

## Coronary Risk Factors in Adolescence. The FRICELA Study

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**Aims.** In a group of adolescents, to examine the prevalence of behaviors and risk factors that predispose to coronary heart disease and ascertain their associations.

**Methods.** A population of 2,599 adolescents, age 12 to 19 years, both sexes, was studied. The study sites were 30 public or private medical centers located in the Federal District and 12 provinces of Argentina.

**Results.** Teenagers with hypercholesterolemia had a greater body mass index, higher incidence of hypertension, and more frequent sedentary lifestyle. There was a positive correlation between hypertension, body mass index, and family history of hypertension, and a negative correlation with physical exercise. Obesity in the young correlated with obesity in their parents. At the age of 19 years, 42% consumed alcohol and 28% smoked. The association between smoking and alcohol consumption was very high ( $P < 0.0001$ ). The smoking habits of parents strongly influenced their children.

**Conclusions.** Early inculcation of a healthy lifestyle, consisting of regular physical exercise, a healthy diet, and no smoking, could be the most important behavioral and risk factor interventions in the effort to curtail atherosclerosis in adults.

**Key words:** *Coronary risk factors. Cardiovascular epidemiology. Adolescence.*

### Factores de riesgo coronario en la adolescencia. Estudio FRICELA

**Objetivos.** Conocer la prevalencia de conductas y factores de riesgo para la enfermedad arterial coronaria en la adolescencia, así como algunas de las asociaciones de dichos factores.

**Pacientes y método.** Se estudió a una población de 2.599 adolescentes de ambos sexos, de 12 a 19 años, procedentes de 30 centros sanitarios, públicos o privados, de la Capital Federal y de 12 provincias de la República Argentina.

**Resultados.** Los pacientes que presentaron hipercolesterolemia resultaron tener un mayor índice de masa corporal, hipertensión arterial y sedentarismo. Se observó una correlación positiva de la hipertensión arterial con el índice de masa corporal y con la historia familiar de hipertensión arterial, y negativa con el ejercicio físico regular. La obesidad de los jóvenes se vinculó con la de sus progenitores. A los 19 años, el consumo regular de alcohol y de tabaco ascendía al 42 y 28%, respectivamente. La asociación del consumo de tabaco y alcohol resultó ser alta ( $p < 0,0001$ ). El hábito tabáquico de los padres en el hogar demostró tener una importante repercusión entre los jóvenes.

**Conclusiones.** Los estilos de vida saludables incorporados de manera temprana, como el ejercicio físico regular, los hábitos alimentarios adecuados y la abstención de tabaco, podrían contribuir a intervenir sobre las más importantes conductas y factores de riesgo para la enfermedad vascular aterosclerótica, con el objeto de disminuir la incidencia de la misma en la edad adulta.

**Palabras clave:** *Factores de riesgo coronario. Epidemiología cardiovascular. Adolescencia.*

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## INTRODUCTION

The first stage of atherosclerosis is now recognized as hypercholesterolemia and the first manifestation of this disease is endothelial dysfunction. Early lesions of the arterial endothelium, generally occurring in lactating infants and chil-

dren, consist of raised formations known as fatty streaks, which are reversible. Their most advanced form, a fibrous plaque, is irreversible, appears in early adulthood and progresses with age. Arterial calcification develops after the fourth decade of life, and when this occurs, the atherosclerotic disease can produce symptoms.

The risk factors for atherosclerosis in general, and for coronary artery disease in particular, are low-density lipoprotein (LDL) cholesterol, smoking, obesity, diabetes mellitus and arterial hypertension. These risk factors have been identified more frequently in the children of parents with coronary disease; thus, the parents of children with elevated risk

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factors present an increased frequency of similar factors and of coronary disease. Excess weight and obesity are the common denominator when various risk factors are present, and physical inactivity is considered to be their cause.

Regular physical exercise and proper eating habits, established at an early age, can have an effect on the most significant behavioral factors and risk factors for developing atherosclerotic vascular disease. This in turn can help decrease its incidence in adulthood.

The FRICAS (Factores de Riesgo Coronario en América del Sur, Coronary Risk Factors in South America) epidemiological study of 1989 to 1994 was carried out to investigate the prevalence and magnitude of risk factors for acute myocardial infarction in the adult population (30-65 years) of Argentina.<sup>1</sup> There are very few studies on the prevalence of coronary risk factors in Argentine adolescents. To fill this need, the FRICELA (Factores de Riesgo Coronario en la Adolescencia, Coronary Risk Factors in Adolescence) study was designed. The proposed objectives were to determine the prevalence of coronary risk factors around the second decade of life according to sex and age, and to study the interrelations among these factors.

## PATIENTS AND METHODS

A cross-sectional, multicenter, national (Argentine Cardiology Society and Argentine Pediatric Society) epidemiological study was designed, with the participation of 88 physicians (investigators) and a cardiologist (general coordinator), from 30 public and private medical centers in the Federal District and 12 provinces of the Republic of Argentina. The study was conducted from July 1994 to August 1997.

A total of 2599 young people of both sexes, from 12 to 19 years of age, underwent a questionnaire interview when they came to the above-mentioned centers to obtain a health certificate, which was mandatory for all students. Those with a preexisting disease such as hyperthyroidism that might cause variations in the risk factors under study were excluded. All those completing the questionnaire were selected, even though 58% were girls or young women and 42% were boys or young men. There were no significant differences in the characteristics (age, social class, education, etc.) of the responders as compared to the nonresponders. The ratio between the size of the sample (N=2599) and the total population of adolescents (N=4 854 932, according to the National Institute of Statistics and Census), was 1:1868. The sample was not representative of the general population, but rather of secondary school students. On the basis of these criteria, 12-year-old students who had started the first year of secondary school early, up to 19-year-olds who had started late and had to repeat a year, were included.

The questionnaire contained items concerning the students' daily and weekly tasks, such as the time devoted to study in school and at home and the time spent on regular physical activity, both in and outside of school. It also included the time spent sleeping and taking naps, and the intake

of food cooked or seasoned at the table with salt. The adolescents were also questioned about the time spent watching television, playing with video games, using a computer, etc. Smokers were defined as persons who regularly smoked at least one cigarette and drinkers were those who regularly drank at least one glass of wine or beer, weekly. These items attempted to give priority to contact with a toxic habit rather than to the amount consumed.

Special care was taken to obtain data on the incidence of coronary disease in the family and on the risk factors present in each parent, including smoking, arterial hypertension, hypercholesterolemia, obesity, physical inactivity and diabetes.

The doctors involved in the study had to have participated in at least one epidemiologic study previously, and were required to record the body parameters (weight, height, heart rate and blood pressure) with instruments validated. Weight was recorded in kilograms to one decimal and height in meters to two decimals. With this data, the body mass index (BMI) ( $\text{kg/m}^2$ ) was calculated. This measure is more easily obtained than skinfold thickness and is now the most frequently used index of excess weight in epidemiological studies.

A highly practical physical inactivity (PI) index was specifically designed for this study. It required dividing the average number of hours spent daily sitting (studying in school and at home, watching television, playing video games and using the computer) by the sum of the hours spent weekly in physical exercise at school and in extracurricular activities. The ideal value was considered to be one, which would mean, empirically, that the average of hours spent daily sitting would be compensated for by an equivalent number of hours per week of physical exercise.

Young people in this series with blood pressure values of 130/85 mm Hg or higher were considered epidemiologically hypertensive, in accordance with the cut-offs for systolic and diastolic arterial pressures established by the Fifth Joint National Committee on High Blood Pressure<sup>2</sup> and used in the CARDIA (Coronary Artery Risk Development In Young Adults) study. Systolic and diastolic arterial pressure were measured with the subject in a sitting position, with the back and feet resting against a support, without crossing the legs and using a cuff of appropriate size for the arm. The Korotkoff first and fifth sounds were recorded in exact numbers, without rounding, and in mm Hg.<sup>3</sup> Heart rate was determined during one minute. The investigators were advised to perform these measurements in a pleasant environment with a comfortable room temperature. The subject should not have smoked during the four hours prior to the examination.

At least one plasma cholesterol determination was made no later than two months after completing the questionnaire. The laboratories performing these analyses used an enzyme-based assay according to the Liebermann-Burchard reaction, which meets the United States National Institute of Health guidelines (1992). Laboratories worked at a coefficient of variation below 15% and participated in an external quality control scheme (e.g., CAP: College of American

Pathologists). Due to the logistics of the country at this time, cholesterol determinations could not be centralized in a single laboratory.

## Statistical analysis

Data were entered in a database with a DBASE format and were analyzed using the EPI INFO and STATISTICA programs. Student's *t* test was used for continuous data and the  $\chi^2$  for qualitative data. Results were expressed as the mean and standard deviation (SD). The Mantel-Haenszel odds ratio (OR) was calculated to quantify excess risk of the presence as related to the absence of the variable under study. Multiple logistic regression was used to adjust for confounding factors.

## RESULTS

The mean age of the 2599 adolescents was  $15 \pm 1.9$  years:  $15.2 \pm 1.9$  for young women and  $14.9 \pm 1.9$  years for young men.

## Alcohol consumption

Among the total, 30% of the young men and 15.5% of the young women were regular drinkers, with an increase in these percentages at 15 to 16 years. At the age of 19, 68% of the young men and 24% of the young women were drinkers (Figure 1).

## Smoking

Regular smoking was recorded in 12.2% of the sample (14.6% of young men and 10.4% of young women), with a marked increase between 15 and 16 years of age. In contrast to the trends seen in alcohol consumption, a plateau was not reached in the last years of adolescence (Figure 2).

At the age of 19, smoking was more common in the young men (37%) than in young women (22%), with a mean for both sexes of 28%, a value close to that estimated by the WHO for this age group in various geographical areas. Among the smokers, 10% of young men and 6% of young women regularly smoked 5 or more cigarettes per day. The overall mean was 2.1 cigarettes per day. In general, young men smoked intermittently during the week, whereas a larger number of young women with this habit smoked daily.

Alcohol consumption was recorded in 68% of the smokers and 18% of the nonsmokers ( $P < .0001$ ). Smoking in adolescents correlated with smoking in their parents. When both parents smoked, the OR was greater than 2 both in young men and young women. Smoking by the mother had a greater influence on young women than on young men. Analysis of each parent separately showed that smoking by the mother was associated with a higher incidence of smoking in adolescents of both sexes (OR=2) than was smoking by the father (OR=1.29) (Table 1).

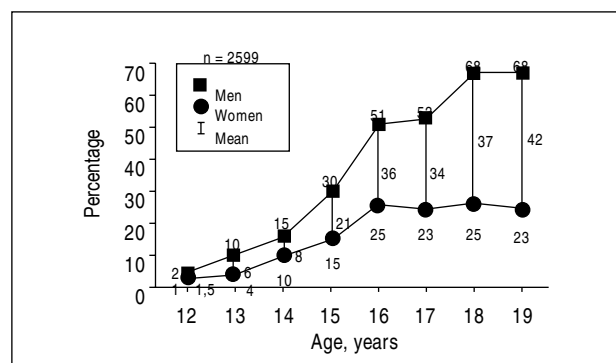


Fig. 1. Alcohol consumption according to sex and age.

## Cholesterolemia

The mean total cholesterol (TC) value for the entire population was 163 mg/dL (161 mg/dL in young men and 165 mg/dL in young women). The higher value in young women is probably attributable to higher levels of high-density lipoprotein (HDL) cholesterol in this group. Distribution according to sex and age showed that the percentage of 19-year-olds with TC values of 200 mg/dL or more was double that of the 18-year-olds, with most of the increase occurring in young men (Figure 3). Among the total, 2.8% (2.6% young men and 2.9% young women) had TC values higher than 235 mg/dL, the cut-off established for detecting family hypercholesterolemia in young people.

There was a direct correlation between TC level and the BMI. Hypercholesterolemia was present in 11.7% of the adolescents with BMI < 25 kg/m<sup>2</sup>, in 18.3% of those with BMI between 25 and 30 kg/m<sup>2</sup>, and in 22% of those with BMI > 30 kg/m<sup>2</sup> ( $P < .05$ ). In the multivariate analysis, after adjusting for the other risk factors, the relative risk of having hypercholesterolemia when BMI was below 25 kg/m<sup>2</sup>, was 1.26 (95% CI, 0.87-1.82) for BMI between 25 and 30 kg/m<sup>2</sup>, and 2.00 (95% CI, 1.10-3.66) for BMI over 30 kg/m<sup>2</sup>. Furthermore, in adolescents with TC values of 200 mg/dL or more, the OR for hypertension was 2.15 (95% CI, 1.6-2.9), ( $P < .001$ ).

Hypercholesterolemia also correlated with physical inactivity according to the pre-established PI index, reaching an OR of 1.58 (95% CI, 1.1-2.3) in the multivariate analysis. This finding suggests that the 255 adolescents with a PI index above 7.5 (10% of the sample) would have a 58% greater chance of having elevated TC.

## Hypertension

Among the adolescents interviewed, 96% consumed food cooked with salt at home and 45% added salt at the table daily; percentages were similar for both sexes.

Adolescent hypertension correlated with the BMI. In adolescents with a BMI < 25, multivariate analysis gave an OR for hypertension of 2.9 (95% CI, 2.16-3.6) for BMI between 25 and 30 kg/m<sup>2</sup>, and an OR of 4.9 (95% CI, 3.07-7.9) for BMI greater than 30 kg/m<sup>2</sup>.

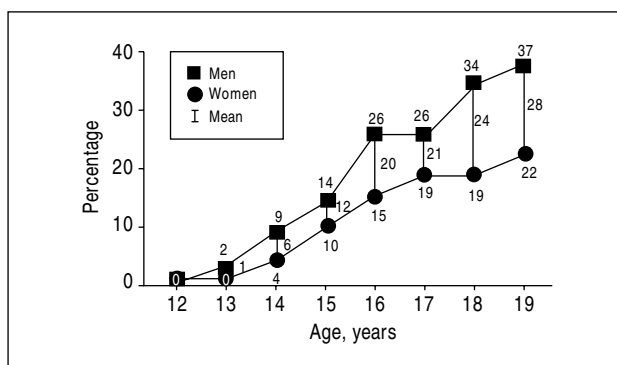


Fig. 2. Smoking according to sex and age.

Adolescents epidemiologically recognized as being hypertensive had hypertensive parents. After adjusting for the remaining risk factors, the OR for this variable was 1.38 (95% CI, 1.09-1.75;  $P<.001$ ) in the multivariate analysis.

There was a positive correlation between maternal hypertension and hypertension in the adolescents, with an OR of 1.38 (95% CI, 1.03-1.86) ( $P=.02$ ). Similarly, a positive correlation was found between paternal hypertension and hypertension in the adolescents, with an OR of 1.32 (95% CI, 0.98-1.78;  $P=.05$ ).

### Physical inactivity-physical exercise

The PI index was below 1.5 in 12% of the adolescents, from 1.5 to 7.5 in 78% and above 7.5 in 10%. In adolescents declaring regular physical exercise (5 h or more per week), the OR for the development of hypertension was 0.77 (95% CI, 0.59-0.99).

### Excess weight-obesity

Among the total, 14% of the adolescents were overweight or obese: 11.1% had BMI between 25 and 30 kg/m<sup>2</sup> and only 3% had BMI greater than 30 kg/m<sup>2</sup>. The mean BMI value was 21.4±3.6 kg/m<sup>2</sup>. In the group with BMI from 25 to 30 kg/m<sup>2</sup>, 59% were young women and 41% were young

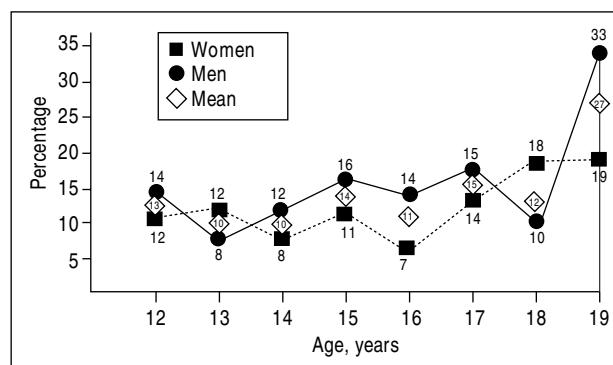


Fig. 3. Hypercholesterolemia (≥200 mg/dL) according to sex and age.

men. In the group with BMI greater than 30 kg/m<sup>2</sup>, 64% were young women and 36% young men.

Obesity in the parents correlated positively with the BMI in both the 25 to 30 kg/m<sup>2</sup> group and the >30 kg/m<sup>2</sup> group ( $P<.0001$ ).

## DISCUSSION

Cardiovascular disease is now the most frequent cause of death worldwide and leaves a large number of patients with chronic incapacity, resulting in elevated health care costs. A predisposition to atherosclerosis may already be present in infants and children; intima-media thickening probably precedes atherosclerosis and its severity can be induced by hereditary and extrinsic factors.<sup>4</sup> Various studies have demonstrated that early atherosclerosis is mainly associated with smoking, elevated LDL-C and arterial hypertension.<sup>5,6</sup> Mahoney et al observed that calcification of the coronary arteries is more prevalent in young men (31%) than in young women (10%). Coronary risk factors seen in children and young adults are associated with early calcification of the coronary arteries. These factors include increased BMI, both in childhood and in adult life, hypertension, and decreased HDL-C.<sup>7</sup>

There is evidence that 100% of adolescents 15 years of age have atherosclerotic aortas and 50% have coronary atherosclerosis. In young people with serum TC values of 140 to 170 mg/dL in life, 25% of the total surface of the aorta is found to be affected by fatty streaks at autopsy, whereas in young people with serum TC concentrations above 200 mg/dL, 50% of the surface of the aorta is affected. The Pathological Determinants of Atherosclerosis in Youth (PDAY) study has shown that a 50-mg/dL increase in LDL-C in adolescents and young adults increases the risk of developing atherosclerotic plaque by 70%, and now this population is considered a high-risk subgroup. These observations clearly demonstrate the importance of cardiovascular risk factors in childhood and adolescence.<sup>5</sup>

### Family history

A history of early or late coronary disease in the grandparents is associated with an increased risk that their grand-

TABLE 1. Risk of smoking in adolescents as related to smoking by their parents

	None	Smoking by the parents		
		Mother	Father	Mother and father
Women	1	2.61 (1.39-4.90)	1.41 (0.79-2.54)	2.35 (1.30-4.28)
Men	1	1.49 (0.74-3.00)	1.17 (0.67-2.06)	2.64 (1.55-4.63)
Both sexes	1	2 (1.26-3.18)	1.29 (0.86-1.93)	2.52 (1.70-3.75)

Odds ratio (95% CI) obtained after adjustment with logistic regression analysis.

children will have low apolipoprotein A and HDL-C values. It is very important for pediatricians to investigate the family history following the guidelines of the National Cholesterol Education Program, in order to identify children belonging to high-risk families.<sup>8</sup>

The CARDIA study highlighted the relation between risk factors in young adults and a family history of cardiovascular disease.<sup>9</sup> In the present study we found that risk factors such as smoking, hypertension and obesity show a family correlation, a finding consistent with previous reports.

## Alcohol consumption

The WHO has recommended abstention from alcohol up to 20 years of age to avoid the risk of addiction and the primary and secondary disorders it produces in young people. The Bogalusa Heart Study showed that alcohol consumption starts at an early age in both sexes and is linked to smoking, demonstrating that among smokers the prevalence of alcohol consumption is increasing. As observed in other ethnic groups, we also found a strong association between drinking and smoking, and an important increase in alcohol use around the age of 16.

## Smoking

Smoking is a "transmittable" and "preventable" risk factor, and the most significant predictor of death due to cardiovascular disease. In Argentina alone it is responsible for 40 000 deaths annually and around 4 000 000 worldwide.

Nicotine and carbon monoxide are the substances most closely linked to the initial endothelial lesion. Smoking increases intravascular coagulability, and stimulates coronary vasoconstriction and ultrastructural changes in the endothelial cells. Smokers can present «premature» rupture of a plaque.<sup>10,11</sup>

Smoking usually starts during childhood or adolescence. Nearly 90% of smokers begin before 20 years of age. Our study showed a significant increase in individuals acquiring the habit between 15 and 16 years of age. The young men reported smoking intermittently during the week, whereas the young women demonstrated a more regular daily habit. The family model, particularly maternal influence, is a factor to keep in mind regarding the initiation of smoking.

As the WHO has declared, primary prevention is the most effective strategy for decreasing the prevalence of smoking. This should be carried out, above all, in primary school and the beginning of secondary school.

## Lipids

Some data seem to indicate a relation between plasma lipid values during childhood and the development of coronary disease. The children of parents who have had an early myocardial infarction (before the age of 50) present cholesterol values close to 195 mg/dL, whereas those parents have not had an early myocardial in-

fraction have levels of 175 mg/dL. Moreover, the medical records of first-degree relatives of children with elevated cholesterol values (above the 95th percentile) present significantly higher cardiovascular mortality. Finally, the probability of elevated cholesterol in children who are born and live in families in which at least one of the parents has elevated cholesterol is double that observed in children whose parents do not have elevated cholesterol. Repeated cholesterol determinations in school-age children have demonstrated that those with high values at the first analysis to maintained increased levels four years later. Moreover, the plasma cholesterol values in children living in populations with low coronary mortality present clearly lower values than those found in children living in countries with high coronary mortality.<sup>12</sup>

The mean cholesterol values we found were similar to those of other developed Western countries such as the United States. In 12 studies carried out in Argentina it was observed that the prevalence of hypercholesterolemia (defined as TC values higher than 200 mg/dL) among adolescents was 5% in the total population, 18% among obese persons and 24% among diabetic persons. In the FRICELA study, 11% of adolescents presented TC values higher than 200 mg/dL and in 35% the value was higher than 170 mg/dL, a level that is considered to indicate the need for an adequate diet and regular physical exercise. In this population sample, cholesterolemia showed a positive correlation with the BMI, an association that is not commonly reported.

## Arterial hypertension

Our findings confirm the correlation between excess weight and hypertension. The origins of hypertension are found in the first two decades of life, suggesting that effective interventions at this time could lead to reductions in the incidence of hypertension. Nevertheless, a decrease in the sodium/potassium ratio during three years in adolescents has been found to decrease blood pressure in young women, but not young men.<sup>13</sup> The underlying mechanisms behind this difference should be investigated.

The INTERSALT international epidemiological study demonstrated a significant independent relation between 24-hour urinary sodium excretion and systolic blood pressure, particularly among populations with exceptionally low sodium excretion values.<sup>14</sup> In contrast, no correlation was found between salt consumption and hypertension in our sample, perhaps because of the short period of exposure to this factor. There was, however, a positive correlation between hypercholesterolemia and hypertension.

## Physical inactivity-physical exercise

It recognized that exercise and physical activity are effective in preventing atherosclerotic coronary disease. The physical activity does not necessarily have to be intense; it can be occupational or recreational, performed during leisure time. In addition to the possible direct effects on the vessel

wall and on coronary atherosclerosis, exercise has a significant influence on other coronary risk factors such as circulating lipids, glucose intolerance and obesity, as well as on certain populations with hypertension.

A relation exists between physical inactivity, coronary artery disease and cardiovascular mortality.<sup>15,16</sup> Our study showed a positive correlation between TC values and physical inactivity. We were not able to measure or quantify the degree of physical activity, since the frequency, intensity and duration were not specified. Other authors have assessed physical activity in terms of kilocalories, distance run, or changes in maximum oxygen consumption.<sup>17</sup> Our data suggest that five hours of regular physical exercise per week would have a protective effect against the appearance of hypertension.

### Excess weight-obesity

In the general population, the genetic components of obesity are hereditary and available evidence indicates that it is a multigenetic disorder.<sup>18</sup>

In the Ten State Nutrition Survey, which involved 30 000 individuals, a high correlation was found between obesity in parents and obesity in their children. In adolescents, 18% of the children of a single obese parent and 40% of children of two obese parents were also obese. Our study also showed a relationship between the obesity of parents and their children.

In keeping with results from previous studies, we found that young people with a BMI of  $<20 \text{ kg/m}^2$  presented a minimum prevalence of coronary risk factors. Girls and young women in our study had a higher BMI than boys and young men in all age groups, and the female predominance grew with each increase in BMI.

As in adults, obesity in young people is related with hypertension and high lipid concentrations. In studies of children with several risk factors, the common factor was obesity, with physical inactivity being the "father" of obesity.

### CONCLUSIONS AND CLINICAL IMPLICATIONS

This national, multicenter, epidemiological study performed by pediatricians and cardiologists determined the prevalence of behavioral habits and risk factors related to coronary artery disease during adolescence. Although it is not possible to extrapolate the conclusions to the general population, we have attempted to encourage the development of other studies and facilitate the possibility of acting upon the most important risk factors in the early stages of life in order to implement prevention programs.

This study evidenced a high prevalence of coronary risk factors and alcohol consumption in children and adolescents, with a marked increase after the age of 16 years. Moreover, we observed a strong correlation between body mass index and both cholesterolemia and blood pressure, and between smoking and alcohol consumption. Finally,

there was a clear association between the prevalence in parents and children of smoking, excess weight, hypercholesterolemia, and arterial hypertension, suggesting that the family exerts a significant influence in this respect.

Interventions on the behavioral habits and risk factors that favor atherosclerotic vascular disease can be initiated in childhood and adolescence, with the aim of decreasing the incidence of atherosclerosis in adults. Our results support adherence to the recommendations of the American Academy of Pediatrics, which promotes the detection of arterial hypertension, the control of obesity, regular exercise and total abstinence from smoking, beginning in childhood.<sup>19</sup>

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