GM. Insulin resistance and hypertriglyceridemia in nondiabetic relatives of patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab 1989; 69:343-357
21. Arslanian SA, Kalhan S. Correlations between fatty acid and glucose metabolism. Potential explanation of insulin resistance of puberty. Diabetes 1994; 43:908-914
22. Franz M, Horton E, Bantle J, Beebe CH, Brunzell J, Coulston A, Henry RR, Hoogwerf BJ, Stacpoole PW. Nutrition principles for management of diabetes and related complications. Diabetes Care 1994; 17:490-518
23. Amiel SA, Caprio S, Sherwin RS, Plewe G, Haymond MW, Tamborlane WV. Insulin resistance of puberty; a defect restricted to peripheral glucose metabolism, J Clin Endocrinol Metab 1991; 72:277-282
24. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000; 320:1240-1243
25. Bergström RW, Nawell-Morris LI, Leonetti DL, Abraham S. Evidence for an increased intra-abdominal fat distribution with development of NIDM in Japanese-American men. Diabetes 1990; 39:104-111
26. Blair D, Habricht VP, Sims EAH, Sylvester D, Abrahan S. Evidence for an increased risk for hypertension with centrally located body fat and the effect of race and sex on this risk. Am J Epidemiol 1984; 119:526-540
27. Burke GL, Webber LS, Srinivasan SR, Radhakrishnamurthy B, Freeman DS, Berenson GS. Fasting plasma glucose and insulin levels and their relationship to cardiovascular risk factors in children: The Bogalusa Heart Study. Metabolism 1986; 35:441-446
28. Freedman DS, Srinivasan SR, Burke GL, Shear CL, Smook CG, Harsha DW, Webber LS, Berenson GS. Relation of body fat distribution of hyperinsulinemia in children and

adolescents: The Bogalusa Heart Study. Am J Clin Nut 1987; 46:403-410

28. Linn T, Geyer R, Prassek S, Laube H. Effect of dietary protein intake on insulin secretion and glucose metabolism in insulin dependent diabetes mellitus. J Clin Endocrinol Metab 1996; 81:3938-3943
30. Kitagawa T, Owada M, Urakami T, Yamauchi K. Increased incidence of non-insulin dependent diabetes mellitus among japanese schoolchildren correlates with an increased intake of animal protein and fat. Clin Pediatr 1998; 37:111-116
31. Regensterner J, Mayer E, Sheherly S, Eckel R, Haskell W, Marshall JA, Baxter J, Hamman RF. Relationship between habitual physical activity and insulin levels among nondiabetic men and women: the San Luis Valley Diabetic Study. Diabetes Care 1991; 14:1066-1074
32. Irwin M, Mayer-Davis E, Addy CH, Pate R, Durstins L, Stolarczyk LM, Ainsworth BE. Moderate-intensity physical activity and fasting insulin levels in women. Diabetes Care 2000; 23:449-454

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