# Association Between Apo B Levels in Mothers and in their Pre-school Age Offspring

VALERIA HIRSCHLER*, MAXIMILIANO MARTIN**, KAREN OESTREICHER*, CLAUDIA MOLINARI*, LAURA BOERO**, WALTER TETZLAFF**, FERNANDO BRITES**, Buenos Aires, Argentina

*University of Buenos Aires. **Laboratory of Lipids and Atherosclerosis, Department of Clinical Biochemistry, School of Pharmacy and Biochemistry, INFIBIOC, University of Buenos Aires. CONICET. Buenos Aires. Argentina.

Running Title: Apo B in mothers and their offspring.

Type of manuscript: Original Article.

Word count: 2967; tables: 3.

Corresponding author: Valeria Hirschler.

Address: Maipu 812, 5M; Buenos Aires (1006), Argentina.

Phone: 54 11 4803 7794; e mail: vhirschler@gmail.com.

Key words: Cardiovascular disease, dyslipidemia, apo B, pre-school children, mothers.

Abbreviations: Cardiovascular disease (CVD), apolipoprotein (apo).

## ABSTARCT

**Objective**: To determine the association between apo B levels in mothers and their pre-school offspring.

**Methods**: Anthropometric measurement (e.g. BMI), lipids, lipoproteins, and apolipoproteins (e.g. apo B) levels were obtained in mothers and their children in November 2015 in Buenos Aires.

**Results**: Eighty-four children (42M) aged 5.3±1.6 years and their mothers aged 33.8±7.2 years were examined. The prevalence of overweight was 39.2% (33) in mothers and 22.6%(19) in children, and the prevalence of obesity was 38.1% (32) in mothers and 10.7% (9) in children. Multiple linear regression analysis showed that maternal apo B levels were associated with apo B levels in their offspring, adjusted for confounding variables (Beta=0.29; p=0.03; $R^2$=0.25). Furthermore, offspring born to mothers with high apo B levels were six times likelier to have high apo B levels (OR), 5.7; (95% CI 1.3-25.5].
**Conclusions**: This study suggests that maternal apo B levels were significantly associated with apo B concentration in their pre-school age children**.**

## Background

The relationship between traditional cardiovascular disease (CVD) risk factors and the occurrence of cardiovascular events is well understood (1). The odds of developing CVD in adulthood are enhanced if risk factors, including dyslipidemia, are present in childhood (1,2). Cardiovascular risk factors are well known to be shared traits between parents and their children (3,4). Many CVD risk factors correlate independently of parent and child BMI (5). In a large group of elementary school children and their mothers, we have previously shown that the increase in a mother's waist circumference was associated with high prevalence of metabolic syndrome in their children (6).

Dyslipidemia, a CVD risk factor, is well known to be a feature shared between parents and their children (7-9). However, studies have clearly shown that traditional determinants, such as total cholesterol, HDL-C, LDL-C and triglycerides are inadequate for assessing the risk for future CVD, especially in children of younger ages (10). Although low density lipoprotein-cholesterol (LDL-C) remains the chief target of therapy to lower CVD events, apolipoprotein B (apo B), the

major apolipoprotein of very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), and LDL particles, has also been proposed as a marker with high predictive value (11). There has been a growing emphasis on the fact that each LDL particle and other lipoproteins such as VLDL and IDL contain a single molecule of apo B, meaning that measurement of apo B concentration constitutes a reliable surrogate of the number of circulating atherogenic lipoprotein particles. Small, dense LDL particles are common and, when present, LDL-C concentration underestimates the number of LDL particles (11). Because risk of atherosclerosis appears to be more directly related to the number of circulating atherogenic particles that enter the arterial wall than to the concentration of LDL-C, apo B would be a better predictor of CVD risk than serum LDL-C in children (12).

Although the amount of CVD risk factors are significantly lower in children than in adults, children with levels at the extremes of the normal range are thought to be at greater future risk (13). A recent study found positive correlations for measures of adiposity, systolic blood pressure (BP), total cholesterol, LDL-C, HDL-C, triglycerides, and insulin sensitivity between parents and their children (6-18 years) (5). The measurement of apo B is standardized, simple, and inexpensive and can be done with samples obtained from non-fasting individuals (11). As fasting is an issue in pre-school aged children, the measurement of apo B levels allows us to circumvent this problem. To the best of our knowledge, there is no information about the association between apo B levels in mothers and their pre-school aged children. The objective of this study was to determine the association between apo B levels in mothers and in their pre-school aged offspring.

**Methods**

*Study design*

A cross-sectional study was designed to determine the association between apo B levels in mothers and their pre-school aged children. The study was approved by the Human Rights Committee. Each parent gave written informed consent after an explanation of the study and before its initiation.

*Study population*

Convenience sampling was used due to economic limitations. Approximately 70% of children attending a pre-school in the northern suburban area of Buenos Aires, Argentina, were included in the sample. Eighty-four mother/child pairs were evaluated. Children aged 3-6 years were examined in November 2015. Age, sex, weight, height, and waist circumference were recorded for all children attending the pre-school (112; 56 males). However, only 84 mother/child pairs were included in the study, as only these pairs were not excluded based on the exclusion criteria below.

*Exclusion criteria*

Exclusion criteria were: 1-missing anthropometric or biochemical data; 2-mothers and/or children not fasting for 12 hours; 3-presence of type 1 or type 2 diabetes or other chronic diseases; 4-mothers being pregnant; 5- the informed consent form not being signed. Furthermore, only one child per mother was included. Given that some families had more than one child, the sample was randomized to determine which child would be included. We chose to study mothers and not both parents, as only mothers could attend the evaluation with their children. Most of the fathers worked full time and could not attend. Therefore, fathers were not included in the study.

*Data Collection*

Three sets of data were collected: demographic data, anthropometric measurements, and blood samples for lipid, lipoprotein, and apolipoprotein analysis. Trained research assistants performed all measurements. Socio-demographic characteristics recorded included age, level of education and the presence or absence of a refrigerator or a dirt floor in the house. These two indicators are used to identify families of very low socioeconomic level by the National Statistics and Censuses Institute of Argentina (INDEC,2010) (14). Height and weight were measured with subjects wearing light clothing and without shoes. Height was recorded to the nearest 0.1 cm with a wall-mounted stadiometer. Weight was measured to the nearest 0.1 kg on a medical balance scale.

*Sample Analysis*

Whole-blood samples were collected from the antecubital vein, after an overnight fast of 12 hours, for measurement of triglycerides, total cholesterol, LDL-C, HDL-C, apo B, and apo A-I levels. In order to avoid technical bias due to possible changes in calibration or internal quality control, all samples were analyzed with a standardized homogeneous assay in a single laboratory. Lipids and lipoproteins were analyzed by standardized methods using the 5800 AU Analyzer (Beckman Coulter, CA, USA). Apo A-I and apo B levels were quantified by immunonephelometry (IMMAGE®, Beckman Coulter, Fullerton, CA, USA). Within and between assay coefficients of variation (CVs) were the following: total cholesterol 1.1 and 1.5 %; high density lipoprotein-cholesterol (HDL-C) 3.2 and 3.8 %; triglycerides 1.3 and 2.4 %, and apo B, 2.41 % and 1.16%, respectively. Concentration of non-HDL-C was calculated as total cholesterol minus HDL-C. LDL-C concentration was calculated with the Friedwald formula given that no participant presented with severe hypertriglyceridemia (15).

*Defining overweight/obesity and dyslipidemia in children*

Body mass index (BMI) was calculated as weight in kilograms divided by height in $m^2$, and z-score (BMI-z) was calculated as the deviation of BMI based on the mean CDC reference values, accounting for age and sex (16). Children were classified as underweight (<5th percentile), normal weight (5th to <85th percentile), overweight (85th to <95th percentile), or obese (≥95th percentile) according to Center for Disease Control (CDC) age- and sex-specific growth chart percentiles (16). Triglyceride concentrations ≥1.69 mmol/L were considered abnormal according to the reference standards of the American Heart Association (17). LDL-C > 3.36 mmol/L and HDL-C <1.04 mmol/L were considered abnormal for children (18).

*Defining overweight/obesity and dyslipidemia in mothers*

Overweight was defined as BMI ≥25 and <30 $kg/m^2$ and obesity as BMI ≥30$kg/m^2$ according to the National Cholesterol Education Program´s Adult Treatment Panel III (19). Abnormal lipid levels were defined as triglycerides >1.69 mmol/L, HDL-C <1.29 mmol/L, and LDL-C >3.36 mmol/L (19).

*Statistical analysis*

Risk factors in children and mothers were described by mean ± standard deviation for continuous variables and percentage for categorical variables.

The fit to normal distribution of continuous variables was assessed using the Shapiro–Wilk test. Variables with a skewed distribution were logarithmically transformed for analysis. After log transformation, the data were tested again to confirm the findings. When comparing two groups with normally distributed data, a student *t*-test was performed. When comparing more than two groups with normally distributed data, one-way analysis of variance (ANOVA) and Student–

Newman–Keuls post hoc tests were used. Bonferroni's adjustment was carried out when many comparisons were performed. All data with skewed distributions were normalized after log transformation. When the homogeneity of the variances could not be proved, the Brown–Forsythe test was employed. In particular in this analysis we applied it in cases where, although homogeneity was not rejected, the p value was not high enough to accept it. In those cases (non-HDL-C and LDL-C) we performed both tests (standard Anova and Brown-Forsythe) in order to determine the consistency of the results. Pearson and Spearman correlation coefficients were calculated to assess the degree of mother-child association in continuously distributed risk factors. Pearson correlation was used for normal data distribution, and Spearman, for skewed distribution. Multiple linear regression analysis was performed to examine the relationship between apo B levels in mothers and their offspring, adjusted for age, sex, and children's and maternal BMI. Multiple logistic regression analysis was performed to examine the relationship between high apo B levels in mothers and their offspring, adjusted for age, sex, and children's and maternal BMI.

All tests were 2-sided, and p-values of less than 0.05 were considered statistically significant. Analyses were performed using the SPSS statistical software package version 22.0 (Chicago, IL, USA). The authors had full access to the data and take responsibility for its integrity.

## Results

*Characteristics of mothers and their children*

Anthropometric measurements were performed in 112 children. However, 28 mother-child pairs were excluded from the study based on the previously stated

exclusion criteria: 6 mothers were pregnant, 14 children only had their father present and not their mother, 3 participants did not sign informed consent forms, and 5 participants were siblings. Therefore 84 mother-child pairs were included in the study.

This information was collected, but was never corrected in analysis. I am assuming this is because these parameters were very similar between all participants. However, this should be stated in the results section after statistics of education level and socioeconomic status are presented.

There was no difference in the mean age and BMI between all children (n=112; 56 males) and those who underwent the complete examination (n=84; 42 males) (p=0.34). All of the pairs belonged to a low socioeconomic level. Ninety percent of the mothers did not have a high school education. None of them had a dirt floor and only one did not have a refrigerator in the house. There was not a significant difference in the socioeconomic levels between families who participated in the study.

Table 1 shows the mean values of all variables for mothers and their children included in the study. Nineteen (22.6%) children were overweight and 9 (10.7%) were obese; whereas 33 (39.2%) mothers were overweight and 32 (38.1%) were obese. The average maternal BMI was approximately 29 $kg/m^2$, indicating that, as a group, they were overweight/obese. Thirty-four children (40%) and 64 (76%) mothers had low HDL-C concentration; whereas 4 children (5%) and 19 (23%) mothers had high triglyceride concentration. Three children (4%) and 16 (19%) mothers had high total cholesterol concentration. In addition, 2 children (2%) and 21 (25%) mothers had high LDL-C concentration. The prevalence of low HDL-C was the most common CVD risk factor among children

and their mothers.

*Univariate associations*

Most variables explored as continuous variables were significantly correlated between mothers and their offspring: BMI (r=0.50) triglycerides (r=0.31), total cholesterol (r=0.31), HDL-C (r=0.29), non-HDL-C (r=0.29), LDL-C (r=0.33), apo B (r=0.34), and apo B/apo AI (r=0.33). However, apo A-I levels were not significantly associated. The sample size was too small to evaluate sex-specific correlations.

*Analysis of CVD risk factors in children according to maternal apo B quartile*

Maternal apo B levels ranged from 0.40 to 2.08 g/L. Children were divided into four groups according to maternal apo B quartiles and the means of several variables were compared between these groups (Table 2). Children's z-BMI total cholesterol, non-HDL-C, LDL-C, and apo B significantly increased as maternal apo B quartiles increased (Table 2). However, mean values of HDL-C, triglycerides, apo A-I, and apo B/apo A-I were not significantly different between maternal apo B quartiles. Children with maternal apo B >III quartile had significantly higher BMI-z (1.2 ± 1.1 *vs.* 0.4 ± 1.2; $p<0.05$), LDL-C (2.73 ± 0.75 *vs*. 2.05 ± 0.57 mmol/L; $p<0.05$), and apo B (0.93 ± 0.20 *vs*. 0.74 ± 0.15 g/L; $p<0.01$) than those with maternal apo B <III quartile (Figure 1).

*Multiple regression analyses*

Multiple linear regression analysis showed that maternal apo B levels were significantly associated with apo B levels in their offspring adjusted for age, sex, and children's and maternal BMI ($R^2=0.25$; $p<0.05$) (Table 3). Furthermore, multiple logistic regression analysis showed a significant increase in the odds ratio for high apo B (> III quartile) among pre-school age children whose mothers had

apo B > III quartile compared with those with maternal apo B< III quartile adjusted for sex, age, and children's BMI [odds ratio (OR), 5.7; (95% CI 1.3-25.5]. In this cohort, an offspring born to a mother with high apo B levels had approximately six times the likelihood of having high apo B, independent of age, sex, and adiposity. This suggests that these pre-school aged children whose mothers have a high apo B concentration are at higher risk for CVD.

**Discussion**

The aim of this study was to determine the association between apo B levels in mothers and in their pre-school offspring. We found that maternal apo B levels were significantly associated with apo B levels in their pre-school age offspring, adjusted for age, sex, and children's and maternal BMI. Therefore, mother-child correlations in apo B levels were independent of mother-child BMI. There is strong evidence demonstrating that higher levels of BMI, BP, and lipids, even within the normal range, tend to track into adulthood, are difficult to reverse, and are associated with increased morbidity over time (20). Previous studies in adults showed that the non-traditional risk factor, apo B, was a better marker of risk for CVD than LDL-C (12,21). Because atherosclerosis begins early in life and remains hidden for many years, screening for modifiable CVD risk factors should be performed (7). Successful prevention of CVD depends on early identification and modification of risk factors. Therefore, measurement of apo B levels in mothers and in their pre-school children may identify individuals with CVD risk who may benefit from early intervention.

There was a high prevalence of overweight/obesity in pre-school children (33%) and in their mothers (77%) in this sample. Furthermore, we found that apo B levels in mothers were significantly associated with apo B levels in their

children. Specifically, the mother-child apo B correlation was independent of adiposity. Furthermore, the multiple linear regression analysis showed that after adjusting for mother and child BMI, the correlation remained significant. Therefore, the implications of our results apply to both obese and non-obese mothers and their offspring. Consistently, a previous longitudinal study in adolescents showed that other mechanisms could act, in part, independently of obesity, as insulin resistance during adolescence did not follow the expected course in relation to developmental changes in adiposity (22). This highlights the importance of shared genetic or environmental traits independent of obesity in the transmission of CVD risk (7). An important genetic influence on BMI and lipid levels is supported by adoption and twin studies, where a strong correlation was found between adopted offspring and their biological parents, and between monozygous twins and other pedigrees (23,24). Studies have suggested that CVD begins during childhood, which may in part be due to genetic susceptibility, while increased CVD risk is also mediated or modulated through environmental/lifestyle factors [25,26].

Our results from a sample of pre-school children with and without risk factors indicate that measurements of apo B concentration correlate between mothers and their offspring. Our findings were consistent with other studies associating parents' lipid profiles with those of their offspring (7,27). In 1984, the Basel Family Study showed that BMI and lipid levels, such as cholesterol, triglycerides, and HDL-C, were strongly correlated between children and parents from 506 Swiss families (28). However, the mean age of children from the Swiss cohort was 17.3 years (28). In addition, Reis et al. described correlations of traditional CVD risk factors between 170 parent-child pairs living in the USA [7]. A

study performed by our group in a large cohort of elementary school children showed that a mother's waist circumference was associated with the presence of the metabolic syndrome in their children (6). However, our study differs from previous studies in that the offspring were pre-school children (under the age of 6 years) and non-traditional risk factors were measured, whereas most previous studies have examined the association between traditional risk factors in parents and their children over six years old. We found that children with mothers with apo B concentrations in the fourth quartile not only had significantly higher apo B levels, but also higher z-BMI, total cholesterol, and LDL-C than children in the other quartiles of maternal apo B. Veerkamp et al. (29) suggested that the most consistent lipoprotein abnormality present across time within and between different affected individuals with familial combined hyperlipidemia was elevated apo B concentration. Consistently, previous studies demonstrated that non-fasting apolipoproteins were superior to any of the lipid levels for estimation of the risk of acute myocardial infarction regardless of ethnicity, age, or sex (11). In the clinical setting, measurement of triglycerides and LDL-C (calculated by Friedewald formula) requires a 12 hour fast. In contrast, measurement of non-traditional risk factors, such as apo B, might be more convenient because they can be measured at any time, regardless of food intake (11,30). The clinical measurement of apolipoproteins is standardized, simple, and inexpensive (11). Therefore, as fasting is an issue in the pediatric population, especially in pre-school ages, measurement of apo B might be a more easily accessible tool for identifying children at risk of CVD. The more accurately risk can be defined, the more cost effective primary prevention will be (11). As far as we know, the association between apo B levels in mothers and their pre-school children has not yet been

described. CVD risk factors in the current health care system focuses on the individuals who present themselves for care. This focus limits the delivery of available preventive healthcare measures, because pre-school children do not seek primary care services. Our study provides additional evidence to support the screening of young parents and their pre-school children to measure apo B levels as it is standardized, simple, inexpensive, and can be measured in non-fasting samples (11). Identification of CVD risk factors in mothers should prompt a recommendation for their children to consult a pediatrician for assessment, diagnosis, prevention, and/or treatment.

Several limitations of this study should be acknowledged. First, it was a cross-sectional study, and thus the directionality of the associations cannot be established. Second, a local sample was recruited from a single geographic area. Third, only mothers and not fathers were able to participate. Based on this study design, we were unable to assess the relative contribution of the risk factor status of fathers and both parents simultaneously on children's risk factors. Because this study was performed in a community from low socioeconomic level, the results cannot be generalized for other communities. The strengths of our study included a population-based sample of only pre-school children, which excluded the influence of puberty on our results. Finally, few, if any, previous studies in pre-school children have examined the association between apo B levels in mothers and their children, taking into account the potential confounding effect of anthropometric measures.

**Conclusions**

Our findings indicate that maternal apo B levels are significantly associated

with apo B levels in their pre-school age children, adjusted for confounding variables. Furthermore, the mother-child correlations in apo B levels were independent of mother-child adiposity. Measurement of apo B levels in mothers may identify both high-risk children and mothers who may benefit from intervention. Further longitudinal studies should be performed to confirm these findings.

There is not any potential conflict of interest

**References**


1- Li, S., Chen, W., Srinivasan S.R., Bond, M.G., Tang, R., Urbina, E.M., & Berenson, G.S.(2003) Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. JAMA, 290, 2271–2276. DOI: 10.1001/jama.290.17.2271

2- Raitakari, O.T., Juonala, M., Kähönen, M., Taittonen, L., Laitinen, T., Mäki-Torkko, N.,… Viikari, J.S. (2003) Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the cardiovascular risk in young finns study. JAMA, 290,2277–83. DOI: 10.1001/jama.290.17.2277

3- Harrap, S.B., Stebbing, M., Hopper, J.L., Hoang, H.N., & Giles, G.G. (2000) Familial patterns of covariation for cardiovascular risk factors inadults: the Victorian Family Heart Study. Am J Epidemiol,152,704-15.

4- Rasmussen-Torvik, L.J., Pankow, J.S., Jacobs, D.R., Steffen, L.M., Moran A.M., Steinberger, J., & Sinaiko, A.R. .(2007) Heritability and genetic correlations

of insulin sensitivity measured by the euglycaemic clamp. Diabet Med, 24,1286-9. DOI: 10.1111/j.1464-5491.2007.02271.

5- Halvorsen, T., Moran, A., Jacobs, D.R. Jr, Steffen, L.M., Sinaiko, A.R., Zhou, X., & Steinberger, J. (2015) Relation of Cardiometabolic Risk Factors between Parents and Children. J Pediatr., 2015,167:1049-56.e2. doi:10.1016/j.jpeds.2015.07.053.

6- Hirschler, V., Roque, M., Calcagno, M.L., Gonzalez, C., Aranda, C.(2007) Maternal waist circumference and the prediction of children's metabolic syndrome Arch Pediatr Adolesc Med,161,1205-10. DOI: 10.1001/archpedi.161.12.1205

7- Reis, E.C., Kip, K.E., Marroquin, O.C., Kiesau, M., Hipps, L. Jr., Peters, R.E., & Reis, S.E. (2006). Screening children to identify families at increased risk for cardiovascular disease. Pediatrics , 118,e1789-97. DOI: 10.1542/peds.2006-0680

8- Schwandt, P., Bischoff-Ferrari, H.A., Staehelin, H.B., & Haas, G.M. (2009). Cardiovascular risk screening in school children predicts risk in parents. Atherosclerosis , 205,626-31. doi: 10.1016/j.atherosclerosis.2009.01.019.

9- Vik, K.L., Romundstad, P., & Nilsen,T.I. (2013). Tracking of cardiovascular risk factors across generations: family linkage within the population- based HUNT study, Norway. J Epidemiol Community Health, 67,564-70. doi: 10.1136/jech-2012-201634.

10- Marma, A.K., Berry, J.D., Ning ,H., Persell, S.D., & Lloyd-Jones, D.M. (2010). Distribution of 10-year and lifetime predicted risks for cardiovascular disease in US adults findings from the National Health and

Nutrition Examination Survey 2003–2006. Circ Cardiovasc Qual Outcomes , 3, 8–14.. doi: 10.1161/CIRCOUTCOMES.109.869727.

11- McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J, et al. (2008) INTERHEART study investigators: Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. Lancet, 372:224–233.

12- Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard PM, Dagenais GR, et al. (1996): Apolipoprotein A-1 and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Quebec Cardiovascular Study. Circulation ,94:273–78.

13- Nguyen QM, Srinivasan SR, Xu JH, Chen W, Berenson GS. (2008) Changes in risk variables of metabolic syndrome since childhood in pre-diabetic and type 2 diabetic subjects: the Bogalusa Heart Study. Diabetes Care, 31:2044-9.

14- INDEC, 2010 National Statistics and Censuses Institute of Argentina (INDEC.2010). http://www.censo2010.indec.gov.ar/ Accessed September 3, 2015.

15- Martin SS, Blaha MJ, Elshazly MB, Brinton EA, Toth PP, McEvoy JW, Joshi PH, Kulkarni KR, Mize PD, Kwiterovich PO, Defilippis AP, Blumenthal RS, Jones SR. (2013). Friedewald-estimated versus directly measured low-density lipoprotein cholesterol and treatment implications. J Am Coll Cardiol. 62:732-9

16- Kuczmarski R, Ogden C, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, et al.: (2002) 2000 CDC growth charts for the United States: methods and development. Vital Health Stat ,246:1–190.

17- Kavey, R.E., Daniels, S.R., Lauer, R.M., Atkins, D.L., Hayman, L.L., & Taubert, K.; American Heart Association. (2003). American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation, 107,1562-6.

18- Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. (2011). Pediatrics. 128 S213-56.

19- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2002) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Choles- terol in Adults (Adult Treatment Panel III) final report. Circulation ,10: 3143–421.

20- Balakrishnan PL. (2014) Identification of obesity and cardiovascular risk factors in childhood and adolescence. PediatrClin North Am,61:153-71.

21- Pencina MJ, D'Agostino RB, Zdrojewski T, Williams K, Thanassoulis G, Furberg CD, Peterson ED, Vasan RS, Sniderman AD. Apolipoprotein B improves risk assessment of future coronary heart disease in the Framingham Heart Study beyond LDL-C and non-HDL-C. Eur J Prev Cardiol. 2015;22:1321-7.

22- Moran A, Jacobs DR Jr, Steinberger J, Steffen LM, Pankow JS, Hong CP, et al. (2008) Changes in insulin resistance and cardiovascular risk during adolescence: establishment of differential risk in males and females. Circulation, 117:2361-2368.

23- Hunt SC, Hasstedt SJ, Kuida H, Stults BM, Hopkins PN, Williams RR. (1989) Genetic heritability and common environmental components of resting and stressed blood pressures, lipids, and body mass index in Utah pedigrees and twins. Am J Epidemiol ,129:625–38.

24- Carmelli D, Cardon LR, Fabsitz R. (1994). Clustering of hypertension, diabetes, and obesityin adult male twins: same genes or same environments? Am J Hum Genet, 55:566–73.

25- Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willet WC. (2000) Primary prevention of coronary heart disease in women through diet and lifestyle. N Engl J Med, 343:16–22.

26- Danner FW. (2008) A national longitudinal study of the association between hours of TV viewing and the trajectory of BMI growth among US children. J PediatrPsychol, 33:1100–8

27- Harrap SB, Stebbing M, Hopper JL, Hoang HN, Giles GG. (2000) Familial patterns of covariation for cardiovascular risk factors in adults: the Victorian Family Heart Study. Am J Epidemiol ,152: 704-15

28- Staehelin HB, Bruppacher R. (1984). The influence of the family on risk factors in children and adolescents—The Basle Family Study. In: Cardiovacular risk factors in children and adolescents. Verlag Hans Huber; p. 88–149 [Book chapter]

29- Veerkamp MJ, de Graaf J, Hendriks JC,Demacker PN, Stalenhoef AF. (2004) Nomogram to diagnose familial combined hyperlipidemia on the basis of results of a 5-year follow-up study. Circulation, 109:2980–2985.

30- Marcovina SM, Albers JJ, Kennedy H, Mei JV, Henderson LO, Hannon WH; (1994) International Federation of Clinical Chemistry Standardization Project for Measurements of Apolipoproteins A-I and B: Comparability of Apo B values by use of international reference material. ClinChem 40:586–592

**Table 1: Clinical and Metabolic Characteristics of Mothers and their Children.**

| | **Children (n=84)** | **Mothers (n=84)** |
|---|---|---|
| **Age (years)** | 5.3±1.6 | 33.8±7.2 |
| **Sex (Male/female)** | 42/42 | 0/84 |
| **Weight ( kg)** | 19.9±4.4 | 70.9±15.6 |
| **Height (cm)** | 108.4±7.4 | 157.6±5.7 |
| **z-Height** | -0.37±1.27 | |
| **BMI (Kg/m$^2$)** | 16.8±2.1 | 28.7±5.8 |
| **z-BMI** | 0.63±1.12 | - |
| **WC (cm)** | 56.0±7.4 | 94.5±13.1 |
| **Systolic BP (mmHg)** | 88.5±11.1 | 114.0±11.8 |
| **Glucose (mmol/L)** | 4.16±0.40 | 4.66±0.48 |
| **TG (mmol/L)** | 0.97±0.43 | 1.22±0.63 |
| **TC (mmol/L)** | 3.83±0.68 | 4.54±2.34 |
| **HDL-C (mmol/L)** | 1.13±0.25 | 1.19±0.49 |
| **LDL-C (mmol/L)** | 2.22±0.67 | 2.96±1.07 |
| **Non-HDL-C (mmol/L)** | 2.82±0.68 | 3.35±1.07 |
| **Apo A-I (g/L)** | 1.38±0.25 | 1.55±0.27 |
| **Apo B (g/L)** | 0.78±0.19 | 0.94±0.30 |

BMI, body mass index; WC, waist circumference; BP, blood pressure, TG, triglycerides, TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; Apo, apolipoprotein. Data are mean ± SD or median (percentile 25-50) values. Z-score is a quantitative measure of the deviation of a specific variable taken from the mean of that population. In particular, CDC z-BMI takes into account age and sex.

**Table 2: Clinical and Metabolic Characteristics in Pre-school Children According to Maternal Apo B Quartiles**.

| | **Quartile I 0.39-0.73** | **Quartile II 0.75-0.87** | **Quartile III 0.88-1.11** | **Quartile IV 1.14-2.08** |
|---|---|---|---|---|
| Age (years) (NS) | 4.7 ± 0.9 | 5.3 ± 1.0 | 5.4 ± 1.1 | 5.4 ± 0.9 |
| z-BMI(b) | 0.1 ±1.19 | 0.40 ± 1.2 | 0.7 ± 0.9 | 1.20 ± 1.10 |
| Systolic BP (NS) | 83.6 ± 8.9 | 90.0 ± 10.5 | 91.2 ± 11.1 | 89.0 ± 12.8 |
| TC (mmol/L)(c) | 3.6 ± 0.649 | 3.77 ± 0.56 | 3.63 ± 0.62 | 4.34 ± 0.67 |
| HDL-C (mmol/L) (NS) | 1.12 ± 0.20 | 1.20 ± 0.26 | 1.05 ± 0.22 | 1.14 ± 0.31 |
| LDL-C (mmol/L) (a) | 1.99 ± 0.70 | 2.05 ± 0.57 | 2.15 ± 0.55 | 2.73 ± 0.75 |
| TG (mmol/L) (NS) | 1.00 ± 0.56 | 0.88 ± 0.34 | 0.90 ± 0.30 | 1.12 ± 0.46 |
| Non-HDL-C (mmol/L)(c ) | 2.64 ± 0.67 | 2.69 ± 0.59 | 2.71 ± 0.57 | 3.27 ± 0.76 |
| Apo-A-I (g/L) (NS) | 1.34 ± 0.20 | 1.43 ± 0.24 | 1.35 ± 0.24 | 1.40 ± 0.31 |
| Apo B (g/L) (a) | 0.70 ± 0.18 | 0.74 ± 0.15 | 0.78 ± 0.17 | 0.92 ± 0.20 |
| Apo B/Apo-A-I (NS) | 0.50 ± 0.20 | 0.50 ± 0.20 | 0.60 ± 0.10 | 0.70 ± 0.10 |

BMI, body mass index; BP, blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein; LDL-C, low density lipoprotein cholesterol; Apo, apolipoprotein; Z-score is a quantitative measure of the deviation of a specific variable taken from the mean of that population. In particular, CDC z-BMI takes into account

age and sex. Mean values ± SD are shown. Quartile I: (0.40–0.73 g/L);.

(a) Significance found in comparison of QIV to QI & II.

(b) Significance found in comparison of Q IV to QI

(c) Significance found in comparison of Q IV to QI & III.

(NS), non significant.

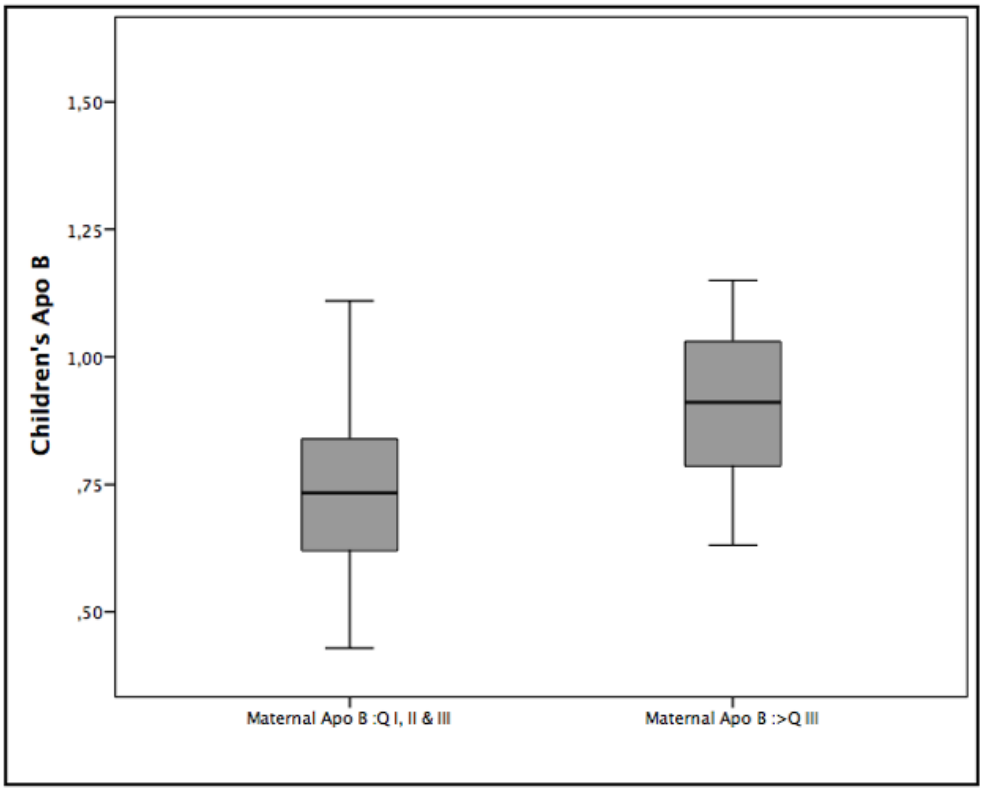
**Table 3: Multiple Regression Analysis**

| | **B (unstandardized coefficient)** | | **B (standardized coefficient)** | **t** | **Significance** |
|---|---|---|---|---|---|
| | B | Standard error | **B** | | |
| Age (years) | -0.08 | 1.42 | -0.01 | -0.06 | 0.95 |
| Sex | 7.64 | 4.91 | 0.20 | 1.56 | 0.13 |
| Maternal Apo- B | 0.19 | 0.09 | 0.29 | 2.17 | 0.03 |
| Maternal BMI | -0.52 | 0.50 | -0.16 | -1.04 | 0.30 |
| Children's BMI | 6.66 | 2.56 | 0.39 | 2.60 | 0.01 |

**$R^2$= 0.25**

BMI, body mass index; Apo, apolipoprotein. Relationship between mother/child Apo B levels adjusted for age, sex, children's BMI, and maternal BMI.

Figure 1: Boxplot. Children's median Apo B levels and interquartile ranges are presented separately according to the presence of maternal high apo B (>III Quartile) among pre-school children. Apo B levels in children with maternal apo B levels >III quartile were significantly higher than in children with maternal apo B levels ≤ III quartile ( $p<0.01$) . The boxes define the 25th and 75th percentiles, and enclose the median; the extensions define the range of values


Children's Apo B
1,50
1,25
1,00
,75
,50
Maternal Apo B :Q I, II & III
Maternal Apo B :>Q III