Proatherogenic Lipid Profile in Early Childhood: Association with Weight Status at 4 Years and Parental Obesity

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Objectives To determine lipid profiles in early childhood and evaluate their association with weight status at 4 years of age. Additionally, we evaluated whether the risk of overweight or having an altered lipid profile was associated with parental weight status.

Study design Five hundred eighty two mothers and their 4-year-old children from 2 Spanish population-based cohorts were studied. Weight status in children at 4 years of age was classified as overweight or obese using the International Obesity Task Force criteria. Plasma total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were determined in children and lipid ratios were calculated. A proatherogenic lipid profile was defined as having the 3 lipid ratios in the third tertile.

Results A total of 12.9% of children were overweight and 6.4% were obese. Weight status at 4 years of age was related to maternal prepregnancy body mass index, paternal body mass index, gestational diabetes, and birth weight, but not with other sociodemographic characteristics of the mother. We found no association with gestational age, sex of the child, or breastfeeding. The risk of overweight/obesity was increased 4.17-fold if mothers were overweight/obese (95% CI 1.76-9.88) and 5.1-fold (95% CI 2.50-10.40) if both parents were overweight/obese. There were 133 children (22.8%) with a proatherogenic lipid profile. The risk of a proatherogenic lipid profile was increased 2.44-fold (95% CI 1.54-3.86) if they were overweight/obese at 4 years of age and 2-fold if the father was overweight/obese (95% CI 1.22-3.35).

Conclusions Four-year-old overweight/obese children have higher lipid risk profiles. Offspring of overweight/obese parents have an increased risk for obesity and a proatherogenic lipid profile. *(J Pediatr 2017;187:153-7).*

The prevalence of overweight and obesity in children is a well-recognized public health problem in Europe,[1] as well as in other developed countries.[2] Obesity persists from childhood to adolescence and into adulthood, and is a leading cause of health problems.[3]

Identification of children at risk for early atherosclerosis is essential because predisposing cardiovascular disease (CVD) risk factors cluster in childhood and persist into adulthood.[4-6] Even though atherogenesis is a multifactorial process, abnormalities in lipoprotein metabolism represented approximately 50% of the population-attributable risk of developing CVD.[7] The best predictor of lipid or lipoprotein levels in adulthood is the level observed in childhood,[6] although the cutoff for defining dyslipidemia in children remains controversial.[8] Several lipoprotein ratios or "atherogenic indices" have been defined in an attempt to optimize the predictive capacity of the lipid profile.[9] The total/high-density lipoprotein (HDL) cholesterol ratio and the low-density lipoprotein/HDL cholesterol ratio are 2 important indicators of vascular risk, with a predictive value greater than the single variables.[10] Furthermore, the association between triglycerides (TG) and HDL cholesterol in late adolescence predicts a proatherogenic lipid profile in adulthood, independent of obesity and weight gain.[11] Associations with insulin resistance have been found in obese children.[12] A high TG/HDL ratio is associated with an unfavorable cardiometabolic profile in a population aged 6 to 16 years.[13] To date, the clinical value of lipid ratios has not been evaluated in younger children.

This study aimed to determine lipid profiles in early childhood and to evaluate their association with weight status at 4 years of age. We also evaluated whether the risk of being overweight/obese or having an altered lipid profile at the age of 4 years was associated with maternal and/or paternal overweight/obesity.

BMI	Body mass index
CVD	Cardiovascular disease
GWG	Gestational weight gain
HDL	High-density lipoprotein
TG	Triglycerides
WHO	World Health Organization

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Methods

This population-based birth cohort study (Infancia y Medio Ambiente [Environment and Childhood Project]) recruited pregnant women during the first trimester of pregnancy from 7 Spanish areas between 2003 and 2008, and followed a common protocol.[14] Inclusion criteria were as follows: age >16 years, singleton pregnancy, no assisted conception, intention to deliver at the reference hospital, and no communication handicap. The population considered in the present study consisted of mothers who agreed to participate in the Infancia y Medio Ambiente cohorts of Asturias and Sabadell, and their children who had lipid data available. A total of 1151 eligible women (494 from Asturias and 657 from Sabadell) agreed to participate. A total of 1044 children (453 from Asturias and 591 from Sabadell) of these women were followed up to 4 years of age. Finally, 582 children (266 from Asturias and 316 from Sabadell) had lipid data available and were included in this study.

The study was approved by the local ethics committee, and all participants signed the informed consent.

Maternal height was measured and prepregnancy weight reported by the mother at the first trimester visit. These values were used to calculate prepregnancy body mass index (BMI) (in kg/m^2). Reported prepregnancy weight was highly correlated with measured weight at 12 weeks of pregnancy ($r^2 = 0.96$; $P < .0001$).[15] Paternal weight and height were reported by the mother at the first trimester visit and used to calculate paternal BMI. Maternal and paternal BMI were grouped according to the World Health Organization (WHO) categories for underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥30 kg/m^2).

Height and weight of children were measured by staff trained in anthropometry. Height was measured twice to the nearest 0.1 cm using a wall-mounted stadiometer after the participant removed their shoes. Weight was measured twice to the nearest 0.1 kg using a digital scale with the participant wearing only light clothes. Overweight/obesity in children were defined using the International Obesity Task Force criteria that enable global comparison of prevalence.[16]

Nonfasting blood samples were collected from children in both cohorts. Serum total cholesterol, TG, and HDL levels were determined using a Roche analyzer (Modular Analytics Serum Work Area, Mannheim, Germany) in Asturias. Plasma total cholesterol, TG, and HDL levels were determined using the ABX-Pentra 400 (HORIBA ABX SAS, Madrid, Spain) in samples from Sabadell. Low-density lipoprotein levels were calculated using the Friedewald formula.[17] Concentrations of all these cardiometabolic biomarkers were homogeneous across cohorts.

Lipid ratios (TG/HDL cholesterol, low-density lipoprotein cholesterol /HDL, and total/HDL cholesterol) were calculated. The variable TG/HDL ratio was not normally distributed and thus underwent a natural logarithmic (ln) transformation. They were also stratified into tertiles to further evaluate their relationship with other variables. A proatherogenic profile was defined as having the 3 lipid ratios in the third tertile of our population.

Questionnaires were administered during the first and third trimesters of pregnancy. We obtained information on maternal and paternal age and education, maternal and paternal occupations, maternal country of birth, maternal smoking during pregnancy, and parity. Social class was defined according to occupation during pregnancy of the mother or the father using a widely used Spanish adaptation of the International Standard Classification of Occupations coding system.[18] Gestational weight gain (GWG) was calculated as the difference between the first prepregnant weight and the last weight measurement before delivery. GWG was classified as low, recommended, and high based on the US Institute of Medicine guidelines.[19] Information on gestational diabetes and on children's birth weight, gestational age, and sex was obtained from clinical records. Data on breastfeeding duration were collected when infants were approximately 6 and 14 months. All questionnaires were conducted face to face by trained interviewers.

Statistical Analyses

Differences between BMI categories were examined by the χ^2 test for categorical variables, and the Student *t* test or ANOVA for continuous variables.

For multivariable analysis, we used logistic regression models to evaluate the risk of the proatherogenic profile on being overweight/obese, initially adjusting for education, mother's BMI, father's BMI, birth weight, weeks of gestation, sex, and predominant breastfeeding. We then used a stepwise procedure under the forward method and variables with a significance of $P < .1$ were maintained in the model according to the likelihood ratio test. We further analyzed the risk of either overweight/obesity and the proatherogenic profile by having overweight/obese parents using the same procedure. Sensitivity analyses using the WHO classification for overweight and obesity in children were performed to assess the robustness of our results. Statistical analyses were conducted using SPSS for Windows, Version 15.0 (SPSS Inc, Chicago, Illinois).

Results

Overall, 12.9% of the 4-year-old children were classified as overweight and 6.4% as obese according to the International Obesity Task Force. The highest prevalence of overweight and obesity was observed in children from Asturias (14.3% and 9.4%, respectively), whereas this prevalence in children from Sabadell was lower (11.7% and 3.8%, respectively). Using the WHO classification, the overall prevalence of overweight was 13.8% and obesity was 14.2%.

Table I (available at www.jpeds.com) shows anthropometric variables, sociodemographic characteristics, and other factors related to gestation and breastfeeding from the 582 mothers in relation to the weight status of their offspring, as well as data of the father's BMI. A total of 20.9% of mothers were overweight and 9.6% were obese, whereas 45.5% of fathers were overweight and 13.9% were obese. A total of 39% of women gained more than the recommended weight during pregnancy (32%, normal weight; 60%, overweight; 44%, obese).