Inter-relationships Between Body Mass Index, C-reactive Protein and Blood Pressure in a Hispanic Pediatric Population

Patricio López-Jaramillo[1,2], Elizabeth Herrera[3], Ronald G. Garcia[1], Paul A. Camacho[1] and Victor R. Castillo[4]

BACKGROUND

The link between inflammation, obesity, and cardiovascular disease (CVD) has been described in adult populations but few data are available with respect to children. The aim of this study was to describe the inter-relationships between adiposity, C-reactive protein (CRP) plasma concentrations, and blood pressure levels in a Hispanic pediatric population.

METHODS

We included 325 schoolchildren (mean age, 10.0 years) selected from the school population of Bucaramanga, Colombia. Blood pressure, lipid profile, glucose, and CRP plasma concentration were measured using standard procedures. Body mass index (BMI) was used for evaluating the children's nutritional condition. Correlation coefficients were calculated for all the variables using Spearman's test.

RESULTS

As expected, a positive correlation was found between BMI and systolic blood pressure (SBP) in both genders, and between CRP and SBP levels in boys. After a multivariate regression analysis, the association between adiposity and blood pressure remained significant, whereas the CRP concentrations were no longer associated with SBP.

CONCLUSIONS

The results obtained in our study of Hispanic school-age children show that adiposity is correlated with CRP concentrations and SBP values as has been earlier described in Caucasian populations. However, we failed to find a significant relationship between low-grade inflammation and SBP levels. Further studies are needed in order to explore alternative pathophysiological mechanisms linking obesity and high blood pressure in children and to define the impact of these associations on the cardiovascular risk of our pediatric population.

Am J Hypertens 2008; **21**:527-532 © 2008 American Journal of Hypertension, Ltd.

Obesity in childhood and adolescence has become a global epidemic over the past few decades.[1] This major health problem is of particular relevance in developing countries, where it coexists with the transplantation of a western lifestyle characterized by a high intake of high-calorie foods, animal fats, and processed sugars, along with deficient physical activity.[2,3] Further, results from the most recent US National Health and Nutrition Examination Survey (NHANES) showed higher rates of overweight and obesity in children from minority groups when compared with non-Hispanic whites, thereby suggesting that the Hispanic pediatric population has an ethnic predisposition to develop increased adiposity.[4]

Overweight and obesity in childhood are factors that induce a high risk of morbidity and mortality from cardiovascular diseases (CVDs).[5] Obesity is a common cause of insulin resistance in children,[6] and is associated with an increasing risk of dyslipidemia,[7] type 2 diabetes mellitus,[8] and atherosclerosis.[9] Essential hypertension, most commonly found in adults, may also have its origins in childhood obesity.[10] It has been earlier reported, in studies of pediatric populations, that systolic and diastolic blood pressures are significantly and positively related to body mass index (BMI).[11,12]

Adipose tissue produces proinflammatory cytokines that stimulate the hepatic synthesis of C-reactive protein (CRP).[13] Plasma concentrations of CRP are a highly sensitive measure of overall inflammatory activity, and are significantly correlated with adiposity levels and components of the metabolic syndrome in adults.[14] A high CRP level has also been shown to be a predictor of CVDs such as myocardial infarction[15] and stroke.[16] Studies performed in pediatric populations from developed countries have shown that the association between cardiovascular risk factors and CRP concentrations in children seems to be similar to that found in adult populations.[17,18]

[1]VILANO Group, Research Institute, Fundación Cardiovascular de Colombia, Bucaramanga, Colombia; [2]Research Department, Medical School, Universidad de Santander (UDES), Bucaramanga, Colombia; [3]School of Nutrition, Universidad Industrial de Santander (UIS), Bucaramanga, Colombia; [4]Pediatric Cardiac Surgery Department, Fundación Cardiovascular de Colombia, Bucaramanga, Colombia. Correspondence: Patricio López-Jaramillo (joselopez@fcv.org)

Received 6 September 2007; first decision 20 September 2007; accepted 22 December 2007; advance online publication 6 March 2008. doi:10.1038/ajh.2007.86

There is a growing body of evidence supporting the hypothesis that the presence of a chronic low-grade inflammatory state with impairment of vascular endothelial function could be the pathophysiological mechanism that links obesity to hypertension.[19,20] However, data about this association in the pediatric population are limited. Therefore the aim of this study was to test whether childhood adiposity and CRP plasma levels are related to blood pressure values in a Hispanic pediatric population.

METHODS

Study population. During 2003–2004, healthy schoolchildren, both boys and girls (9–11 years old) were included in a cross-sectional study to evaluate the influence of low birth weight on vascular endothelial function. The initial sample consisted of 375 children who were randomly selected from the total school population (n = 15,830) from Bucaramanga, Colombia. All the children included in the study were nonsmokers and took no medications. None had a history of diabetes mellitus, endocrinologic disorders, or hereditary or CVDs. The race/ethnicity of children was recorded on the basis of their mothers' self-reports. All the children included were classified as Hispanics with mixed ancestry. For this study we excluded 50 children with history of menarche, acute inflammatory, or infectious diseases during the previous 10 days, leukocyte count >15,000 cells/mm^3 or differential white cell count of eosinophils over 10%. This reduced the study sample to 325 children.

Measurements. Anthropometric measurements were part of a physical examination performed in the morning after a 10-h overnight fast. Venous blood samples were then taken for determination of total and differential leukocyte count, hemoglobin, glucose, lipid profile, and high-sensitivity CRP determinations. Hemoglobin, total cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured using an automated colorimetric method (Biosystems, Barcelona, Spain), and plasma glucose concentration was measured using the glucose–oxidase method. low-density lipoprotein cholesterol was calculated using the Friedewald equation. High-sensitivity CRP in plasma was determined using chemiluminescent immunometric assay (IMMULITE 1000, DPC, Los Angeles, CA) with a functional sensitivity of <0.02 mg/dl.

After the child had rested for 5 min in a quiet environment, blood pressure was measured using a mercury sphygmomanometer with an appropriate-sized cuff on the right arm, with the child in a seated position. The first and fifth Korotkoff sounds were recorded as systolic blood pressure (SBP) and diastolic blood pressure, respectively, in accordance with the recommendations of the National High Blood Pressure Education Program Working Group in its Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents.[21] The children were weighed wearing light clothes, without shoes, and after emptying the bladder, using an electronic scale with a precision of 100 g, TANITA BF-556 (Tanita Corporation of America, Arlington Heights, IL). Heights were measured to the nearest 0.1 cm using a stadiometer; BMI was calculated as weight in kilograms divided by the square of the height in meters. Abdominal circumference (AC) was determined at the middle point between the lower edge of the ribs and the iliac anterior spine. Triceps (TSF) and abdominal skin folds (ASF) were determined using a Lange Skinfold Caliper (Lange, Beta Technology, Cambridge, MD) with constant standard pressure of 10 g/mm^2 and 1 mm accuracy. The experimental protocols and the process for obtaining informed consent were approved by the Institutional Review Board of the Fundación Cardiovascular de Colombia, Bucaramanga, Colombia. The children expressed their interest in participating in the study, and parents or legal guardians gave written informed consent, before the children were included in the study.

Statistical analysis. Statistical analysis was carried out using the SPSS software (version 14.0, SPSS, Chicago, IL). Normality of distribution was checked for all variables using the Kolmogorov–Smirnov test. Descriptive statistics were computed for variables of interest, and included mean values and s.d. of continuous variables and absolute and relative frequencies of categorical factors. Student's t-test and Mann–Whitney U-test were used to investigate the differences in continuous variables based on gender. The data were also divided by tertiles of BMI and AC, and bivariate associations were analyzed stratified by gender. Testing for differences in continuous variables across BMI tertiles was accomplished using the one-way analysis of variance or the Kruskal–Wallis one-way analysis of variance, ranked appropriately. In addition, Spearman correlation coefficient was used for examining the relationships among variables. The association of anthropometric measures (BMI, AC, TSF, and ASF) and CRP (as independent variables) with SBP (as a dependent variable) was explored using a multivariate linear regression adjusted for age and stratified by gender. Statistical significance was set at $P < 0.5$.

RESULTS

Out of the total population of 375 children, 325 fulfilled the inclusion criteria. These children had a mean age of 10.0 (s.d. 0.6) years, weight 33.6 (s.d. 7.7) kg, height 137.4 (s.d. 7.6) cm, BMI 17.6 (s.d. 2.7), and AC 63.6 (s.d. 7.6) cm. The median CRP concentration of the patients was 0.47 (Interquartile range: 0.15–1.3) mg/l. The study population comprised 169 girls (52%) and 156 boys (48%), and there were no significant gender-based differences in the distribution of any of the study variables (**Table 1**). Eighteen children had a history of low birth weight (5.5%); however, there were no significant differences in anthropometric measures, biochemical parameters, or blood pressure values between these subjects and the children with normal birth weight (data not shown).

An expected significant correlation was found between BMI and the other anthropometric measurements (AC, ASF, and TSF) (**Table 2**). All anthropometric variables were positively correlated with CRP concentrations and SBP ($P < 0.01$). There was also a positive correlation between low-density lipoprotein cholesterol values and anthropometrical parameters in

Table 1 | Distribution of study variables among children with gender specifications

	Boys ($n = 156$)	Girls ($n = 169$)
Age (years)	10.0 ± 0.5	10.1 ± 0.6
Body mass index (kg/m^2)	17.9 ± 2.8	17.4 ± 2.6
Abdominal circumference (cm)	64.3 ± 7.9	63.0 ± 7.3
ASF (cm)	12.9 ± 8.0	13.5 ± 7.1
TSF (cm)	11.5 ± 4.4	12.4 ± 4.3
CHOL (mg/dl)[a]	156.7 ± 26.7	159.9 ± 25.8
HDL-C (mg/dl)[a]	49.0 ± 9.7	49.0 ± 8.2
LDL-C (mg/dl)[a]	90.1 ± 24.4	92.8 ± 23.3
Triglycerides (mg/dl)[a]	84.6 ± 23.6	90.0 ± 27.1
Glucose (mg/dl)[a]	83.6 ± 7.9	82.7 ± 9.0
CRP (mg/l)	1.2 ± 2.6	1.5 ± 2.0
Systolic blood pressure (mm Hg)	97 ± 10	97 ± 10
Diastolic blood pressure (mm Hg)	63 ± 9	64 ± 8

Values represent means ± s.d.
ASF, abdominal skin fold; CHOL, cholesterol; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TSF, triceps skin fold.
[a]To obtain mmol/l values for cholesterol, HDL-C and LDL-C multiply values by 0.0259; for triglycerides, multiply values by 0.0113, and for glucose, multiply values by 0.0555.

Table 2 | Spearman correlation between BMI, AC, ASF, TSF, and other study variables among children with gender specification

	BMI	AC	ASF	TSF
Boys				
BMI (kg/m^2)	1	0.74*	0.65*	0.58*
AC (cm)	0.74*	1	0.82	0.81*
ASF (cm)	0.65*	0.82	1	0.86*
TSF (cm)	0.58*	0.81*	0.86*	1
CHOL (cm)	0.15	0.16**	0.13	0.19**
HDL-C (mg/dl)	−0.10	−0.13	−0.19	−0.09
LDL-C (mg/dl)	0.16**	0.19**	0.21*	0.22*
Triglycerides (mg/dl)	0.18**	0.20**	0.15	0.10
Glucose (mg/dl)	0.17**	0.10	0.10	0.07
CRP (mg/l)	0.29*	0.32*	0.29*	0.33*
SBP	0.39*	0.30*	0.26*	0.30*
DBP	0.12	0.08	0.09	0.16**
Girls				
BMI (kg/m^2)	1	0.81*	0.71*	0.71*
AC (cm)	0.81*	1	0.82*	0.75*
ASF (cm)	0.71*	0.82*	1	0.84*
TSF (cm)	0.71*	0.75*	0.84*	1
CHOL (cm)	0.69	0.03	−0.05	−0.01
HDL-C (mg/dl)	−0.06	−0.04	−0.17	−0.17
LDL-C (mg/dl)	0.02	−0.01	−0.05	−0.01
Triglycerides (mg/dl)	0.15**	0.13	0.10	0.06
Glucose (mg/dl)	0.02	0.06	−0.10	−0.07
CRP (mg/l)	0.31*	0.23*	0.30*	0.31*
SBP	0.42*	0.31*	0.23*	0.31*
DBP	0.27*	0.16**	0.12	0.15**

AC, abdominal circumference; ASF, abdominal skin fold; BMI, body mass index; CHOL, cholesterol; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TSF, tricipital skin fold.
*$P < 0.01$, **$P < 0.05$.

boys. Among girls, BMI and AC also correlated with diastolic blood pressure ($P < 0.05$). We also found a significant correlation between CRP and SBP levels, but only in boys ($P = 0.01$).

We decided to divide the study children into three subgroups on the basis of their BMIs. **Table 3** shows a comparison of the study variables among these BMI tertiles with gender specification. In both genders, AC, CRP, and SBP showed a statistically significant increase along BMI tertiles. diastolic blood pressure, ASF, and TSF were significantly different only among the girls. Neither lipid profiles nor glucose plasma levels showed significant differences among groups. In both genders, the significant association between the anthropometric measures and SBP persisted after a multivariate linear regression analysis, adjusted for age, among both boys and girls. However, the relationship of CRP values with SBP levels lost statistical significance (**Table 4**).

DISCUSSION

This study shows direct and progressive correlations among adiposity (in terms of BMI), CRP concentrations, and SBP levels in a group of school-age Colombian children. Our findings are consistent with those of earlier studies performed in pediatric populations from developed countries.[17,18,22,23] To our knowledge, these are the first results from a Hispanic pediatric population living in a developing country, that show a positive relationship between adiposity and increase in subclinical inflammation. We also observed a direct relationship between CRP concentrations and SBP levels in boys; however this association lost significance after a multivariate analysis.

Although the role of obesity in the increasing risk of CVD is well recognized, the underlying etiological mechanisms are not well understood. In children, as in adults, excess adiposity is a consistent determinant of chronic low-grade inflammation.[17,23] The adipose tissue is not merely a reservoir of energy but also an active secretory organ that releases complement factors and proinflammatory cytokines in the circulation,[13] particularly IL-6 and TNF-α which, in turn, stimulate hepatic production of CRP, a highly sensitive measure of overall inflammation.[24]

There have been several studies that evaluated CRP concentrations in schoolchildren from developed countries.[17,18,22,23] Cook *et al.*[23] measured CRP concentrations in a population-based sample study that included 699 children of ages 10–11 years from ten population centers in England and Wales. This study reported that serum concentrations of CRP were positively correlated with BMI, heart rate, SBP, fibrinogen and high-density lipoprotein cholesterol, but not with other lipid parameters. Interestingly, it was found that a small

Table 3 | Distribution of study variables among children with gender specifications according to BMI tertiles

	T1	T2	T3
Boys			
n	48	56	52
BMI	15.1	17.0	21.2
Age (years)	9.9 ± 0.2	10.0 ± 0.3	10.1 ± 0.2
History of low birth weight	2 (4.1%)	4 (7.1%)	2 (3.8%)
AC (cm)[a]	58.7 ± 4.6	61.7 ± 3.8	72.1 ± 7.5
ASF (cm)	8.3 ± 4.8	10.4 ± 4.3	19.8 ± 8.8
TSF (cm)	9.2 ± 3.5	10.2 ± 2.2	15.1 ± 4.8
CHOL (mg/dl)[b]	152.1 ± 28.6	155.9 ± 25.3	161.7 ± 26.1
HDL-C (mg/dl)[b]	48.8 ± 8.6	50.4 ± 11.1	47.6 ± 8.9
LDL-C (mg/dl)[b]	87.0 ± 26.2	87.2 ± 22.2	95.9 ± 24.7
Triglycerides (mg/dl)[b]	81.3 ± 21.1	81.6 ± 21.2	90.7 ± 27.1
Glucose (mg/dl)[b]	82.2 ± 8.8	83.3 ± 7.6	85.2 ± 7.1
CRP (mg/l)[c]	0.6 ± 0.9	1.1 ± 2.2	1.9 ± 3.7
SBP (mm Hg)[a]	92 ± 9	97 ± 10	102 ± 10
DBP (mm Hg)	62 ± 7	63 ± 10	65 ± 8
Girls			
n	55	56	56
BMI	14.8	16.9	20.4
Age (years)	10.0 ± 0.1	10.1 ± 0.4	10.1 ± 0.2
History of low birth weight	3 (5.4%)	4 (7.1%)	3 (5.3%)
AC (cm)[a]	57.4 ± 4.3	61.5 ± 4.4	70.0 ± 6.3
ASF (cm)[a]	9.1 ± 3.5	11.4 ± 4.5	20.0 ± 7.4
TSF (cm)[a]	9.4 ± 2.2	11.6 ± 3.1	16.1 ± 4.4
CHOL (mg/dl)[b]	154.2 ± 26.4	167.5 ± 28.0	157.8 ± 21.2
HDL-C (mg/dl)[b]	49.0 ± 9.3	49.4 ± 8.7	48.7 ± 9.6
LDL-C (mg/dl)[b]	88.3 ± 22.7	99.8 ± 24.7	90.3 ± 21.1
Triglycerides (mg/dl)[b]	84.7 ± 20.1	91.9 ± 29.1	93.4 ± 30.4
Glucose (mg/dl)[b]	82.2 ± 6.4	83.1 ± 8.0	83.0 ± 11.9
CRP (mg/l)[c]	1.0 ± 1.6	1.3 ± 2.4	2.2 ± 3.3
SBP (mm Hg)[a]	92 ± 10	98 ± 9	102 ± 10
DBP (mm Hg)[c]	60 ± 8	66 ± 6	65 ± 9

Values represent means ± SD and *n* (%).
AC, abdominal circumference; ASF, abdominal skin fold; BMI, body mass index; CHOL, cholesterol; CRP, C-reactive protein; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TSF, triceps skin fold.
[a]Means are significantly different at 0.0001 level. [b]To obtain mmol/l values for cholesterol, HDL-C and LDL-C multiply values by 0.0259; for triglycerides, multiply values by 0.0113, and for glucose, multiply values by 0.0555. [c]Means are significantly different at 0.05 level.

number of children of South Asian origin presented CRP values 2.04 times (95% CI 1.23–3.36) higher than those found in Caucasian children of the same age, sex, and ponderal index. Ford *et al.*[17] in a study involving 2,486 boys and girls of ages 3–17 years who participated in a cross-sectional survey of the US population (NHANES, 1999–2000), reported, after a multiple linear regression analysis, that BMI was the best predictor of CRP. They also found some ethnicity-dependent differences in this association between the parameters in boys of ages 8–17 years and in girls of ages 8–11 years. Specifically, a higher concentration of CRP was observed in Mexican Americans (geometric mean values 0.60 and 0.76 mg/l, $P = 0.023$ and 0.015) in comparison with Caucasian children (geometric mean values 0.35 mg/l and 0.39 mg/l).

We found a significant positive correlation between BMI and CRP and, consequently, higher values of CRP among both boys and girls in the upper tertiles of BMI distribution. It is important to note that the CRP concentrations found in the second BMI tertile of both genders in our population are as high as those reported for overweight and obese subjects of similar age in some studies with Caucasian children.[25,26] Despite possible differences in methodology between the various studies, on the basis of our data and earlier findings[17,23] it is attractive to hypothesize that the Hispanic pediatric population in our study and children of South Asian origin share an ethnic predisposition to present a higher inflammatory response with lower adiposity levels than those reported for Caucasian populations. This ethnic predisposition has been previously demonstrated in Hispanic adults, who are more prone to develop insulin resistance, low-grade inflammation and high cardiovascular risk with smaller abdominal perimeters when compared with Caucasian populations.[27,28]

Our study showed that, as with BMI, central obesity (in terms of AC) also was positively associated with CRP plasma levels. Earlier, Gillum[18] had evaluated the association between waist-to-hip ratio, BMI, and CRP in a sample of Mexican American children included in the US Third NHANES, and found that central obesity measurements correlated well with CRP levels even after controlling for BMI. However, a limitation of this study was the low sensitivity of the nepholometric CRP assay used, which precluded researchers from analyzing CRP values as a continuous variable. In this study in a sample of Hispanic boys and girls, we used a high-sensitivity CRP test and confirmed that central obesity is significantly associated with CRP concentrations.

In our study, CRP concentrations were 25% higher in girls than in boys; however, this difference did not reach statistical significance. In adults, several reports have indicated that CRP levels are higher, and correlations between BMI and CRP response are stronger, in women compared with men.[29,30] Ford *et al.*[17] made similar observations in adolescents in the 1999–2000 US NHANES, and reported that female subjects of ages 16–19 years had higher CRP concentrations than male subjects of the same age group. Furthermore, in a representative sample of youths in the province of Quebec, Canada, Lambert *et al.*[31] found that CRP concentrations were higher in 9- to 16-year-old girls than in boys of the same age group. It has been suggested that these sex differences in CRP concentrations can be explained by the fact that women have a higher percentage of body fat as compared to men for a given BMI.[32] The increase in the levels of sex hormones during puberty could create these differences in fat

Table 4 | Multiple regression coefficients for systolic blood pressure on anthropometrics variables, before and after adjusting for CRP values and age

Independent variables	Boys				Girls			
	Univariate		Multivariate		Univariate		Multivariate	
	β	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value
BMI (kg/m^2)	1.567	0.0001	1.485	0.0001	1.669	0.0001	1.678	0.0001
AC (cm)	0.473	0.0001	0.461	0.0001	0.437	0.0001	0.421	0.0001
ASF (cm)	0.392	0.0001	0.381	0.0001	0.347	0.002	0.340	0.003
TSF (cm)	0.795	0.0001	0.738	0.0001	0.742	0.0001	0.740	0.0001
CRP (mg/l)[a]	4.396	0.197	4.741	0.145	2.729	0.391	3.202	0.309

β, regression coefficient; AC, abdominal circumference; ASF, abdominal skinfold; BMI, body mass index; CRP, C-reactive protein.
[a]CRP was adjusted for age.

distribution, which are reflected in a higher amount of adipose tissue in girls and consequently in elevated concentrations of inflammatory markers.[33] Because we included subjects at the preadolescent stage, when the differences in body fat distribution between boys and girls are not as obvious as they are later in life, smaller gender differences in CRP values than previously reported could be expected. However, it is important to note that, even at this early age in girls, a tendency to higher values of CRP concentrations exists.

Circulating CRP is not only a marker of chronic low-grade inflammation, but also a proposed key factor in the development of vascular disease.[34] A chronic low-grade inflammation, characterized by high levels of CRP, may produce disturbances in endothelial function, impairing endothelial ability to produce nitric oxide, leading to vasoconstriction.[19] A positive association has been consistently found between elevated CRP levels and higher blood pressure in adults, and elevated levels of CRP have been associated with an increased risk of developing hypertension.[19,20] The few studies analyzing this relationship in children have produced conflicting results.[17,23,31] Ford *et al.*,[17] in a large representative sample of US children, reported an independent association between CRP and SBP among girls of ages 12–17 years. In another study among 2,224 Canadian children, Lambert *et al.*[31] found an association between increased CRP and high SBP. However, this relationship was no longer statistically significant after adjusting for BMI. We observed, in our population, a direct relationship between CRP plasma concentration and SBP among boys; however, this association lost statistical significance after a multivariate regression analysis.

These conflicting results suggest a modest role for CRP in the association between obesity and blood pressure levels in children, and underlines the need to explore possible alternative pathophysiological mechanisms that would explain this relationship. Although the alteration in vascular function on account of chronic low-grade inflammation could be a predisposing factor for high blood pressure in obese children, other mechanisms such as disturbances in autonomic function and/or insulin resistance could also play a role. Childhood obesity has been associated with increased activity of the sympathetic nervous system.[35] The chronic sympathetic activation could produce elevation of blood pressure values by increasing renal tubular sodium reabsorption and peripheral vasoconstriction.[36] Evidence suggests that this autonomic imbalance caused by obesity could be related to high circulating levels of leptin and insulin.[37,38] However, these mechanisms have not been completely elucidated. Recently, the activation of the renin–angiotensin system has also been reported to be involved in the pathophysiology of obesity-associated hypertension.[39] Angiotensin receptors (AT_1 and AT_2 types), angiotensin converting enzyme, and angiotensinogen, are widely expressed in the human adipose tissue.[40,41] Further, the angiotensinogen gene expression is directly related to the degree of abdominal obesity.[42] These data demonstrate that the visceral adipocyte is both a generator and a target tissue of angiotensin II through the activation of AT_1 and AT_2 receptors. It has been suggested that increased angiotensin II stimulates adipocyte growth and differentiation and also sodium reabsorption, and raises the blood pressure in obese subjects.[43] There is also considerable evidence that activation of the renin–angiotensin system may contribute to the glomerular injury and nephron loss associated with obesity.[44] However, the exact role of the renin–angiotensin system in the relationship between adiposity and blood pressure in children remains to be determined.

In summary, the results obtained in our study of Hispanic school-age children show that adiposity is correlated with CRP concentrations and SBP values as previously described in Caucasian populations. However, after carrying out a multivariate analysis, we failed to find a significant relationship between low-grade inflammation and SBP levels. Further studies with larger sample sizes, that explore alternative pathophysiological mechanisms, are needed in order to elucidate the link between obesity and high blood pressure in children. This would help in defining early preventive and therapeutic strategies in childhood so as to diminish the high morbidity and mortality rates that occur in later life due to insulin resistance, hypertension, and atherosclerosis in our population.

Acknowledgments: We express our gratitude to Ofir Macias, Lilibeth Cuello and Sandra Pico, for their help in data collection, and to Jean Noël Guillemot for reviewing the article for language and style.

Disclosure: The authors declared no conflict of interest.

1. Strauss RS, Pollack H. Epidemic increase in childhood overweight, 1986–98. *JAMA* 2001; 286:2845–2848.
2. López-Jaramillo P, Pradilla LP, Castillo VR, Lahera V. Socioeconomic Pathology as a cause of regional differences in the prevalence of metabolic syndrome and pregnancy-induced hypertension. *Rev Esp Cardiol* 2007; 60:168–178.
3. Caballero B. A nutrition paradox—underweight and obesity in developing countries. *N Engl J Med* 2005; 352:1514–1516.
4. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. *JAMA* 2002; 288:1728–1732.
5. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics* 1998; 101:518–525.
6. Caprio S. Insulin resistance in childhood obesity. *J Pediatr Endocrinol Metab* 2002; 15:487–492.
7. Goran MI, Ball GD, Cruz ML. Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents. *J Clin Endocrinol Metab* 2003; 88:1417–1427.
8. Arslanian S. Type 2 diabetes in children: clinical aspects and risk factors. *Horm Res* 2002; 57:19–28.
9. Berenson GS, Srinivasan SR, Bao W, Newman WP, III, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med* 1998; 338:1650–1656.
10. Burke V, Beilin LJ, Dunbar D. Tracking of blood pressure in Australian children. *J Hypertens* 2001; 19:1185–1192.
11. Ribeiro J, Guerra S, Pinto A, Oliveira J, Duarte J, Mota J. Overweight and obesity in students and adolescents: relationship with blood pressure, and physical activity. *Ann Hum Biol* 2003; 30:203–213.
12. Falkner B, Gidding SS, Ramirez-Garnica G, Wiltrout SA, West D, Rappaport EB. The relationship of body mass index and blood pressure in primary care pediatric patients. *J Pediatr* 2006; 148:195–200.
13. Wellen KE, Hotamisligil GS. Obesity-induced inflammatory changes in adipose tissue. *J Clin Invest* 2003; 112:1785–1788.
14. Festa A, D'Agostino R Jr, Howard G, Mykkanen L, Tracy RP, Haffner SM. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). *Circulation* 2000; 102:42–47.
15. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A, Lowe GD, Pepys MB, Gudnason V. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *N Engl J Med* 2004; 350:1387–1397
16. Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, D'Agostino RB, Franzblau C, Wilson PW. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. *Stroke* 2001; 32:2575–2579.
17. Ford ES. C-Reactive protein concentration and cardiovascular disease risk factors in children: findings from the National Health and Nutrition Examination Survey 1999–2000. *Circulation* 2003; 108:1053–1058.
18. Gillum RF. Association of serum C-reactive protein and indices of body fat distribution and overweight in Mexican American children. *J Natl Med Assoc* 2003; 95:545–552.
19. Bautista LE, López-Jaramillo P, Vera LM, Casas JP, Otero AP, Guaracao AI. Is C-reactive protein an independent risk factor for essential hypertension? *J Hypertens* 2001; 19:857–861.
20. Bautista LE, Vera LM, Arenas IA, Gamarra G. Independent association between inflammatory markers (C reactive protein, interleukin-6, and TNF-α) and essential hypertension. *J Hum Hypertens* 2005; 19:149–154.
21. National High Blood Pressure Education Program Working Group. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics* 2004; 114:555–576.
22. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Low-grade systemic inflammation in overweight children. *Pediatrics* 2001; 107:E13.
23. Cook DG, Mendall MA, Whincup PH, Carey IM, Ballam L, Morris JE, Miller GJ, Stracham DP. C-reactive protein concentration in children: relationship to adiposity and other cardiovascular risk factors. *Atherosclerosis* 2000; 149:139–150.
24. Baumann H, Gauldie J. Regulation of hepatic acute phase plasma protein genes by hepatocyte stimulating factors and other mediators of inflammation. *Mol Biol Med* 1990; 7:147–159.
25. Aeberli I, Molinari L, Spinas G, Lehmann R, l'Allemand D, Zimmermann MB. Dietary intakes of fat and antioxidant vitamins are predictors of subclinical inflammation in overweight Swiss children. *Am J Clin Nutr* 2006; 84:748–755.
26. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, Allen K, Lopes M, Savoye M, Morrison J, Sherwin RS, Caprio S. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; 350:2362–2374.
27. Perez M, Casas JP, Cubillos-Garzon LA, Serrano NC, Silva F, Morillo CA, López-Jaramillo P. Using waist circumference as a screening tool to identify Colombian subjects at cardiovascular risk. *Eur J Cardiovasc Prev Rehabil* 2003; 10:328–335.
28. Garcia RG, Cifuentes AE, Caballero RS, Sanchez L, Lopez-Jaramillo P. A proposal for an appropriate central obesity diagnosis in Latin American population. *Int J Cardiol* 2006; 110:263–264.
29. Lear SA, Chen MM, Birmingham L, Frohlich JJ. The relationship between simple anthropometric indices and C-reactive protein: ethnic and gender differences. *Metabolism* 2003; 52:1542–1546.
30. Khera A, McGuire DK, Murphy SA, Stanek HG, Das SR, Vongpatanasin W, Wians FH, Grundy SM, de Lemos JA. Race and gender differences in C-reactive protein levels. *J Am Coll Cardiol* 2005; 46:464–469.
31. Lambert M, Delvin EE, Paradis G, O'Loughlin J, Hanley JA, Levy E. C-reactive protein and features of the metabolic syndrome in a population-based sample of children and adolescents. *Clin Chem* 2004; 50:1762–1768.
32. Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol* 1996; 143:228–239.
33. He Q, Horlick M, Thornton J, Wang J, Pierson RN, Heshka S, Gallagher D. Sex-specific fat distribution is not linear across pubertal groups in a multiethnic study. *Obes Res* 2004; 12:725–733.
34. de Ferranti S, Rifai N. C-reactive protein and cardiovascular disease: a review of risk prediction and interventions. *Clin Chim Acta* 2002; 317:1–15.
35. Rabbia F, Silke B, Conterno A, Grosso T, De Vito B, Rabbone I, Chiandussi L, Veglio F. Assessment of cardiaca autonomic modulation during adolescent obesity. *Obes Res* 2003; 11:541–548.
36. Esler M, Straznicky N, Eikelis N, Masuo K, Lambert G, Lambert E. Mechanisms of sympathetic activation in obesity-related hypertension. *Hypertension* 2006; 48:787–796.
37. Eikelis N, Schlaich M, Aggarwal A, Kaye D, Esler M. Interactions between leptin and the human sympathetic nervous system. *Hypertension* 2003; 41:1072–1079.
38. Guizar JM, Ahuatzin R, Amador N, Sanchez G, Romer G. Heart autonomic function in overweight adolescents. *Indian Pediatr* 2005; 42:464–469.
39. Rahmouni K, Correia ML, Haynes WG, Mark AL. Obesity-associated hypertension: new insights into mechanisms. *Hypertension* 2005; 45:9–14.
40. Engeli S, Gorzelniak K, Kreutz R, Runkel N, Distler A, Sharma AM. Co-expression of renin-angiotensin system genes in human adipose tissue. *J Hypertens* 1999; 17:555–560.
41. Karlsson C, Lindell K, Ottosson M, Sjostrom L, Carlsson B, Carlsson LM. Human adipose tissue expresses angiotensinogen and enzymes required for its conversion to angiotensin II. *J Clin Endocrinol Metab* 1998; 83:3925–3929.
42. Giacchetti G, Faloia E, Sardu C, Camilloni MA, Mariniello B, Gatti C, Garrapa GG, Guerrieri M, Mantero F. Gene expression of angiotensinogen in adipose tissue of obese patients. *Int J Obes Relat Metab Disord* 2000; 24:S142–S143.
43. Segura J, Ruilope LM. Obesity, essential hypertension and renin-angiotensin system. *Public Health Nutr* 2007; 10:1151–1155.
44. Wofford MR, Hall JE. Pathophysiology and treatment of obesity hypertension. *Curr Pharm Des* 2004; 10:3621–3637.