Insulin Resistance Syndrome in Adolescents

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To explore whether the so-called insulin resistance syndrome can be identified in adolescents, serum insulin level was measured in 842 healthy Swedish adolescents (462 boys and 380 girls) and the values were related to current serum lipoprotein and apolipoprotein values (triglyceride [TG], total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], apolipoprotein [apo] A-I, apo B, and lipoprotein(a)), blood pressure (BP), and anthropometric measurements and previous physical growth. Mean serum insulin values were higher in 14-year-olds as compared with 17-year-olds and were highest in midpuberty. Adolescents with a high serum insulin had a higher attained height and weight during infancy and childhood. Obesity (body mass index [BMI] > 30 kg/m^2) was found in 1% of both boys and girls, and hypertensive BP levels were found in 3% of the boys and 1% of the girls. Controlling for age, serum insulin correlated positively with BMI (r = .36 and .25 in boys and girls, respectively), TG (r = .32 and .14), LDL-C (r = .17 and .24), and apo B (r = .23 and .23) and negatively with HDL-C (r = −.13 and −.21). High serum insulin, TG, LDL-C, and BP and low HDL-C clustered in adolescents with high BMI. In conclusion, the findings of this study indicate that features typical of the insulin resistance syndrome are already present in adolescents.

CARDIOVASCULAR DISEASE (CVD) obesity with or without non–insulin-dependent diabetes mellitus, hyperlipoproteinemia, and hypertension are major health problems in the adult population of most industrialized countries.[1-4] There is increasing evidence that acquired cellular resistance to serum insulin, leading to impaired glucose tolerance, hyperglycemia, hyperinsulinemia, dyslipidemia, and sodium retention, may be a common denominator linking these conditions together into the so-called insulin resistance syndrome, or syndrome X. Although the pathogenesis of this syndrome is multifactorial, genetic factors in combination with a sedentary life-style, including a high-energy diet rich in saturated fat leading to obesity, are regarded as major determinants.[5-8]

With few exceptions, the clinical features of CVD are not apparent until the third or fourth decade of life, but there is substantial evidence that the atherosclerotic process is already initiated during childhood.[9-11] Information on the early stages of the insulin resistance syndrome is scarce, but there are studies indicating that hyperinsulinemia, hyperlipoproteinemia, obesity, and hypertension cluster already in childhood and adolescence[12-15] and that these factors track into young adulthood,[16] and furthermore, that these factors are influenced by heredity.[17-23]

The present study is part of a larger prospective study on risk indicators for future CVD in Swedish adolescents—The Umeå Youth Study.[24-26] The objectives of the present study were (1) to determine serum insulin, serum lipids, blood pressure (BP), and anthropometric measurements of Swedish adolescents; (2) to evaluate the association between previous physical growth and current serum insulin levels; and (3) to determine if the insulin resistance syndrome can be identified in adolescence.

SUBJECTS AND METHODS

Study Area and Study Population

The study was performed in the municipality of Umeå, a city of 90,000 inhabitants in northern Sweden. The study area and study population have been described in detail previously.[24-26] Two groups of adolescents (N = 1,032) were invited to participate in the study, 14-year-olds (n = 439: 225 boys and 214 girls; mean age, 14.4 years; range, 13.5 to 15.7) and 17-year-olds (n = 593: 342 boys and 251 girls; mean age, 16.8 years; range, 15.9 to 18.2).

The study was approved by the research ethics committee of the Medical Faculty, Umeå University. All participants received verbal and written information on the purpose and content of the study, and participation was voluntary.

Measurements

The procedures used for blood sampling, serum lipid analyses, assessment of current height, weight, and pubertal stage, and collection of data on chronic disease history, medication, physical activity, and previous physical growth were recently described.[24-26] Serum insulin level was measured on fasting morning samples using an enzyme-linked immunosorbent assay test.[27,28] Clinical examination was performed by only one research nurse. Anthropometric and BP measurements were made singly. Pubertal stage was estimated by inspection according to Tanner's criteria. Twenty-three percent of the 14-year-old boys and 88% of the 17-year-old boys were classified as being past puberty (defined as Tanner genital stage 5). Eighty-six percent of the 14-year-old girls and 97% of the 17-year-old girls had passed menarche. 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 skinfold caliper according to the method described by Tanner.[29] Systolic (SBP) and diastolic ([DBP] Korotkoff 4th and 5th phases) BP were measured in the right arm in the sitting position after 5 minutes' rest using a standard mercury sphygmomanometer.

Participation

Blood samples were obtained and analyzed from 879 adolescents, 477 boys and 402 girls (85% of the study population). Of 879

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Submitted September 19, 1995; accepted December 21, 1995.

Supported by the Swedish Council for Social Research, the Joint Committee of the Northern Health Region, the Swedish Medical Research Council (19X-05708), the Medical Faculty of Umeå University, Förstamajblommans Riksförbund, Riksförbundet för Hjärt-och Lungsjuka, and the National Public Health Institute.

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0026-0495/96/4507-0020$03.00/0

subjects, serum lipoproteins and apolipoproteins were analyzed from almost all (98% to 100%) of the subjects, serum insulin from 845 (96%), birth weight from 854 (97%), birth length from 846 (96%), growth data up to adolescence from 9,671 measurements from 819 individuals (93%), current anthropometric measurements from 859 (98%), pubertal stage from 852 (97%), SBP and DBP (Korotkoff 4) 848 (98%), and DBP (Korotkoff 5) from 643 (73%). Two girls and one boy were excluded from serum insulin analyses due to diabetes mellitus, leaving 842 subjects (96%) for further analysis.

Statistical Analysis

Analyses were made using SPSS for Windows version 6.1 software (SPSS, Chicago, IL). For normally distributed data, the difference between means was evaluated with ANOVA. For non–normally distributed data, differences between medians were evaluated with the Median test, and differences between distributions with the Mann-Whitney U and the chi-square test. Standard deviation scores (z scores) for height, weight, and weight/height were calculated using the Epi-Nut software (National Center for Health Statistics, Centers for Disease Control, Atlanta, GA), comparing the obtained measurements on weight and height with the Centers for Disease Control/National Center for Health Statistics reference values.[30] Bivariate correlations were calculated for boys and girls separately with Pearson correlation coefficients. Associations between serum insulin, serum lipids, BP, and anthropometric measurements were analyzed in a partial correlation analysis. Since age showed a stronger association than pubertal stage with these different parameters, the analysis was made controlling for age (decimal).

RESULTS

Serum Insulin and Lipid Values

The 14-year-old adolescents showed higher mean serum insulin values than the 17-year-olds (Table 1). Fourteen-year-old girls had higher mean serum insulin values than 14-year-old boys ($P = .002$), whereas there was no significant difference between boys and girls in the 17-year-old age group. In both boys and girls, serum insulin values showed a tendency to be higher during midpuberty (data not shown). The data on serum lipid values have been presented in a previous report.[26] These data showed that mean total cholesterol (TC) was significantly higher in girls than in boys (4.4 and 4.2 mmol/L, respectively, both age groups together). TC and LDL-C values were lower during midpuberty in both boys and girls. In boys but not in girls, mean HDL-C values decreased and TG values increased successively with increasing pubertal stage. Four percent of the boys and 2% of the girls had HDL-C values <0.9 mmol/L, 9% of the boys and 10% of the girls had LDL-C values >3.4 mmol/L, and 1% of both boys and girls had TG values >2.3 mmol/L.[26]

Current Anthropometric Measurements and BP Values

As expected, 17-year-old adolescents had significantly higher mean values for all anthropometric measurements than the 14-year-olds, except for biceps and triceps skinfolds in boys (Table 1). BMI was also higher in 17-year-olds compared with 14-year-olds, but there were no significant differences between boys and girls. Boys had larger waist and smaller hip circumferences ($P < .001$) than girls, and consequently a higher waist to hip ratio ($P < .001$). Furthermore, as expected, girls had significantly higher mean values for all skinfold measurements compared with boys ($P < .001$). The same differences between boys and girls were seen in both age groups. Central fat distribution, estimated as the subscapular to triceps skinfold ratio, increased with age and the increase was more pronounced

Table 1. Anthropometry, Clinical Chemistries, and BP in Swedish Adolescents

	14-Year-Olds				17-Year-Olds			
	Boys		Girls		Boys		Girls	
Parameter	Median	Mean ± SD	Median	Mean ± SD	Median	Mean ± SD	Median	Mean ± SD
Anthropometry								
Height (cm)	168.8	168.2 ± 8.4	164.5	163.8 ± 6.6	178.5	178.5 ± 6.9	165.8	166.1 ± 6.2
Weight (kg)	54.3	55.2 ± 10.3	53.5	53.5 ± 8.3	65.6	66.8 ± 9.5	57.2	58.6 ± 8.7
BMI (kg/m²)	19.0	19.4 ± 2.7	19.5	19.9 ± 2.5	20.7	20.9 ± 2.3	20.8	21.2 ± 3.0
Waist (cm)	70.0	71.3 ± 7.5	66.5	67.0 ± 5.9	74.3	75.0 ± 6.3	68.2	68.9 ± 6.0
Hip (cm)	86.0	86.8 ± 6.5	89.3	89.7 ± 6.5	91.5	92.2 ± 5.3	92.5	93.4 ± 6.3
Waist-to-hip ratio	0.82	0.82 ± 0.04	0.74	0.75 ± 0.05	0.81	0.81 ± 0.03	0.74	0.74 ± 0.04
Skinfold (mm)								
Biceps	6.0	6.7 ± 3.1	9.2	10.3 ± 4.3	4.7	5.3 ± 2.1	10.0	10.8 ± 4.6
Triceps	8.3	9.2 ± 3.8	12.5	13.5 ± 4.2	7.6	8.3 ± 3.2	14.6	15.3 ± 4.7
Subscapular	7.0	7.9 ± 3.7	9.6	10.9 ± 4.8	7.8	8.6 ± 3.0	12.2	13.0 ± 5.0
Suprailiac	10.4	12.2 ± 5.9	13.7	14.5 ± 5.5	11.4	13.0 ± 5.9	16.5	17.4 ± 5.8
Clinical chemistries								
Insulin (mU/L)	10.1	11.1 ± 5.5	11.7	12.2 ± 4.3	8.5	8.9 ± 3.6	8.9	9.2 ± 3.2
TG (μmol/L)	0.68	0.78 ± 0.34	0.76	0.84 ± 0.36	0.80	0.86 ± 0.33	0.77	0.87 ± 0.44
TC (μmol/L)	4.05	4.09 ± 0.69	4.30	4.39 ± 0.74	4.20	4.22 ± 0.73	4.40	4.48 ± 0.78
HDL-C (μmol/L)	1.27	1.32 ± 0.30	1.43	1.43 ± 0.26	1.26	1.30 ± 0.33	1.49	1.49 ± 0.30
LDL-C (μmol/L)	2.38	2.41 ± 0.60	2.49	2.56 ± 0.68	2.48	2.51 ± 0.68	2.52	2.58 ± 0.67
BP (mm Hg)								
SBP	115	115 ± 10	110	111 ± 8	120	119 ± 9	110	109 ± 8
DBP*	80	78 ± 9	80	77 ± 8	75	75 ± 7	70	72 ± 6

*Korotkoff phase 4.

Table 2. Associations Between Anthropometric Measurements and Serum Insulin, Serum Lipids, and BP

	Insulin	TG	TC	HDL-C	LDL-C	Apo A-I	Apo B	Lp(a)	SBP
Boys									
Weight	.28‡	.25‡	.09	−.15‡	.11*	−.11*	.16‡	−.01	.18‡
BMI	.36‡	.28‡	.15‡	−.13†	.17‡	−.06	.23‡	.02	.16‡
Waist circumference	.36‡	.33‡	.17‡	−.16‡	.17‡	−.06	.24‡	.00	.16‡
Waist to hip ratio	.27‡	.26‡	.15‡	−.12†	.18‡	.02	.24‡	−.01	.10*
Subscapular skinfold	.38‡	.33‡	.17‡	−.13†	.20‡	−.02	.27‡	.02	.09*
Subscapular to triceps ratio	−.02	.09	.06	−.06	.04	−.08	.05	.00	.09*
Girls									
Weight	.24‡	.14†	.11*	−.17†	.15†	−.05	.12*	.09	.05
BMI	.25‡	.21‡	.19‡	−.21‡	.24‡	−.05	.23‡	.11	.03
Waist circumference	.25‡	.23‡	.18‡	−.17‡	.20‡	−.03	.20‡	.09	.01
Waist to hip ratio	.06	.15†	.11*	−.04	.10	.01	.13*	.01	−.01
Subscapular skinfold	.23‡	.21‡	.19‡	−.17‡	.22‡	−.05	.23‡	.07	.04
Subscapular to triceps ratio	.06	.14†	.05	−.13*	.07	−.10*	.11*	.03	.02

*$P \leq .05$.
†$P \leq .01$.
‡$P \leq .001$.

in boys ($r = .39$, $P < .001$ and $r = .15$, $P = .003$, for boys and girls, respectively). However, the waist to hip ratio did not show any significant change with age. BMI was highly correlated with both circumference and skinfold measurements in boys and girls (BMI/subscapular skinfold, $r = .77$ for both boys and girls; BMI/waist, $r = .77$ and .70 for boys and girls; BMI/hip, $r = .66$ and .67 for boys and girls, respectively; $P < .001$). Overweight defined as BMI greater than 25 kg/m^2 was found in 4% of the boys and 6% of the girls, and obesity defined as BMI greater than 30 kg/m^2 in 1% of both boys and girls. Mean SBP was higher in boys than in girls in both age groups and DBP was also higher in boys than in girls in the 17-year-old age group, whereas there was no difference in the 14-year-olds. Sex-related differences in BP were independent of differences in height. Hypertensive BP values (14-year-olds, SBP $\geq$ 136 and/or DBP $\geq$ 86; 17-year-olds, SBP $\geq$ 142 and/or DBP $\geq$ 92)[31] were found in 3% of the boys and 1% of the girls.

Associations Between Current Serum Insulin, Serum Lipids, BP, and Anthropometric Measurements

In both boys and girls, anthropometric measurements, independently of age, correlated positively with serum insulin, TC, LDL-C, TG, and apo B values and negatively with HDL-C (Table 2). In boys, anthropometric measurements also correlated positively with BP. There were no apparent differences in the associations between serum insulin, serum lipids, and BP values on the one side and BMI, waist circumference, or subscapular skinfold on the other. The same pattern was seen in both boys and girls, although the correlations were generally stronger in boys. Furthermore, when the mean values of serum insulin, TG, LDL-C, HDL-C, and SBP for different BMI quartiles calculated for 14- and 17-year-old boys and girls separately (BMI quartiles: 14-year-old boys, <17.7, 17.7 to 19.0, 19.1 to 20.7, >20.7; 14-year-old girls, <18.3, 18.3 to 19.5, 19.6 to 21.1, >21.1; 17-year-old boys, <19.5, 19.5 to 20.7, 20.8 to 22.6, >22.6; and 17-year-old girls, <19.3, 19.3 to 20.8, 20.9 to 22.6, >22.6 kg/m^2, respectively) were compared, it showed that both boys and girls in the highest BMI quartile had significantly higher serum insulin, TG, and LDL-C values and lower HDL-C values compared with adolescents in the lowest quartile. Boys in the highest quartile also had higher mean TG and SBP (Table 3). Moreover, independently of age and BMI, there were significant correlations between serum insulin and serum lipid values in boys (serum insulin/TG, $r = .24$, $P < .001$; TG/HDL-C,

Table 3. Serum Insulin, TG, LDL-C, HDL-C, and BP Values by BMI Quartiles

	BMI Quartiles									
	Boys					Girls				
	1	2	3	4	Variation	1	2	3	4	Variation
Insulin (mU/L)	9.0	8.7	9.2	9.5	4 > 1,* 4 > 2,† 4 > 3‡	9.7	9.9	10.5	11.0	4 > 1†
TG (mmol/L)	0.70	0.76	0.75	0.79	4 > 1†	0.75	0.78	0.74	0.80	4 > 1‡
HDL-C (mmol/L)	1.38	1.31	1.31	1.27	4 < 1†	1.54	1.44	1.45	1.41	4 < 1,* 4 < 2,‡ 3 < 1†
LDL-C (mmol/L)	2.42	2.37	2.49	2.61	4 > 2‡	2.42	2.54	2.54	2.82	4 > 1,* 4 > 2,† 4 > 3†
SBP (mm Hg)	115	117	117	120	4 > 1,* 4 > 2,† 4 > 3‡	111	110	109	111	NS

NOTE. BMI quartiles were calculated separately for 14- and 17-year-old boys and girls. Median values are shown for insulin and TG, and mean values for LDL-C, HDL-C, and SBP.
*$P \leq .001$.
†$P \leq .01$.
‡$P \leq .05$.

$r = -.25, P < .001$; TG/LDL-C, $r = .20, P < .001$; HDL-C/LDL-C, $r = -.12, P = .011$). In contrast to boys, there were no significant correlations between serum insulin and serum lipid values in girls, but similar to boys, there were significant correlations between TG values on the one side and HDL-C and LDL-C values on the other (TG/HDL-C, $r = -.30$, $P < .001$; TG/LDL-C, $r = .30$, $P < .001$), but there was no significant association between HDL-C and LDL-C.

Clustering of High Insulin, TG, LDL-C, and BP and Low HDL-C Values

The proportion of elevated serum insulin values cannot be estimated, since there are presently no set cutoff values for serum insulin in adolescents. Only a minor proportion of this adolescent population had TG, LDL-C, or BP values greater than, and HDL-C values less than, the internationally accepted reference values.[4] Consequently, even fewer had values for several parameters beyond these cutoff limits (data not shown). To assess the degree of clustering of unfavorable values, the presence of one or more high values (> 75th percentile for serum insulin, TG, LDL-C, and SBP) or low values (HDL-C < 25th percentile) was assessed in the same individuals (14-year-old boys: serum insulin > 12.3 mU/L, TG > 0.89 mmol/L, LDL-C > 2.72 mmol/L, HDL-C < 1.12 mmol/L, SBP > 120 mm Hg; 14-year-old girls: serum insulin > 14.5 mU/L, TG > 0.92 mmol/L, LDL-C > 2.92 mmol/L, HDL-C < 1.26 mmol/L, SBP > 120 mm Hg; 17-year-old boys: serum insulin > 10.2 mU/L, TG > 1.04 mmol/L, LDL-C > 2.97 mmol/L, HDL-C < 1.09 mmol/L, SBP > 125 mm Hg; 17-year-old girls: serum insulin > 10.7 mU/L, TG > 1.00 mmol/L, LDL-C > 2.93 mmol/L, HDL-C < 1.28 mmol/L, SBP > 115 mm Hg). It appeared that 26% of the boys and 30% of the girls had none and only 1% of the boys and girls had all of these indicators (Table 4). When the clustering status of unfavorable TG, HDL-C, LDL-C, and SBP values was assessed in relation to serum insulin level (quartiles), there were no significant differences in clustering between the insulin strata. On the other hand, when clustering was assessed in relation to BMI (quartiles), the clustering of unfavorable TG, HDL-C, LDL-C, SBP, and serum insulin values was more pronounced in adolescents with higher BMI (Table 4).

Table 4. Clustering of Indicators of the Insulin Resistance Syndrome

No. of Indicators	BMI Quartiles 1 No.	1 Col%	2 No.	2 Col%	3 No.	3 Col%	4 No.	4 Col%	Total No.	Total Col%
Boys										
0	41	36	31	27	29	26	19	17	120	26
1	36	32	56	48	48	43	36	32	176	39
2	32	28	23	20	22	20	30	27	107	24
3	3	3	6	5	9	8	20	18	38	8
4	1	1	0	0	4	4	5	4	10	2
5	0	0	0	0	0	0	3	3	3	1
Girls										
0	30	32	42	44	22	23	18	20	112	30
1	44	47	22	23	36	38	22	25	124	33
2	9	10	20	21	27	28	31	35	87	23
3	10	11	7	7	10	10	12	14	39	10
4	1	1	4	4	1	1	5	6	11	3
5	0	0	1	1	0	0	1	1	2	1

NOTE. Indicators are insulin, TG, LDL-C, or SBP > 75th percentile, or HDL-C < 25th percentile. Differences between BMI quartiles 1 and 4 ($\chi^2 = 26.4, P < .001$ and $\chi^2 = 26.2, P < .001$ for boys and girls, respectively).

Abbreviation: col%, column percent.

Associations Between Serum Insulin and Previous Physical Growth

In a previous report, we demonstrated that a high LDL-C level in adolescents was associated with low attained height during infancy and childhood.[26] When the same analysis was made for serum insulin, it appeared that adolescents with high serum insulin values (> 75th quartile) were longer and heavier at birth, although not significantly, compared with those having serum insulin values not higher than the 75th quartile. Also, they had higher mean standard deviation scores on height and weight for age and also higher weight for height as compared with the lower insulin quartiles throughout infancy and childhood (Fig 1). The differences in height and weight were small but consistent, and the same pattern was seen in both boys and girls. Significant differences were found in weight for age between 6 and 12 years and in weight for height between 4 and 6 years, whereas the differences in height did not reach significance. Moreover, weight and length at birth correlated positively with current weight and height (weight at birth *v* current weight, $r = .27$ and .20, and length at birth *v* current height, $r = .40$ and .22, for boys and girls, respectively). However, there was no correlation between weight or length at birth and current BP. Furthermore, there were no differences in clustering of unfavorable serum insulin, serum lipid, and SBP values between adolescents with different heights and weights during childhood (quartiles of individual means of standard deviation scores for heights and weights).

DISCUSSION

Measuring serum insulin concentration is an accepted way of estimating insulin resistance,[32] but there are currently no available reference values for adolescents. As reported by others,[14,33,34] serum insulin values in adolescence are highly dependent on age and sex (Table 1). The difference in serum insulin between boys and girls probably reflects differences in maturation. There is also an interindividual diurnal variation in serum insulin partly caused by variation in daily dietary intake. These different variations make comparisons between different studies difficult. Serum insulin values were higher in the younger age group, with the highest level in midpuberty for both boys and girls. It has been suggested that the peak in serum insulin level in midpuberty results from an increased resistance to insulin.[35,36] However, the reason for and the physiological meaning of an increased cellular resistance to insulin in

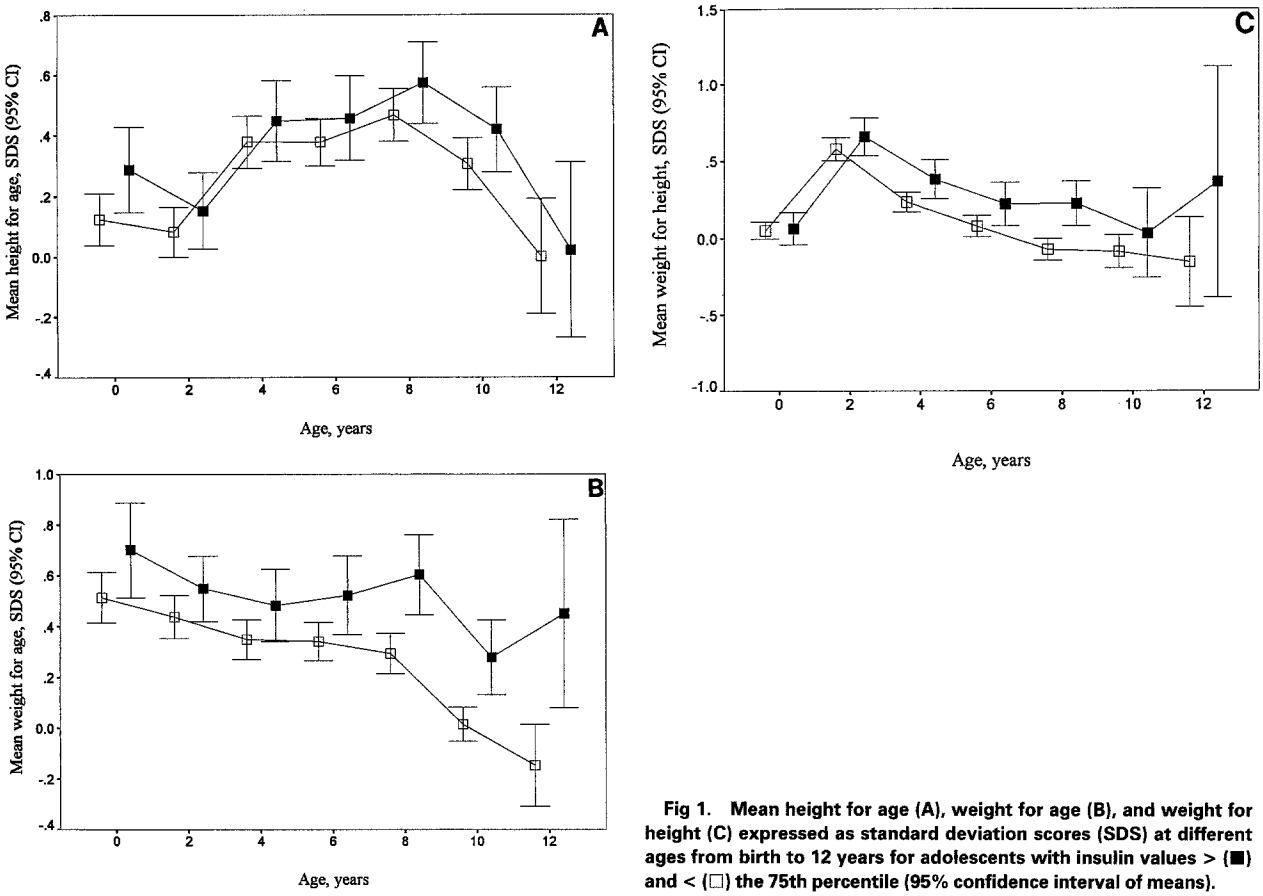

Fig 1. Mean height for age (A), weight for age (B), and weight for height (C) expressed as standard deviation scores (SDS) at different ages from birth to 12 years for adolescents with insulin values > (■) and < (□) the 75th percentile (95% confidence interval of means).

puberty is not known. Still, insulin is known to have a growth hormone–like effect, and increased levels may be caused by an increased secretion of insulin related to the pubertal growth spurt. However, this study was not designed to evaluate these different possible mechanisms. It should be noted that compared with serum insulin, serum lipid values show an opposite pattern, with a decrease in TC and LDL-C values in midpuberty.[26]

The hypothesis that fetal and infant exposures influence the risk of subsequent adult CVD was first proposed by Forsdahl in 1977.[37] In later studies referring to animal experiments and retrospective ecological studies in humans, Barker et al[38-40] have reported associations between reduced physical growth in early life and higher CVD mortality, elevated serum lipids, higher BP, and also impaired glucose tolerance, higher incidence of non–insulin-dependent diabetes mellitus in adulthood, and even syndrome X. However, their conclusions have been disputed; the main criticism is that the studies lack proper control for confounding by later dietary and other socially determined environmental factors.[41-44]

As reported previously, we found no correlations between weight or length at birth and adolescent serum lipid values, but subjects with high LDL-C values were shorter during infancy and childhood.[26] As for serum lipids, no significant correlations were found between weight or length at birth and current serum insulin or BP values. However, we found that adolescents with high serum insulin values (> 75th quartile) were taller and heavier later during infancy and childhood compared with those having lower serum insulin values ($\leq$75th quartile). There are several probable explanations for this finding. High insulin values may stimulate growth—alternatively, tall and heavy children may have higher insulin values. Although consistent, the differences in height and weight were small and the findings must be interpreted with caution. Still, a corresponding finding, illustrating the association between insulin and physical growth, with higher linear growth before the onset of insulin-dependent diabetes in children, has been reported.[45] Hence, our findings are in contrast to the hypothesis that poor physical growth in early life increases the risk of insulin resistance in adulthood.[40]

Obesity in childhood and adolescence is related to CVD morbidity and mortality in adult life,[46] but there is presently no clear consensus on how obesity should be measured or classified. In agreement with others,[47,48] our findings indicate that measures of central body fat distribution such as the waist to hip ratio or subscapular/triceps skinfold thickness show no advantages over BMI or waist circumference as indicators of unfavorable metabolic or physiologic values in adolescents. This view is also supported by the high correlations between BMI and CVD risk factors in adults.[49] The waist to hip ratio seemed to be especially inappropriate in girls, the reason being that waist and hip

circumference measurements also reflect normal changes in body shape during adolescence. These findings indicate that BMI and waist circumference[50] seem adequate to measure obesity in adolescents. It should be noted that BMI and waist circumference are easy to obtain, which makes these measurements suitable for epidemiological studies. However, it is important to emphasize that these measurements must be evaluated against age- and sex-specific reference figures or curves.

Moreover, our findings show that there were few subjects with very high serum lipid[26] or BP values, and relatively few adolescents could be classified as obese. However, parameters linked to insulin resistance (serum insulin, TG, HDL-C, and BP) were related to each other, and these parameters, except for BP in girls, were all related to BMI. Also, LDL-C values were positively correlated with BMI (Table 2). The importance of BMI was also verified by the higher mean serum insulin, serum lipid, and BP values in the upper BMI quartile (Table 3). The finding that high serum insulin, TG, LDL-C, and BP values and low HDL-C values clustered in subjects with high BMI values (Table 4) further emphasizes the importance of overweight, as also shown by others.[13,22,50,51]

In conclusion, this study shows that serum insulin values in adolescents relate to sex, age, maturation, and early physical growth, and also to current serum lipid values, BP, and anthropometric measurements. Although the proportion of adolescents with extreme values was small, our findings indicate that the entity of metabolic alterations typical of an insulin resistance syndrome can already be demonstrated in adolescence. The study stresses the importance of obesity, especially in boys, as a major determinant of these metabolic alterations. However, we do not yet know at what levels of serum insulin, serum lipids, BP, or overweight the risk of later adult disease becomes significant.

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