Obesity indicators and cardiometabolic status in 4-y-old children[1–3]

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ABSTRACT

Background: In adults and adolescents, obesity is positively associated with cardiovascular disease risk factors; however, evidence in preschool children is scarce.

Objective: The objective was to assess the relations between obesity indicators and cardiometabolic risk factors in 324 Chilean children 4 y of age.

Design: We collected anthropometric measurements and calculated general indicators of obesity [weight, body mass index (BMI), sum of 4 skinfold thicknesses, percentage fat, and body fat index] and central obesity (waist circumference, waist-to-hip ratio, waist-to-height ratio, and truncal fatness based on skinfold thickness). We measured blood sample concentrations of C-reactive protein, interleukin-6, homeostasis model assessment of insulin resistance, triglycerides, and total, LDL, and HDL cholesterol. We used correlation and multiple linear regression analyses.

Results: The prevalence of obesity (BMI-for-age z score >2, World Health Organization 2006), central obesity ($\geq$90th percentile, third National Health and Nutrition Examination Survey), and lipid disorders was high (13%, 11%, and $\geq$ 20%, respectively), and 70% of the children had at least one cardiometabolic risk factor. Most correlations between obesity and central obesity indicators were moderate to strong ($0.40 < r < 0.96$). Obesity was positively but weakly associated with C-reactive protein in both sexes and with homeostasis model assessment of insulin resistance only in girls (all $r < 0.3$, $P < 0.05$). Obesity indicators were unrelated to interleukin-6 and lipid concentrations ($P > 0.05$). Overall, obesity indicators explained, at most, 8% of the variability in cardiometabolic risk factors.

Conclusions: Obesity and central obesity were common, and most of the children had at least one cardiometabolic risk factor, particularly lipid disorders. Obesity and central obesity indicators were highly intercorrelated and, overall, were weakly related to cardiometabolic status. At this age, body mass index and waist circumference were poor predictors of cardiometabolic status. *Am J Clin Nutr* 2010;91:166–74.

INTRODUCTION

Childhood obesity is a major public health problem worldwide. In past decades, prevalence has increased relentlessly in almost all countries of the world, including developing countries (1). Of particular concern is the fact that obesity-related risk factors that were traditionally thought of as exclusive of adults are now increasingly observed among children (2).

Although several large cohort studies support an association between childhood obesity and prevalence of cardiovascular disease (CVD) risk factors [ie, high C-reactive protein (CRP), interleukin-6 (IL-6), diabetes, dyslipidemia, and hypertension] in childhood and adulthood, none have specifically focused on the preschool years (3–6). The few studies that have described cardiometabolic status in young children have shown conflicting results on the relation between fatness and CVD risk factors (7–11). In the ALSPAC cohort study, body mass index (BMI) was unrelated to blood lipid concentrations at 32 and 43 mo of age, and higher waist circumference (WC) was weakly associated with higher triglyceride and lower HDL-cholesterol concentrations only in boys (7). In contrast with these findings, the Healthy Start project reported that obesity was positively associated with triglycerides, negatively associated with HDL-cholesterol concentrations, and unrelated to total cholesterol (TC) in preschoolers attending the US Head Start program (11). Another study conducted in 2–3-y-old US children showed that weight, BMI, WC, and skinfold thickness were positively but weakly related to fasting insulin and were unrelated to homeostasis model assessment of insulin resistance (HOMA-IR) and CRP (9). The Early Bird study reported positive relations between BMI and HOMA-IR and triglyceride among 5-y-old children; however, obesity accounted for only a small proportion of the variability in the outcomes (10). More recently, a study in Swedish children found no association between BMI or weight and fasting insulin, HOMA-IR, TC, and triglycerides at 4 y of age (8). Thus, the contribution of fatness to cardiometabolic risk status in preschool children remains uncertain. Clarifying these associations is particularly relevant to define early screening guidelines for CVD risk as well as for targeting preventive interventions. Therefore, the aims of this study were *1*) to characterize the obesity and cardiometabolic status of 4-y-old Chilean children, and *2*) to assess the relations of obesity indicators with cardiometabolic markers. We placed special emphasis on BMI and WC because these measures are simple to

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collect and use to monitor children in a clinical setting or public health evaluation.

SUBJECTS AND METHODS

Subjects

Our study sample was drawn from children enrolled in a cohort study that assesses the association of early postnatal growth and timing of adiposity rebound. All children aged 3.0–4.9 y who attended nursery schools of the National Nursery Schools Council Program (JUNJI) from the south area of Santiago, Chile, in September 2006; were singletons born between >37 and ≤42 wk gestational age; had a birth weight ≥2500 g (data retrieved from medical registries; national prevalence of birth weight <2500 g is 5.0%) (12); and had no physical or psychological conditions that could severely affect growth were eligible for the study. Almost 85% of the total eligible population agreed to participate (n = 1121), and there were no significant differences in age, sex, birth, or anthropometric measures at 4 y between participants and nonparticipants. For the current analyses, we recruited the first 325 children aged 3.5–4.5 y who signed up for the primary study and who had a negative history of genetic metabolic diseases (eg, type 1 diabetes and genetic dyslipidemias) or chronic conditions that might increase systemic inflammation (eg, asthma and arthritis) or who reported oral or inhaled steroid use. For these analyses, we excluded one child whose blood sample we were unable to obtain; thus, our final sample size was 324 children. Assuming 80% power and a 2-tail significance level of 0.05, the smallest correlation we could detect with this sample size was 0.20 in girls and 0.18 in boys; these correlations are considered to correspond to a small effect size (13). The study protocol was approved by the Executive Director of the JUNJI Program, the Institutional Review Board of Emory University and that of the Institute of Nutrition and Food Technology of the University of Chile. Informed consent was obtained from all parents or guardians of the children.

Anthropometric measures

A single registered dietitian measured weight; height; waist, hip, and calf circumferences; and triceps, biceps, subscapular, suprailiac, and abdominal skinfold thicknesses using standardized procedures. Weight was measured with a portable electronic scale (Seca 770; Seca, Hamburg, Germany) with a precision of 0.1 kg, height was measured with a portable stadiometer (Harpenden 603; Holtain Ltd, Crosswell, United Kingdom) to the nearest 0.1 cm, and waist (ie, minimum circumference between the iliac crest and the rib cage), hip, and calf circumferences were measured with a metal inextensible tape (Lufkin W606PM; CooperTools, Raleigh, NC) to the closest 0.1 cm. Skinfold thicknesses were measured in triplicate on the right side of the body with a Lange caliper to the nearest 0.5 mm; the mean value was used in the analyses. The intraobserver technical error of measurement and the mean average bias of the observer were within the limits suggested by the World Health Organization (WHO) in the Growth Reference Study (14).

Blood sample

A trained nurse collected a 12-mL fasting venous sample from the children at arrival to the nursery school. Mothers were contacted the day before the sample was drawn to confirm the absence of fever (>37.5°C) or symptoms of acute infection in the children and to advise them not to provide foods or liquids to the child before arriving to the nursery school the next day. These conditions were rechecked by the nurse at the time of the blood collection and, if not met, exams were rescheduled. Analyses were conducted at the Nutrition Laboratory of the Catholic University of Chile. This laboratory conducts daily assessments of the accuracy of the measurements using quality-control software (Bio-Rad Laboratories Inc, Hercules, CA) and for lipid measurements, has a Certificate of Traceability periodically updated by the Center for Disease Control and Prevention (CDC) (15, 16). Serum IL-6 concentrations were measured with an enzyme-linked immunosorbent assay kit (R&D Systems Inc, Minneapolis, MN) and CRP concentrations with a highly sensitive enzyme-linked immunosorbent assay kit (Biomerica Inc, Newport Beach, CA). Serum glucose concentrations were measured by using enzymatic colorimetric techniques (HUMAN; Gesellschaft für Biochemica und Diagnostica, Wiesbaden, Germany). The HOMA-IR was calculated as fasting glucose (mmol/L) × fasting insulin (μU/mL)/22.5. TC and triglycerides were measured by using enzymatic colorimetric techniques (HUMAN). HDL cholesterol was isolated by precipitation with a sodium phosphotungstate and magnesium chloride solution (17). LDL cholesterol was calculated according to the Friedewald formula (ie, all triglyceride concentrations were < 400 mg/dL) (18). Serum insulin concentrations were measured by using a radioimmunoassay kit (Linco Research Inc, St Charles, MO).

Computed indexes

Anthropometric indicators

We divided weight (kg) by height squared (m) to calculate BMI. We estimated weight-for-age (WAZ), height-for-age (HAZ), and BMI-for-age (BAZ) z scores on the basis of the WHO 2006 growth standards (19). We defined 2 levels of obesity (BAZ > 1 SD and BAZ > 2 SD) and 2 levels of central obesity: WC ≥ 75th percentile (NHANES III: 54.3 cm for girls and 53.9 cm for boys) and WC ≥ 90th percentile (NHANES III: 58.3 cm for girls and 57.6 cm for boys) (20). WC divided by height and hip circumference served to calculate waist-to-height and waist-to-hip ratio, respectively. Triceps, biceps, suprailiac, and subscapular skinfold thicknesses and abdominal, suprailiac, and subscapular skinfold thicknesses were used to estimate fatness and truncal fatness, respectively. To estimate percentage body fat, we used a predictive equation previously developed in a sample of JUNJI children (3–4 y) and validated by using deuterium dilution (21). The equation uses age, sex, weight, calf circumference, and triceps and subscapular skinfold thicknesses. The mean difference in fat mass estimates between the 2 methods was −0.07 kg with a precision (SD) of 0.77; the equations explained 72% of the variation in fat mass. We divided body fat by height squared to calculate the body fat index. We considered indicators of general obesity: weight, BMI, sum of 4 skinfold thicknesses, percentage body fat, and body fat index. The indicators of central obesity used were WC, waist-to-hip ratio, waist-to-height ratio, and truncal fatness.

Cardiometabolic risk factors

Cutoffs used to define abnormal metabolic status were as follows: glucose concentration ≥ 100 mg/dL (22); HOMA-IR ≥ 3.2 (23); total cholesterol, LDL cholesterol, and triglycerides ≥95th percentile [American Academy of Pediatrics: girls (total cholesterol ≥197 mg/dL, LDL cholesterol ≥140 mg/dL, and triglycerides ≥120 mg/dL) and boys (total cholesterol ≥186 mg/dL, LDL cholesterol ≥129 mg/dL, and triglycerides ≥85 mg/dL) (24)]; HDL cholesterol ≤5th percentile [AAP: girls (38 mg/dL) and boys (36 mg/dL) (24)]; and CRP ≥3 mg/L (25).

Statistical analyses

Nonnormal variables (ie, sum of 4 skinfold thicknesses, truncal fat, CRP, IL-6, insulin, HOMA-IR, and triglyceride) were logarithmically transformed. We present data as means ± SDs or frequency distributions; differences by sex were tested by using Student's *t* test for continuous variables or chi-square and Fisher's exact tests for dichotomous variables. We used chi-square and the Fisher's exact test to compare the observed prevalence of 0, 1, 2, and >2 risk factors with the expected prevalence under the assumption that risk factors were independent of each other. Pearson's partial correlation was used to assess associations between *1*) obesity and central obesity indicators and *2*) obesity indicators and cardiometabolic markers. Differences in mean values and prevalence of cardiometabolic markers across BMI and WC levels were tested by using analysis of variance and chi-square or Fisher's exact test, respectively. The relative contribution of obesity and central obesity indicators on the variability of each of the outcomes was evaluated defining 3 blocks of variables: block 1 (weight and BMI), block 2 (sum of 4 skinfold thicknesses, percentage fat, and body fat index), and block 3 (WC, waist-to-hip ratio, waist-to-height ratio, and truncal fatness). Multiple linear regression models that sequentially incorporated one variable from each block were run. Models with all possible combinations of variables were tested; however, most of the models revealed multicollinearity problems (ie, variance inflation factors >10 and condition indexes >30). In all models, adding a quadratic term did not significantly improve the fit. Thus, in the final analysis only linear associations were considered in the models. All analyses were adjusted for age and stratified by sex based on previous studies that showed sex differences in the association of anthropometric indicators and cardiometabolic markers (26, 27). Associations were considered significant if $P < 0.05$. Analyses were done by using SAS (version 9.2; SAS Institute, Cary, NC).

TABLE 1
Anthropometric characteristics of 324 child beneficiaries of the Chilean National Nursery School Council Program (2006), by sex[1]

Anthropometric characteristic	Girls (n = 143)	Boys (n = 181)	P value[2]
Age (y)	4.26 ± 0.3[3]	4.24 ± 0.3	0.71
Weight (kg)	18.19 ± 2.8	17.84 ± 2.5	0.24
Weight-for-age *z* score	0.54 ± 1.0	0.38 ± 1.0	0.15
Height (cm)	103.77 ± 4.4	103.77 ± 4.1	0.99
Height-for-age *z* score	−0.16 ± 0.9	−0.26 ± 0.9	0.32
BMI (kg/m^2)	16.83 ± 1.8	16.53 ± 1.6	0.11
BMI-for-age *z* score	0.94 ± 1.0	0.83 ± 1.1	0.36
Waist circumference (cm)	52.94 ± 4.1	52.77 ± 3.7	0.7
Waist-to-hip ratio	0.904 ± 0.0	0.929 ± 0.0	<0.0001
Waist-to-height ratio	0.51 ± 0.0	0.51 ± 0.0	0.66
Sum of 4 skinfold thicknesses (mm)[4]	35.60 ± 13.1	28.30 ± 10.6	<0.0001
Truncal fat (%)[5]	29.60 ± 13.5	22.10 ± 10.3	<0.0001
Total fat (%)[6]	25.30 ± 4.2	21.00 ± 3.6	<0.0001
Body fat index (kg/m^2)	4.31 ± 1.2	3.53 ± 1.0	<0.0001
Overweight [% (*n*)]			
BMI-for-age *z* score >1 SD (WHO 2006)	48.2 (69)	41.4 (75)	0.26
BMI-for-age *z* score >85th percentile (CDC 2000)	49.0 (70)	35.1 (64)	<0.05
Overweight (IOTF)	35.0 (50)	22.0 (40)	<0.05
Obesity [% (*n*)]			
BMI-for-age *z* score >2 SD (WHO 2006)	12.6 (18)	13.8 (25)	0.86
BMI-for-age *z* score >95th percentile (CDC 2000)	19.6 (28)	17.0 (31)	0.66
Obesity (IOTF)	9.8 (14)	3.3 (6)	<0.05
Central obesity [% (*n*)]			
Waist circumference >75th percentile (NHANES III)	23.8 (34)	30.2 (55)	0.21
Waist circumference >90th percentile (NHANES III)	11.9 (17)	7.7 (14)	0.25

[1] WHO 2006, World Health Organization growth standards (19); CDC 2000, Centers for Disease Control and Prevention growth charts (28); IOTF, International Obesity Task Force (29); NHANES III, third National Health and Nutrition Examination Survey. Girls: obesity IOTF BMI = 19.12, overweight IOTF BMI = 17.28 (29); waist circumference 75th percentile = 54.3 cm and 90th percentile = 58.3 cm (20). Boys: obesity IOTF BMI = 19.29, overweight IOTF BMI = 17.55 (29); waist circumference 75th percentile = 53.9 cm and 90th percentile = 57.6 cm (20).

[2] Sex differences assessed by using Student's *t* test or chi-square test.

[3] Mean ± SD (all such values).

[4] Calculated by summing triceps, biceps, suprailiac, and subscapular skinfold thicknesses.

[5] Calculated by summing abdominal, suprailiac, and subscapular skinfold thicknesses.

[6] Estimated on the basis of a predictive equation that uses age, sex, weight, calf circumference, and triceps and subscapular skinfold thicknesses.

RESULTS

Children enrolled in this substudy did not differ significantly in terms of sex, age, and anthropometric measures at birth and at 4 y when compared with children in the primary study. Selected anthropometric characteristics of the participants are presented in **Table 1**. A total of 324 children (44% girls) participated in the study. The mean age of the participants was slightly >4.0 y. Both girls and boys had heights similar to the WHO reference population, but were considerably heavier and fatter than the standard. Girls had significantly higher adiposity than boys on the basis of skinfold thicknesses and total fat estimated from the predictive equation ($P < 0.0001$). However, no significant differences in mean BMI were found ($P > 0.05$). Fat distribution did not differ by sex (all $P > 0.05$), except for the waist-to-hip ratio, which was greater in boys ($P < 0.0001$). The prevalence of excess weight was high (>40% per WHO 2006 or CDC 2000 criteria and close to 30% per IOTF criteria), and the percentage of children with a high WC was similar to that observed in the United States 10 y ago (10%). General and central obesity were higher in girls than in boys ($P < 0.05$). Cardiometabolic characteristics of participants are presented in **Table 2**. Mean insulin values were higher in girls than in boys, whereas the opposite was the case for glucose concentrations ($P < 0.05$). None of the other markers differed significantly by sex ($P > 0.05$). Nearly 25% of the children had an elevated CRP concentration. One of every 5 children had a high TC, high LDL-cholesterol, and high triglyceride concentration, whereas close to 50% had a low HDL-cholesterol concentration. High glucose concentrations and insulin resistance were uncommon (<3%). Overall, ≈70% of all children had at least one cardiometabolic risk factor. The prevalence of lipid disorders and the sum of cardiometabolic risk factors were higher in boys than in girls ($P < 0.05$). The observed prevalences of 0, 1, 2, and >2 risk factors were significantly different from the expected prevalence assuming that risk factors were independent of each other ($P < 0.05$).

Correlations between general obesity and central obesity indicators are presented in **Table 3**. Correlations between general obesity indicators were consistently strong (r between 0.66 and 0.95), whereas correlations between central obesity indicators were less consistent, ranging from 0 to 0.8. Correlations between general obesity and central obesity indicators were moderate to strong in magnitude ($0.40 < r < 0.96$), except for those involving the waist-to-hip ratio ($r < 0.30$). Correlations between obesity indicators and cardiometabolic markers are presented in **Table 4**. In general, the correlations were weak ($r < 0.3$), although some were statistically significant. Whereas several correlations in boys and girls between obesity indicators and CRP concentrations were positive and significant ($P < 0.05$), none were significant in the case of IL-6 ($P > 0.05$). Several correlations between obesity indicators and HOMA-IR were positive and significant in girls ($P < 0.05$) but not in boys. In both sexes, obesity indicators were not associated with blood lipid indexes ($P > 0.05$).

Mean concentrations and prevalence of cardiometabolic markers by BMI levels are presented in **Table 5**. Obese girls had higher mean values of fasting insulin and HOMA-IR as well as a higher prevalence of high HOMA-IR than girls with lower BMIs (all $P < 0.05$). In girls, the remaining cardiometabolic risk factors did not differ by BMI level (all $P > 0.05$). In boys, differences in mean concentrations and prevalence of cardiometabolic risk factors were all nonsignificant ($P > 0.05$). Similar results were obtained when BMI categories were defined according to the CDC and IOTF cutoffs (data not shown).

Mean concentrations and prevalences of cardiometabolic risk factors by WC levels are presented in **Table 6**. Girls with larger WCs had higher mean values of fasting insulin and HOMA-IR and a higher prevalence of high CRP than did girls with smaller WCs (all $P < 0.05$). In girls, the remaining cardiometabolic risk factors did not differ by WC level (all $P > 0.05$). In boys, differences in mean concentrations and in the prevalence of cardiometabolic risk factors were all nonsignificant ($P > 0.05$).

TABLE 2
Cardiometabolic characteristics of 324 child beneficiaries of the Chilean National Nursery School Council Program (2006), by sex[1]

				Above cutoffs[2]		
Cardiometabolic characteristic	Girls (n = 143)	Boys (n = 181)	P value[3]	Girls (n = 143)	Boys (n = 181)	P value[4]
				% (n)		
C-reactive protein (mg/L)	1.87 ± 2.2[5]	2.18 ± 2.8	0.29	21.4 (28)	27.0 (47)	0.26
Interleukin-6 (pg/mL)	2.62 ± 2.6	2.85 ± 2.5	0.46	—	—	—
Fasting insulin (μU/mL)	6.24 ± 1.2	5.86 ± 1.0	0.003	—	—	—
Fasting glucose (mg/dL)	77.9 ± 6.2	79.9 ± 7.0	0.02	1.4 (2)	2.8 (5)	0.41
HOMA-IR	1.19 ± 0.3	1.15 ± 0.2	0.15	2.1 (3)	1.1 (2)	0.46
Total cholesterol (mg/dL)	169.0 ± 26.8	163.2 ± 27.6	0.06	14.7 (21)	20.3 (37)	0.19
LDL cholesterol (mg/dL)	114.3 ± 26.2	110.2 ± 25.8	0.18	16.1 (23)	23.6 (43)	0.09
HDL cholesterol (mg/dL)	37.6 ± 9.2	36.9 ± 9.5	0.51	42.1 (59)	57.0 (102)	0.01
Triglycerides (mg/dL)	85.8 ± 34.9	78.7 ± 33.6	0.07	13.3 (19)	30.4 (55)	0.00

[1] HOMA-IR, homeostasis model assessment of insulin resistance.
[2] Cutoffs for risk factors were as follows: C-reactive protein ≥3 mg/L (25); glucose ≥100 mg/dL (22); HOMA-IR ≥3.2 (23); total cholesterol, LDL cholesterol, and triglycerides ≥95th percentile [American Academy of Pediatrics: girls (total cholesterol ≥197 mg/dL, LDL cholesterol ≥140 mg/dL, and triglycerides ≥120 mg/dL) and boys (total cholesterol ≥186 mg/dL, LDL cholesterol ≥129 mg/dL, and triglycerides ≥85 mg/dL) (24)]; and HDL cholesterol ≤5th percentile [American Academy of Pediatrics: girls (38 mg/dL) and boys (36 mg/dL) (24)].
[3] Sex differences assessed by using Student's t test.
[4] Sex differences assessed by using chi-square test or Fisher's exact test.
[5] Mean ± SD (all such values).

TABLE 3
Pearson's partial correlation coefficients among obesity anthropometric indicators in 324 preschool child beneficiaries of the Chilean National Nursery School Council Program (2006), by sex[1]

	BMI	Sum of 4 skinfold thicknesses[2,3]	%Fat[4]	Body fat index	Waist	Waist-to-hip ratio	Waist-to-height ratio	Truncal fat[2,5]
Girls (n = 143)								
Weight	0.80[6]	0.70[6]	0.92[6]	0.82[6]	0.84[6]	−0.08	0.48[6]	0.72[6]
BMI		0.79[6]	0.85[6]	0.93[6]	0.81[6]	−0.01	0.78[6]	0.79[6]
Sum of 4 skinfold thicknesses[2,3]			0.89[6]	0.93[6]	0.73[6]	0.01	0.65[6]	0.96[6]
%Fat[4]				0.95[6]	0.84[6]	−0.04	0.60[6]	0.87[6]
Body fat index					0.83[6]	0.01	0.74[6]	0.91[6]
Waist						0.34[6]	0.81[6]	0.74[6]
Waist-to-hip ratio							0.47[6]	0.00
Waist-to-height ratio								0.66[6]
Boys (n = 181)								
Weight	0.76[6]	0.66[6]	0.93[6]	0.83[6]	0.77[6]	−0.24[6]	0.41[6]	0.68[6]
BMI		0.75[6]	0.81[6]	0.91[6]	0.73[6]	−0.15[6]	0.75[6]	0.76[6]
Sum of 4 skinfold thicknesses[2,3]			0.84[6]	0.91[6]	0.67[6]	−0.07	0.61[6]	0.96[6]
%Fat[4]				0.95[6]	0.79[6]	−0.19[6]	0.51[6]	0.83[6]
Body fat index					0.77[6]	−0.15[6]	0.66[6]	0.89[6]
Waist						0.26[6]	0.79[6]	0.71[6]
Waist-to-hip ratio							0.40[6]	−0.04
Waist-to-height ratio								0.65[6]

[1] Values were adjusted for age.
[2] Log-transformed variables.
[3] Calculated by summing triceps, biceps, suprailiac, and subscapular skinfold thicknesses.
[4] Estimated based on a predictive equation that uses age, sex, weight, calf circumference, and tricipital and subscapular skinfold thickneses.
[5] Calculated by summing abdominal, suprailiac, and subscapular skinfold thicknesses.
[6] $P < 0.001$.

Multiple linear regression analyses indicated that obesity indicators explained between 1% and 8% of the variability of cardiometabolic risk factors; the associations were significant only for CRP, fasting insulin, and HOMA-IR (data not shown).

DISCUSSION

We found that obesity indicators were at best weakly related to cardiometabolic status at 4 y of age; in contrast with what has been reported in school-age children and adolescents. These findings, however, are in line with the few studies that have assessed the relation of obesity indicators and cardiometabolic risk in preschool children (7–10). These studies indicate that, for this age group, obesity explains a small proportion of the variability of cardiometabolic risk factors. The most recent US Expert Committee recommends conducting metabolic screening in obese children, with no qualification by age (30). Our results indicate that, at least in preschool children, interventions should follow a population-based approach instead of being targeted to overweight or obese children.

Our findings can be partially explained by the age of our study population. It has been suggested that lifetime obesity exposure influences concurrent cardiometabolic status (6, 31, 32). The Bogalusa Heart Study showed that tracking of BMI from childhood to adulthood not only determines the age-related clustering of CVD risk factors but also the degree of tracking of the metabolic syndrome (29). Recently, similar findings, but in relation to clustering of CVD risk factors in adolescence, were reported in a birth cohort study conducted in Australia (30). NHANES III data also show an age effect on the magnitude of the associations and the relative importance of fatness and fat distribution in determining concentrations of cardiometabolic risk factors (33). Unfortunately, the cross-sectional design of this study does not allow us to test this hypothesis nor does it allow us to assess the direction of the associations and, thus, precludes any causal inference. We expect that the planned follow-up studies of the children being reported here will contribute to answering these questions.

We found no association between obesity and lipid concentrations, as reported in previous studies (7, 8), but in contrast with the results of others studies (10, 11). This might be related to the fact that HDL-cholesterol and LDL-cholesterol disorders were surprisingly high in this population, likely because of specific components of the local diet. HDL-cholesterol concentrations were particularly low compared with those of US children, but were similar to values reported by previous studies conducted in preschool children living in other industrialized countries (7, 34, 35). Evidence indicates that in Chile there is a high consumption of both saturated fat and *trans* fatty acids (36–38). Saturated fats increase LDL-cholesterol concentrations, whereas *trans* fatty acids increase LDL cholesterol and decrease HDL cholesterol, giving a pattern similar to that observed in our population (39, 40). In the specific case of our study sample, meals provided at the JUNJI program have <30% fat and <10% saturated fat; however, the quality of the fats provided by the school meal program or consumed at home was neither controlled nor evaluated. Population trends of childhood obesity and mean lipid values in the United States show that factors other than obesity are also important in determining blood lipid concentrations in children. According to NHANES data, although BMI and WC increased from 1990 to 2000, mean triglyceride values decreased and total, LDL, and HDL cholesterol remained stable (41).

TABLE 4
Pearson's partial correlation coefficients among obesity anthropometric indicators and cardiometabolic markers in 324 preschool child beneficiaries of the Chilean National Nursery School Council Program (2006), by sex[1]

	CRP[2]	IL-6[2]	HOMA-IR[2]	TC	HDL cholesterol	TG[2]
Girls (n = 143)						
Weight	0.12	0.14	0.27[3]	−0.02	−0.06	0.10
BMI	0.08	0.05	0.23[3]	0.04	−0.08	0.12
Sum of 4 skinfold thicknesses[2,4]	0.20[5]	0.06	0.18[5]	−0.07	−0.11	0.10
Body fat index	0.15	0.08	0.20[5]	−0.03	−0.09	0.10
Waist	0.13	0.12	0.21[5]	−0.06	−0.14	0.09
Waist-to-hip ratio	0.02	0.04	0.07	−0.11	−0.12	0.02
Waist-to-height ratio	0.08	0.03	0.13	−0.01	−0.14	0.08
Boys (n = 181)						
Weight	0.10	0.00	0.09	−0.04	0.00	0.07
BMI	0.13	0.03	0.02	−0.01	0.09	−0.01
Sum of 4 skinfold thicknesses[2,4]	0.17[5]	0.02	0.06	−0.03	0.06	0.07
Body fat index	0.15	0.03	0.07	0.00	0.06	0.05
Waist	0.17[5]	0.00	0.05	0.00	−0.01	0.06
Waist-to-hip ratio	0.09	0.04	−0.06	0.03	0.06	0.02
Waist-to-height ratio	0.18[5]	0.04	−0.04	0.04	0.06	−0.01

[1] All analyses were adjusted for age. CRP, C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; IL-6, interleukin-6; TC, total cholesterol; TG, triglycerides.
[2] Log-transformed variables.
[3] $P < 0.01$.
[4] Calculated by summing triceps, biceps, suprailiac, and subscapular skinfold thicknesses.
[5] $P < 0.05$.

The use of BMI as a surrogate marker of adiposity during preschool age is complicated by the fact that during this period the so-called adiposity rebound takes place (42). Normally, BMI decreases from infancy to the fifth year of life and increases thereafter (43). However, some children may lose less fat in their early years (ie, smaller BMI decrease) and have an earlier

TABLE 5
Mean concentrations and prevalence of cardiometabolic risk factors in 324 preschool child beneficiaries of the Chilean National Nursery School Council Program (2006), by categories of BMI-for-age z score (BAZ; World Health Organization 2006) and sex[1]

	Girls			Boys		
Cardiometabolic characteristic	BAZ < 1 (n = 74)	1 ≤ BAZ ≤ 2 (n = 51)	BAZ > 2 (n = 18)	BAZ < 1 (n = 106)	1 ≤ BAZ ≤ 2 (n = 50)	BAZ > 2 (n = 25)
Mean C-reactive protein (mg/L)	1.85	1.79	2.16	2.00	2.60	2.20
C-reactive protein ≥3 mg/L [% (n)]	18.8 (14)	22.0 (11)	28.0 (5)	24.5 (26)	30.0 (15)	32.0 (8)
Mean IL-6 (pg/mL)	2.93	2.66	2.75	2.73	3.36	2.50
Mean fasting insulin (μU/mL)	5.96	6.51	6.61[2]	5.80	5.94	5.94
Mean fasting glucose (mg/dL)	77.2	78.8	77.7	80.7	79.2	77.5
Fasting glucose ≥100 mg/dL [% (n)]	1.4 (1)	0.0 (0)	5.6 (1)	4.7 (5)	0.0 (0)	0.0 (0)
Mean HOMA-IR	1.13	1.26	1.26[2]	1.15	1.15	1.13
HOMA-IR ≥3.2 [% (n)]	1.4 (1)	0.0 (0)	11.2 (2)[3]	1.9 (2)	0.0 (0)	0.0 (0)
Mean total cholesterol (mg/dL)	167.9	172.6	163.7	164.3	163.6	155.8
Total cholesterol ≥95th percentile [% (n)]	13.5 (10)	17.7 (9)	11.2 (2)	18.9 (20)	24.0 (12)	16.0 (4)
Mean LDL cholesterol (mg/dL)	112.7	118.6	108.6	111.2	110.2	104.0
LDL cholesterol ≥95th percentile [% (n)]	16.2 (12)	19.6 (10)	5.6 (1)	23.6 (25)	26.0 (13)	16.0 (4)
Mean HDL cholesterol (mg/dL)	38.0	38.8	38.0	36.3	39.3	36.9
HDL cholesterol ≤5th percentile [% (n)]	44.4 (33)	43.1 (22)	28.0 (5)	60.4 (64)	50.0 (25)	52.0 (13)
Mean triglycerides (mg/dL)	84.3	85.9	91.6	82.2	70.2	81.5
Triglycerides ≥95th percentile [% (n)]	19.5 (14)	6.3 (3)	5.6 (1)	35.9 (38)	16.0 (8)	36.0 (9)
One risk factor [% (n)][4]	25.8 (19)	33.5 (17)	39.0 (7)	32.1 (34)	32.0 (16)	32.0 (8)
Two risk factors [% (n)][4]	13.5 (10)	29.5 (15)	5.6 (1)	33.0 (35)	33.0 (13)	24.0 (6)
Three or more risk factors [% (n)][4]	16.1 (12)	8.0 (4)	17.0 (3)	20.8 (22)	17.0 (9)	24.0 (6)

[1] All analyses were adjusted for age. IL-6, interleukin-6; HOMA-IR, homeostasis model assessment of insulin resistance.
[2] $P < 0.05$ (F test).
[3] $P < 0.05$ (Fisher's exact test).
[4] The risk factors were as follows: C-reactive protein ≥3 mg/L (25); glucose ≥100 mg/dL (22); HOMA-IR ≥3.2 (23); total cholesterol, LDL cholesterol, and triglycerides ≥95th percentile [American Academy of Pediatrics: girls (total cholesterol ≥197 mg/dL, LDL cholesterol ≥140 mg/dL, and triglycerides ≥120 mg/dL) and boys (total cholesterol ≥186 mg/dL, LDL cholesterol ≥129 mg/dL, and triglycerides ≥85 mg/dL) (24)]; and HDL cholesterol ≤5th percentile [American Academy of Pediatrics: girls (38 mg/dL) and boys (36 mg/dL) (24)].

TABLE 6
Mean concentrations and prevalence of cardiometabolic risk factors in 324 preschool child beneficiaries of the Chilean National Nursery School Council Program (2006), by categories of waist circumference (WC) and sex[1]

	Girls			Boys		
Cardiometabolic characteristic	WC < 75th percentile (n = 109)	75th ≤ WC < 95th percentile (n = 17)	WC ≥ 95th percentile (n = 17)	WC < 75th percentile (n = 126)	75th ≤ WC < 95th percentile (n = 41)	WC ≥ 95th percentile (n = 14)
Mean C-reactive protein (mg/L)	1.71	1.98	2.71	2.21	2.00	2.58
C-reactive protein ≥3 mg/L [% (n)]	17.4 (19)	23.5 (4)	47.5 (8)[2]	27.5 (35)	22.5 (9)	37.5 (5)
Mean IL-6 (pg/mL)	2.44	2.82	4.22	3.35	2.54	3.15
Mean fasting insulin (μU/mL)	6.11	6.40	7.12[3]	5.81	5.97	5.99
Mean fasting glucose (mg/dL)	77.6	78.1	79.5	80.5	77.8	79.6
Fasting glucose ≥100 mg/dL [% (n)]	0.9 (1)	5.9 (1)	0.0 (0)	3.9 (5)	0.0 (0)	0.0 (0)
Mean HOMA-IR	1.16	1.22	1.39[3]	1.15	1.14	1.17
HOMA-IR ≥ 3.2 [% (n)]	0.9 (1)	5.9 (1)	5.9 (1)	1.6 (2)	0.0 (0)	0.0 (0)
Mean total cholesterol (mg/dL)	169.9	174.7	157.1	165.2	158.4	155.5
Total cholesterol ≥95th percentile [% (n)]	14.7 (16)	23.5 (4)	5.9 (1)	22.1 (28)	17.5 (7)	15.0 (2)
Mean LDL cholesterol (mg/dL)	114.7	122.7	103.1	111.7	107.6	101.4
LDL cholesterol ≥95th percentile [% (n)]	16.5 (18)	29.4 (5)	0.0 (0)	25.2 (32)	22.5 (9)	15.0 (2)
Mean HDL cholesterol (mg/dL)	38.0	35.5	36.6	37.5	35.6	39.6
HDL cholesterol ≤ 5th percentile [% (n)]	42.2 (46)	41.2 (7)	47.5 (8)	57.5 (73)	57.5 (23)	50.0 (7)
Mean triglycerides (mg/dL)	85.1	82.9	93	78.8	75.8	87.4
Triglycerides ≥95th percentile [% (n)]	11.0 (12)	17.7 (3)	5.5 (1)	30.7 (39)	22.5 (9)	50.0 (7)
One risk factor [% (n)][4]	30.3 (33)	17.7 (3)	35.5 (6)	30.7 (39)	30 (12)	45.0 (6)
Two risk factors [% (n)][4]	17.5 (19)	29.4 (5)	12.0 (2)	26.0 (33)	42.5 (17)	17.5 (3)
Three or more risk factors [% (n)][4]	11.2 (12)	17.7 (3)	17.8 (3)	24.4 (31)	7.5 (3)	27.5 (4)

[1] All analyses were adjusted for age. IL-6, interleukin-6; HOMA-IR, homeostasis model assessment of insulin resistance. WC percentiles were calculated on the basis of the third National Health and Nutrition Examination Survey (75th percentile: 54.3 cm for girls and 53.9 cm for boys; 90th percentile: 58.3 cm for girls and 57.6 cm for boys) (20).

[2] $P < 0.05$ (Fisher's exact test).

[3] $P < 0.05$ (F test).

[4] The risk factors were as follows: C-reactive protein ≥3 mg/L (25); glucose ≥100 mg/dL (22); HOMA-IR ≥3.2 (23); total cholesterol, LDL cholesterol, and triglycerides ≥95th percentile [American Academy of Pediatrics: girls (total cholesterol ≥197 mg/dL, LDL cholesterol ≥140 mg/dL, and triglycerides ≥120 mg/dL) and boys (total cholesterol ≥186 mg/dL, LDL cholesterol ≥129 mg/dL, and triglycerides ≥85 mg/dL) (24)]; and HDL cholesterol ≤5th percentile [American Academy of Pediatrics: girls (38 mg/dL) and boys (36 mg/dL) (24)].

adiposity rebound. Thus, at a similar BMI, a child who has already rebounded might have different associated risks than a child who has not yet rebounded. Maturation and growth of the different corporal segments does not takes place at a uniform rate during early life. This also may confound the use of WC as an indicator of obesity in preschool children (44, 45). In the present study we used several anthropometric indicators of obesity (including a validated predictive equation) and central obesity and we found that they were highly correlated. This precluded any assessment of the differential effect of fatness and fat distribution on CVD status in our sample. Our results, however, should be interpreted with caution because we did not have direct body-composition measurements.

In this study we defined obesity according to WHO standards because these were developed based on the optimal growth of well-to-do healthy breastfed infants from 6 countries around the world (46). Although these cutoffs have not been validated as predictors of future metabolic risk, it has been shown that growth references have minimal differences in their capacity to predict CVD risk factors in adulthood (47). Using different definitions of excess weight, we found that the prevalence of obesity in our sample was twice that of preschool children from Latin American countries (48) and similar to that found in developed countries (49). This is in line with the evidence that indicates that as countries improve their economic condition, obesity tends to disproportionally affect low-income people (50). Growing evidence indicates that early childhood obesity tracks into later life (51, 52) and that obesity at school age or adolescence is associated with concurrent and future metabolic abnormalities (6, 32, 53). Recently, it was also shown that obesity at 5 y of age is predictive of the metabolic status at 9 y of age (49). Therefore, the high prevalence of obesity found in 4-y-old children may predict a high burden of metabolic complications in the future. Moreover, interventions to treat obesity once it has been already been established show only modest and short-term effects, which highlights the need to start primary prevention as early as possible (54).

The recent emergence of the childhood obesity epidemic poses the challenge of defining diagnostic criteria for CVD risk factors traditionally observed only in adults (55, 56). In children, this is complicated not only because of growth and maturity changes but also because long-term follow-up studies are needed to establish the validity of the proposed criteria. Presently, there is no consensus and multiple recommendations and cutoffs are in use. This complicates assessing trends or differences between populations (57). The utility of diagnosing the metabolic syndrome among children and adolescents has been questioned because of its instability and the lack of evidence of its clinical significance (58). We found only one child that had the metabolic syndrome using the International Diabetes Federation criteria, but replacing

blood pressure with insulin concentration [ie, ≥3 of the following: HDL cholesterol <40 mg/dL + triglycerides ≥150 mg/dL + glucose ≥100 mg/dL + insulin ≥15 mU/L (59) + WC ≥ NHANES III 90th percentile (60)]. We chose instead to assess the presence of cumulative cardiometabolic risk factors using well-accepted pediatric cutoffs. Our results indicate that risk factors tend to cluster (ie, they are not independent of each other) and that this clustering is, at least at this age, unrelated to fatness.

In conclusion, we found that obesity and central obesity were prevalent in low-income 4-y-old children attending a welfare program and that most of the children already had at least one cardiometabolic risk factor. Overall, BMI and WC were poor indicators of cardiometabolic risk factors for this age group, which indicated that these anthropometric measurements should not be used for cardiometabolic screening or for targeting CVD preventive interventions. Conversely, these results indicate that population-based prevention through changes in diet and physical activity are the preferred approaches to lowering mean values for cardiometabolic risk factors, including obesity (61). The JUNJI program in Chile, as well as similar programs in other countries, provides a unique opportunity to achieve these goals in a timely manner. The macronutrient quality and portion sizes of the meals provided, the recreational activities programmed, and the education provided to families should be aimed at promoting healthy diets and lifestyles, not only while the children are at the nursery school but also when they are at home.

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