Alanine Aminotransferase and High Sensitivity C-Reactive Protein: Correlates of Cardiovascular Risk Factors in Youth

Antônio C. Oliveira, MD, Ana M. Oliveira, MD, Marcele S. Almeida, RN, Agnaluce M. Silva, PhD, Luis Adan, PhD, and Ana M. Ladeia, MD, PhD

Objective The association between high-sensitivity C-reactive protein (hs-CRP) and alanine aminotransferase (ALT) with clinical/metabolic variables was evaluated in overweight Brazilian children and adolescents.

Study design Oral glucose tolerance test was performed in 407 students (273 overweight/obese, 11.3 ± 3.1 y). Measurements included body mass index (BMI), waist circumference (WC), blood pressure, lipids, insulin, hs-CRP, and ALT. Overweight/obese was defined using BMI *z*-score; insulin resistance (IR) by homeostatic model assessment: insulin resistance (HOMA-IR); and metabolic syndrome (MS) in accordance with the modified NCEP-ATPIII.

Results As weight increased, systolic blood pressure (SBP), diastolic blood pressure (DBP), triglycerides (TG), insulin, HOMA-IR, hs-CRP, ALT, ALT, hs-CRP, and AST and the number of MS components (nMSc) also increased ($P \leq .001$ for all). Subjects with hs-CRP and ALT above the median had higher BMI *z*-score, WC, SBP, DBP, TG, AST, insulin, HOMA-IR, and nMSc than those with both markers below the median ($P \leq .002$ for all). After adjustment for age, sex and ethnicity, BMI *z*-score (OR, 1.5; CI, 1.38 to 1.86; $P < .001$), WC (OR,1.3; CI, 1.19 to 1.43; $P < .001$) SBP (OR, 1.2; CI, 1.03 to 1.38; $P = .015$), DBP (OR, 1.4; CI, 1.15 to 1.69; $P < .001$), TG (OR, 1.8; CI, 1.29 to 2.62; $P < .001$), insulin (OR, 1.4; CI, 1.23 to 1.71; $P < .001$), HOMA-IR (OR, 1.2; CI, 1.09 to 1.29; $P < .001$) and nMSc (OR, 2; CI, 1.16 to 3.47; $P = .012$) were independently associated with high ALT and hs-CRP. For every 5-cm increase in WC and every 1-point increase in BMI *z*-score, there were a 1.3- and 1.5-fold greater chance of having increased ALT and hs-CRP, respectively.

Conclusions Simultaneous measurements of ALT and hs-CRP should be considered as a screening test for metabolic syndrome and cardiovascular disease risk factors in overweight/obese children/adolescents. *(J Pediatr 2008;152:337-42)*

Obesity is on the rise in youth[1,2] and is a predictor of adulthood obesity.[3,4] Abdominal obesity is an independent and modifiable risk factor for cardiovascular disease (CVD) and type 2 diabetes mellitus (DM2).[5] The adipose tissue may play a role in the development of a chronic low-grade inflammatory state that may lead to endothelial dysfunction and vascular damage.[7] Some studies have shown a relationship between high sensitivity C-reactive protein (hs-CRP) and CVD,[8,9] as well as DM.[10]

Recent evidence suggests that elevated liver enzymes, especially alanine aminotransferase (ALT) may serve as a surrogate marker for DM2.[11] The Insulin Resistance Atherosclerosis Study demonstrated that individuals with the highest levels of ALT had significantly greater risk of developing diabetes, irrespective of CRP[10] levels, and therefore, when used in combination, these two markers may have additive predictive ability for identifying subjects at risk of developing DM.[10]

We hypothesized that clinical and metabolic risk factors for cardiovascular disease, such as obesity, abdominal obesity, dyslipidemia, glucose metabolism disturbances, insulin resistance (IR), and metabolic syndrome are associated with increased ALT and hs-CRP. Thus, the association between hs-CRP and ALT with clinical and metabolic measures was evaluated in a sample of overweight Brazilian children and adolescents.

ALT	Alanine aminotransferase	hs-CRP	High-sensitivity C-reactive protein
BMI	Body mass index	IR	Insulin resistance
CVD	Cardiovascular disease	MS	Metabolic syndrome
DBP	Diastolic blood pressure	SBP	Systolic blood pressure
HOMA	Homeostatic model assessment	TG	Triglycerides

From the Bahian School of Medicine and Public Health (A.C.O., A.M.L.), Science Development Foundation of Bahia, Bahia, Brazil; Department of Health (A.C.O., A.M.O., M.S.A.), State University of Feira de Santana, Feira de Santana, Bahia, Brazil; Department of Pediatrics (A.M.O., L.A.), Federal University of Bahia School of Medicine, Salvador, Bahia, Brazil; and Department of Clinical Pathology Laboratory (A.M.S.), Salvador, Bahia, Brazil.

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Reprint requests: Dr. Antonio C. Oliveira, Av. Senhor dos Passos, 407, Feira de Santana-BA - Brazil 44010-230. E-mail: leegoza@uol.com.br.

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METHODS

Study Participants and Procedures

The study was conducted in Feira de Santana, Bahia, Brazil, at state and private schools. Selection was based on lists provided by the schools in the proportion of 2 overweight or obese to 1 normal weight subject. 407 students (229 girls; 273 with excessive weight; mean age ± SD, 11.3 ± 3.1 years) were included in the protocol. Subjects were eligible if they were healthy, 4 to 18 years of age, had no history of current or past excessive alcohol drinking, as defined by and average daily consumption of more than 20 g alcohol, or no history of chronic liver disease, and were not taking medication that might affect liver function tests. Exclusion criteria were smoking, any acute illnesses, or any treatment of inflammatory or chronic infectious disease during the previous 3 months.

Anthropometric measurements were obtained in triplicate and the mean value was used. Body weight was measured to the nearest 0.1 kg using a digital scale, and height was measured to the nearest centimeter, in the standing position, using a wall stadiometer. The waist circumference (WC) was measured by using a tape measure situated midway between the last rib and the upper edge of the right iliac crest, at the end of a normal expiration, and was recorded to the nearest millimeter, as described by the National Center of Health Statistics.[11] The blood pressure (BP) was measured, after a period of rest, three times consecutively, at five minute intervals, in accordance with the method and criteria established by the Task Force on Blood Pressure Control in Children.[12]

The students were invited to the clinic at 8:00 AM after an overnight 12-hour fast. Their weight, height, WC, and BP were measured, and their body mass index (BMI) was calculated. Baseline fasting measurements of plasma glucose, insulin, HDL-cholesterol (HDL-C), triglycerides (TG), ALT and hs-CRP were obtained. A standard 2-hour oral glucose tolerance test (OGTT) was performed, in accordance with the American Diabetes Association guidelines,[13] and blood samples were obtained at 120 minutes to measure plasma glucose.

The local Human Research Ethics Committee reviewed and approved the study, and written informed consent/assent was obtained from guardians and children/adolescents.

Metabolic Phenotyping

The criteria used to diagnose the metabolic syndrome (MS) were modified from those of the National Cholesterol Education Program's Adult Treatment Panel,[14] and the students were diagnosed by the concomitant presence of at least three of the following five clinical features: waist circumference (WC) more than 75th percentile[15]; fasting plasma glucose ≥100 mg/dL, or 2-hour glucose post-challenger ≥200 mg/dL[16]; TG >100 mg/dL and >130 mg/dL for younger than 10 years and between 10 to 19 years, respectively[15]; HDL-C <40 mg/dL and <35 mg/dL for younger than 10 years and between 10 to 19 years, respectively[17]; and systolic/diastolic BP ≥95th percentile by height percentile for age and sex.[18]

To compare BMI across different ages and in both boys and girls, BMI *z*-score was calculated, and a threshold of 1.5 or more defines excess weight. The subjects were then classified as overweight (*z*-score of 1.5 to 2) or obese (*z*-score above 2.0).

The degree of insulin resistance was determined with the use of a homeostatic model (homeostatic model assessment: insulin resistance) (HOMA-IR), based on serum fasting glucose and insulin levels (product of glucose concentrations [expressed as milligrams per deciliter], and insulin [expressed as milliunits per milliliter] divided by a constant [405]) was used as a measure of IR. The cutoff used was 3.16, as described by Keskin et al.[19]

Biochemical Analysis

Sera were stored at −70°C until they were analyzed. Plasma glucose, HDL-C, TG, and concentrations were measured by automated enzymatic photometry; ALT using a standard automatic kinetic enzymatic assay; serum insulin levels with a solid phase radioimmunoassay unit (Linco Laboratories); hs-CRP by fixed time nephelometry (reporting range 0.2 mg/L to 10 mg/L, coefficient of variation [CV] < 7%) (Dade Behring, Deerfield, IL). The population was classified into four groups based on the ALT and hs-CRP median: group 1, integrating individuals below median of both variables; group 2 subjects with ALT above and hs-CRP below median; group 3 with ALT below and hs-CRP above median and group 4 with both features above median.

Statistical Analysis

A descriptive analysis was performed, and the data were expressed either as frequencies or as mean values ± standard deviation (SD) with 95% confidence intervals. Geometric means were reported for hs-CRP. Quartiles of BMI *z*-score were computed and the subjects were classified into these quartiles. Differences between quartiles were tested with analysis of variance (ANOVA) for continuous variables and by the χ^2 test for proportions. Mantel-Haenszel χ^2 statistics were used to evaluate trends in proportions across ALT and hs-CRP categories. Multivariate analysis was done, using logistic regression to model categorized hs-CRP and ALT. In the model, variables that attained 20% of significance in the univariate analysis were included. In the final model only the statistically significant covariables were maintained. SPSS (Statistical Packard for Social Sciences) for Windows statistical software version 10.0 was used for all calculations. A value of $P < .05$ defined statistical significance.

RESULTS

Seventy-two subjects (17.7%) fulfilled the MS diagnosis and their hs-CRP and ALT means were 3.4 ± 2.9 mg/L and 29.2 ± 15.6 U/L, respectively. Anthropometric and metabolic

Table I. Baseline anthropometric and metabolic characteristics of the population according to the weight

Variables	Excessive weight (n = 273)	Normal weight (n = 134)	P value†
Age (y)	11.1 ± 3.1	11.7 ± 3.2	.072
Sex (boys) n (%)	128 (46.9)	50 (37.3)	.067
Ethnic group (white) n (%)	133 (48.7)	34 (25.4)	<.001*
BMI (z-score)	3.4 ± 1.1	–0.2 ± 1.1	<.001*
Waist circumference (cm)	87.6 ± 13.4	65.9 ± 9.1	<.001*
Systolic blood pressure (mm Hg)	110.7 ± 16.3	98.2 ± 13.4	<.001*
Diastolic blood pressure (mm Hg)	69.5 ± 12.4	60.9 ± 9.8	<.001*
Fasting plasma glucose (mg/dL)	74.7 ± 10.2	75.8 ± 9.8	.393
Triglycerides (mg/dL)	120.8 ± 69.4	77.8 ± 32.4	<.001*
HDL-cholesterol (mg/dL)	39 ± 8.5	43.4 ± 9.2	<.001*
Fasting plasma insulin (mg/dL)	21.2 ± 15.2	7.2 ± 4.8	<.001*
HOMA-IR means	3.9 ± 2.9	1.3 ± 0.9	<.001*
hs-CRP (geometric mean) (mg/L)	1.3	0.7	<.001*
hs-CRP (median) (mg/L)	2.5	0.4	<.001*
hs-CRP (>median) n (%)	176 (64.5)	27 (20.1)	<.001*
ALT (median) (U/L)	25	21.5	.001*
ALT means (U/L)	26 ± 11.2	22 ± 6.6	.001*
ALT (>median) n (%)	146 (53.5)	52 (38.8)	.005*
ALT plus hs-CRP (>median) n (%)	104 (38.1)	12 (9)	<.001*
MS n (%)	72 (26.4)	0 (0)	<.001*
MS components (n)	1.9 ± 0.9	0.3 ± 0.6	<.001*

Data are expressed as mean ± SD (range) and frequencies (%).
*Frequencies for "yes" group.
†Comparison of group with excessive weight and with lean group.

data are shown in Table I. Values for BMI *z*-score ($P <$ .001), WC ($P <$ .001), SBP ($P <$ .001), DBP ($P <$ .001), TG ($P <$ .001), insulin ($P <$ .001), and HOMA-IR ($P <$ .001) increased significantly with increasing weight and HDL-C ($P <$ .001) decreased. There were no differences between age ($P =$ .072), sex, ($P =$ .067), and fasting glucose ($P =$ .393). There were no cases of DM, IGT and IFG. The hs-CRP geometric means (1.3 vs 0.7, $P <$ .001) and median (2.5 vs 0.4, $P <$ .001) were higher in the excessive weight group, irrespective of whether or not MS was present. Whites were predominant among the overweight group ($P <$ .001). Overweight was strongly associated with the severity of IR ($P <$ .001), diagnosis of MS ($P <$ .001) and the number of MS components (nMSc) ($P <$ .001).

When the subjects were classified into 4 groups by BMI *z*-score quartiles and were compared with demographic, anthropometric, and metabolic variables, it was observed that as weight increased, SBP ($P <$ .001), DBP ($P <$ .001), TG ($P <$ .001), fasting insulin ($P <$ .001), HOMA-IR ($P <$ .001), hs-CRP ($P <$ .001), ALT ($P <$ .001), ALT and hs-CRP ($P <$ .001), AST ($P =$ .001) and nMSc increased significantly, as shown in Table II.

To identify the association between high levels of CRP and ALT and the risk factors for metabolic and CVD, the authors elected to further classify the sample, based on the median of ALT (23 U/L) and hs-CRP (1.49 mg/L) into 4 groups: low ALT and low hs-CRP (group 1), high ALT and low hs-CRP (group 2), low ALT and high hs-CRP (group 3), and high ALT and high hs-CRP (group 4). When differences in demographic, anthropometric, and metabolic variables (Table III) were assessed across the subgroups, significant differences were found for ethnic group (P for trend = .04) and the presence of MS (P for trend < .001). Furthermore, weight categories (P for trend < .001), WC (P for trend <0.001), SBP (P for trend < .001), DBP (ρ for trend < .001), levels of TG (P for trend < .001), insulin (P for trend < .001), HOMA-IR (P for trend < .001), and TG/HDL-C ratio (P for trend < .001) rose to significantly higher levels from group 1 to 4. The variables with significant elevations across the groups are demonstrated in the Figure.

ALT and hs-CRP were positively correlated with BMI *z*-score ($r = 0.35$, $P <$ .001), WC ($r = 0.33$, $P <$ .001), TG ($r = 0.20$, $P <$ .001), TG/HDL-C ratio ($r = 0.19$, $P <$ .001), insulin ($r = 0.22$, $P <$ .001), HOMA-IR ($r = 0.21$, $P <$ .001), and nMSc ($r = 0.27$, $P <$ .001) in the whole population.

Furthermore, in a multiple logistic regression analysis, adjusted for age, sex, and ethnic group, high levels of ALT and hs-CRP were independently associated with high SBP (OR, 1.2; CI,1.03 to 1.38; $P =$ .015), and DBP (OR, 1.4; CI, 1.15 to 1.69; $P <$ .001), hypertriglyceridemia (OR, 1.8; CI, 1.29 to 2.62; $P <$ .001), high levels of insulin (OR, 1.4; CI, 1.23 to 1.71; $P <$ .001), and HOMA-IR (OR, 1.2; CI, 1.09 to 1.29; $P <$ .001), as well as with the nMSc (OR, 2; CI, 1.16 to 3.47; $P =$ .012).

For every 5-cm increase in WC, there was a 1.3-fold greater chance of having increased ALT and hs-CRP (OR, 1.3; CI, 1.19 to 1.43; $P <$ .001) and for every 1-point increase in BMI *z*-score there was 1.5-fold greater chance of having the same alteration (OR, 1.5; CI, 1.38 to 1.86; $P <$ .001).

Table II. Baseline anthropometric and metabolic characteristics of the population according to the weight in quartiles

Variables	Quartile 1 (≤0.68) (n = 102)	Quartile 2 (0.69-2.59) (n = 103)	Quartile 3 (2.60-3.79) (n = 102)	Quartile 4 (≥3.80) (n = 100)	*P* value†
Age (y)	11.5 ± 3.2	11.9 ± 3.1	11.4 ± 2.8	10.2 ± 3.3	.001*
Sex (boys) n (%)	39 (38.2)	36 (35)	48 (47.1)	55 (55)	.004*
Ethnic group (white) n (%)	23 (22.5)	46 (44.7)	47 (46.1)	51 (51)	<.001*
BMI (z-score)	-0.6 ± 0.9	1.8 ± 0.5	3.2 ± 0.3	4.6 ± 0.7	<.001*
Waist circumference (cm)	63.5 ± 7.8	78.1 ± 10.3	87.7 ± 10.2	92.7 ± 15.8	<.001*
Systolic blood pressure (mm Hg)	96.2 ± 13	105.2 ± 12.4	108.6 ± 14.5	116.7 ± 18.8	<.001*
Diastolic blood pressure (mm Hg)	60.2 ± 9.7	65.1 ± 10.3	68.3 ± 11.5	73.4 ± 13.5	<.001*
Fasting plasma glucose (mg/dL)	76.2 ± 9.3	74.1 ± 10.6	74.6 ± 11.1	75.5 ± 9.2	.462
Triglycerides (mg/dL)	73.5 ± 25	101.4 ± 67.7	119.6 ± 66.2	132.8 ± 67	<.001*
HDL-cholesterol (mg/dL)	43.2 ± 9.3	40.5 ± 8.2	40.2 ± 10.1	37.9 ± 7.5	<.001*
TG/HDL-C ratio	1.7 ± 0.7	2.6 ± 1.9	3.1 ± 1.9	3.7 ± 2.2	<.001*
Fasting plasma insulin (mg/dL)	7.1 ± 4.7	13.6 ± 11.4	21.7 ± 14.5	24.3 ± 16.8	<.001*
HOMA-IR means	1.3 ± 0.9	2.4 ± 2.1	4.1 ± 2.9	4.5 ± 3.1	<.001*
hs-CRP (geometric mean) (mg/dL)	0.7	1	1.3	1.5	<.001*
hs-CRP (median)	0.3	1.3	2.5	3.6	<.001*
hs-CRP (>median) n (%)	16 (15.7)	48 (46.6)	65 (63.7)	74 (74)	<.001*
ALT means (U/L)	22.1 ± 6.7	22.6 ± 7.1	26.5 ± 11.3	27.5 ± 13	<.001*
ALT (>median) n (%)	41 (40.2)	41 (39.8)	49 (48)	67 (67)	<.001*
ALT plus hs-CRP (>median) n (%)	9 (8.8)	23 (22.3)	34 (33.3)	50 (50)	<.001*
MS n (%)	0 (0)	7 (6.8)	22 (21.6)	43 (43)	<.001*
MS components (n)	0.2 ± 0.4	1.1 ± 0.9	1.8 ± 0.8	2.3 ± 0.8	<.001*

Data are mean ± SD for continuous variables and n (%) for categorical. *P* values are based on analysis of variance for continuous variables and *P* for trend for categorical variables.

In a multiple logistic regression now including MS as the dependent variable and ALT and hs-CRP as the independent variables, also adjusted for age, sex, and ethnic group, subjects with increased ALT and hs-CRP had an almost 2-fold greater chance of having MS (OR, 1.9; CI, 1.12 to 3.34; $P = .016$) when compared with those with both ALT and hs-CRP in a normal range.

DISCUSSION

Chronic conditions, such as CVD, are now affecting young people and generally require ongoing treatment for many years. In developing countries, these diseases alone account for nearly 27% of all deaths, and 9% of all years of healthy life lost to disease worldwide.[20] Despite this, there are some limitations of current risk strategies to predict CVD.[21]

CVD is increasing in young people and it has been confirmed that children with high systolic blood pressure are at increased risk of hypertension and metabolic syndrome later in life.[22] Thus, it is of paramount importance to find a cost-effective marker that could predict chronic diseases in youth, especially in low and lower-middle socioeconomic status countries.

Recent findings indicate that there is a relationship between elevated levels of inflammatory markers, such as hs-CRP, and increased risk of DM and CVD. In clinical practice, the usefulness of predicting MS and cardiovascular risk has also been demonstrated in adults.[23] Some of the cardiovascular risk factors are related to IR.[5] Several reports indicate that inflammation may be driven by IR and suggest that low-grade inflammation and IR may be pathogenic bases of DM rather than its outcome.[6] The relationship between high levels of CRP and ALT with uric acid, a nontraditional new marker of inflammation, MS, and subclinical coronary atherosclerosis,[24] found in this study, emphasizes the potential role of these combined markers as a screening test to identify children at risk for CVD.

Hypertriglyceridemia, prediabetic state, and DM, as well as fatty liver disease,[25] are all related to IR.[2,26] Nonalcoholic fatty liver disease (NAFLD) may play a role in the development of the metabolic syndrome, IR and type 2 DM.[5] This relationship may involve elevation of ALT levels. The International Diabetes Federation also included this disorder as a new component of the MS and an Italian study concluded that NAFLD should rank as an additional CV and metabolic risk factor, because it correlates with decreased insulin sensitivity independently of BMI.[27] In this study, a positive correlation between ALT and CRP and triglycerides and TG/HDL ratio was found. It is interesting to note that hypertriglyceridemia is also associated with both NAFLD and CVD.[5,28] Furthermore, the TG/HDL ratio has emerged as a new marker of atherogenic dyslipidemia, inversely related to LDL size and positively related to LDL concentration.[29]

MS is a cluster of CV risk factors composed of hypertriglyceridemia, low HDL-C levels, and carbohydrate metabolic disturbances, including impaired fasting glucose, impaired glucose tolerance, and DM2. Therefore, the asso-

Table III. Baseline anthropometric, clinical, and metabolic characteristics of subjects based on the ALT plus hs-CRP median (above or below)

Variables	Group 1 ALT ↓ + PCR ↓ (n = 122)	Group 2 ALT ↑ + PCR ↓ (n = 82)	Group 3 ALT ↓ + PCR ↑ (n = 87)	Group 4 ALT ↑ + PCR ↑ (n = 116)	*P* value†
Age (y)	11.4 ± 3.1	10.9 ± 3.1	11.2 ± 3.2	11.4 ± 3.2	.725
Sex (boys) n (%)	47 (38.5)	40 (48.8)	33 (37.9)	58 (50)	.183
Ethnicity (white) n (%)	47 (38.5)	29 (35.4)	30 (34.5)	61 (52.6)	.040*
Overweight n (%)	9 (7.4)	4 (4.9)	5 (5.7)	7 (6)	.715
Obesity n (%)	46 (37.7)	38 (46.3)	67 (77)	97 (83.6)	<.001*
BMI (kg/m^2)	19.9 ± 4.7	21.3 ± 5.7	24.5 ± 5.8	26.4 ± 6.1	<.001*
BMI (z-score)	1.1 ± 1.9	1.6 ± 2.2	2.8 ± 1.4	3.3 ± 1.7	<.001*
WC (cm)	73.2 ± 13.4	76.5 ± 15.8	84.1 ± 14.9	88.2 ± 14.8	<.001*
Systolic BP (mm Hg)	102.3 ± 13.2	104 ± 17.3	109.9 ± 18	110.4 ± 16.6	<.001*
Diastolic BP (mm Hg)	63.1 ± 10.6	64.8 ± 10.7	69 ± 12.6	70.2 ± 13.4	<.001*
Glucose (mg/dL)	74.8 ± 10.4	75.8 ± 10.7	76.3 ± 10.1	73.9 ± 9.2	.331
Triglycerides (mg/dL)	87.7 ± 43.4	106.4 ± 58.1	106.6 ± 63.4	126.9 ± 76.9	<.001*
HDL-C (mg/dL)	42.1 ± 9.1	40 ± 8.8	39 ± 7.1	40.1 ± 10	.069
TG/HDL-C	2.2 ± 1.4	2.9 ± 2	2.9 ± 2.1	3.3 ± 2.0	<.001*
Uric acid (mg/dL)	3.5 ± 1	3.6 ± 1	3.8 ± 1	4.1 ± 1.2	<.001*
Insulin (mg/dL)	12.2 ± 9.6	13.2 ± 11.3	18.8 ± 15.4	22.7 ± 17	<.001*
HOMA-IR (means)	2.2 ± 1.8	2.4 ± 2	3.6 ± 3.1	4.1 ± 3.1	<.001*
MS	7 (5.7)	15 (18.3)	20 (23)	30 (25.9)	<.001*
MS components (n)	0.8 ± 0.9	1.2 ± 1.2	1.7 ± 1	1.8 ± 0.9	<.001*

Data are mean ± SD for continuous variables and n (%) for categorical.
↓ = below median; ↑ = above median.
†*P* based on analysis of variance for continuous variables and *P* for trend for categorical variables.

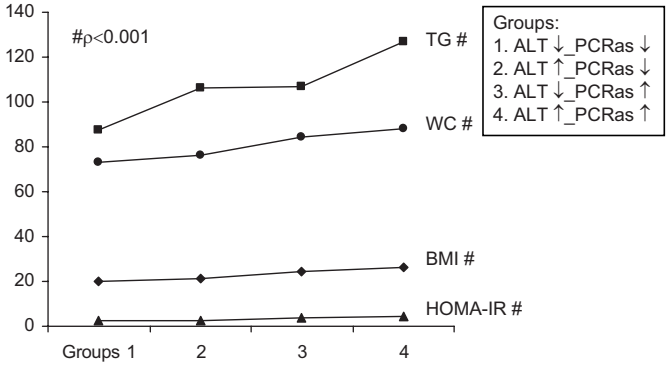

Figure. Clinical and metabolic parameters of subjects based on the ALT plus hs-CRP medians.

ciation between nMSc with ALT and CRP supports the inclusion of both as part of a routine for pediatricians. In youth, MS is on the rise[2] but still underdiagnosed.[30]

Thus, the main finding of this study is that ALT and hs-CRP is a better marker of IR than each of them separately. This is clearly demonstrated by the association between these combined markers and clinical and laboratorial measures of IR, thus emerging as a marker of CV and metabolic disorders. When the sample was classified into 4 groups, based on the ALT and hs-CRP median, a progressive increase in the SBP and DBP values, TG, uric acid, insulin, and HOMA-IR levels was found, demonstrating the usefulness of these markers together. The fact that there was no statistical significance with each variable alone emphasizes the importance of this finding.

Given the limitations of current risk assessment strategies, adjunctive markers are needed to improve the prediction of cardiovascular and metabolic disorders. In clinical practice it may be useful to include both ALT and hs-CRP as a screening test for cardiovascular risk factors in overweight/obese children and adolescents.

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