Material and Methods

The trial was previously approved by the Research and Ethics Committee from Instituto Mexicano del Seguro Social and Instituto Nacional de Perinatología, México. Afterward, a cross-sectional study was carried out, including 6-18 year old children and adolescents, presumably healthy, by means of a non-probabilistic sampling of consecutive cases in primary schools, social security centers and outpatient visit in a second level care hospital who attended spontaneously by any other reason. Inclusion criteria comprised no intake of any drug, signed an agreement to participate in the study, and informed consent by their parents. Exclusion criteria were obesity-associated syndromes, drug intake that could modify arterial blood pressure, lipids, or glucose metabolism.

*Clinical evaluation.*

Anthropometric studies were achieved without shoes and with light clothes, by trained nutritionists, according to conventional procedures. Weight was obtained with a portable SECA digital scale model 803 and height with a SECA stadiometer model 0123. Each measure was performed twice. BMI (kg/m2) was determined using Anthro Plus software (<http://www.who.int/growthref/tools/en/>). The classification of overweight and obesity was based on the calculation of the Z score of the Body Mass Index (BMI) for age and was classified as overweight above +1 standard deviation and, with obesity, above +2 standard deviations of the population WHO reference ([18](#_ENREF_18), [19](#_ENREF_19)).

Arterial blood pressure was assessed using a mercury sphygmomanometer and a suitable bracelet for each patient’s age and complexion, measuring twice with 5 minutes between both and taking the average value.

*Laboratory tests.*

After 12 hours of fasting, blood samples were taken by venipuncture using a vacuum collection system. Tubes were centrifuged at 500 g for 10 min to obtain serum. Glucose concentration, total cholesterol, high density lipoprotein-cholesterol (HDL), and triglycerides (enzymatic colorimetric DiaSys Lory 2000 Alte Strasse 965558 Holzheim Germany); were quantified. Low-density lipoproteins (LDL) were calculated by Friedewald formula. Insulin quantitative measure was determined by chemiluminescent immunoassay (Inmunolite 1000 Siemens NY, USA).

# Metabolic phenotypes of obesity

# To define the metabolic status of each of the participants, 4 cardiometabolic risk factors were taken into account([13](#_ENREF_13)): HDL <40 mg / dl (or <1.03 mmol/L) , triglycerides ≥ 150 mg/dl (or ≥ 1.7 mmol/ L), high blood pressure (systolic blood pressure and/or diastolic blood pressure): ≥90 percentile for age and sex, and fasting glucose ≥ 5.6 mmol/Ll (≥ 100mg/dL). Accordingly, participants were dichotomized as "metabolically healthy" or "metabolically unhealthy" depending on the absence or presence of cardiometabolic risk factors, respectively. Likewise, the metabolic state was analyzed using HOMA-IR (fasting insulin [mUI/ml] × fasting glucose [mmol/L] /22.5)([20](#_ENREF_20)), considering as absence of insulin resistance if the result was <1.95. Cutoff value of 3.16 was chosen according to previous studies in obese children and adolescents([12](#_ENREF_12), [16](#_ENREF_16), [21](#_ENREF_21), [22](#_ENREF_22)). Other indices used to indirectly estimate the action of insulin were the triglycerides/HDL ratio, and triglycerides and glucose index ([23](#_ENREF_23)).

*Statistical analysis*

Results obtained from quantitative variables were shown as mean ± standard deviation or median with its interquartile interval (IQI) just if they fulfilled or not a normal distribution according to the Shapiro-Wilk test. Results from nominal or ordinal scale variables were reported as absolute number of cases and their percentage [n (%)]. Chi-square test was used for bivariate analysis of nominal qualitative variables and Mann-Whitney U test for ordinal qualitative as well as quantitative variables. A size effect estimation was reported with a z statistic, considering 0.1, 0.3, and 0.5 as threshold values to estimate low, medium, and large size effects, respectively([24](#_ENREF_24)). A multivariable logistic regression analysis was performed to examine the association between the MHO and MONW phenotypes, and the explanatory variables (sex, age, nutritional status, waist circumference, HOMA-IR, product of triglycerides and glucose, leptin/adiponectin ratio, and triglyceride/HDL ratio). All tests considered significant when p <0.05. The same analyses were performed for both definition criteria of metabolically healthy status. Statistical analysis used Stata-14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCo LP).