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Interpretation of Findings in the Context of Adolescent Cardiovascular Risk

Interpretación de los hallazgos en el contexto del riesgo cardiovascular en adolescentes

Cuba is developing a system to achieve the public health goals set for 2020, from primary to tertiary care, with an assessment that includes improving the quality of life of patients with both vascular and cerebrovascular diseases through adequate medical care. Research projects are being carried out using current methods and modern approaches to achieve these goals and thus reduce these diseases.[24,28]

The National Program for the Prevention of Cerebral and Vascular Diseases in Cuba has contributed to curbing mortality from such causes owing to actions developed from primary health care, with an increase in life expectancy to approximately 73 years, which has increased as a result of the development of medicine and improved socioeconomic conditions. However, the incidence of death from these diseases has still shadowed over the last years of life in our population.[102]

In recent years, the population and public health authorities have shown an interest in learning about these metabolic disorders owing to their relationship with diet and atherosclerosis. Recent studies have shown that early diagnosis and timely treatment of children can prevent the onset of clinical manifestations and prevent cardiovascular disease.[77,98,103]

In this context, research indicates that hyperlipidemia is a disorder that affects both sexes equally, and although it can occur at any age, it is more prevalent in adulthood.[9,40,41,104]

Over the last few decades, vascular conditions have become the true disease of the century.[76] Recent studies suggest that the pathophysiology in target organs such as the heart and peripheral vessels may begin as early as the first or second year after the onset of the disease and not after 10 or 15 years, as suggested in epidemiological studies conducted by Jiménez Acosta et al.[3].

Lipoprotein concentrations increase gradually from childhood to adulthood. A considerable jump in magnitude occurs in the first week of life, with cholesterol levels reaching twice the value at birth and normal values being present in the first month of life, remaining constant with little variation until approximately 20 years of age. Triglycerides behave in a similar but more modest way, with little significant difference in their sex-age relationship.[35,37,49,105,106]

Castillo Herrera et al.[40] suggested that the number of CVD events is significantly lower in adolescents than in adults, with an annual incidence in children under 15 years of age ranging from 2,5 to 13 per 100 000 children, representing 65 new cases each year (2,4 million).

According to the report in a study conducted in Venezuela, boys maintained high triglyceride averages until the ages of 5-11 years, decreased slightly from the age of 6 years, placed them in the “risk” zone, and then rose from the age of 9 years to levels considered “high” according to the established cutoff points. In females, average values remained in the “risk” zone, with lower values found in the 6-year-old groups and higher values again from age 12 onward.

In this country, health education programs have been developed to increase awareness of cardiovascular risk factors in young patients[107,108] given the high incidence of cardiovascular disease in children.[109,110,111,112]

A study conducted in the province of Cáceres in Spain analyzed the prevalence of hyperlipidemia in adolescents, described changes according to age and sex groups and compared the overall results with those of other local studies. The sample studied included 7,5 % women and 4,7 % men. Twenty-seven point nine percent of the children had total cholesterol values >200 mg/dL. In the same study, the overall prevalence of hypercholesterolemia (cholesterol >200 mg/dL) was 27,9 %, predominantly in females (29,67 % vs. 26,14 %), although the differences were significant only when a cholesterol level above 230 mg/dl was considered, which was 7,53 % in females and 4,74 % in males (p<0,01). Notably, 58 % of our child population has levels above 175 mg/dl, above which dietary advice is recommended.[113]

A study highlighted relatively constant cholesterol levels in children up to the age of 11, with a tendency to increase with age and correspond to the female sex. After puberty, sex begins to determine some changes between males and females that have thus far been attributed to sex hormones, with values remaining the same until menopause, when women reach higher cholesterol levels. The prevalence of hyperlipidemia is greater in prepubertal females, with the most discriminative risk ratios.

An analysis of the different age and sex groups revealed that the prevalence of hypercholesterolemia (>200 or >230 mg/dL) was greater in prepubertal women than in males of the same age, although the difference was not significant. From puberty onward, the prevalence decreases significantly in both sexes, but in this case, it remains clearly higher in females.[114]

When the prevalence of hyperlipidemia according to LDL level (>130 mg/dL) was analyzed, the results were similar: a greater number of cases in the prepubertal stages, a circumstance already referred to in other studies and probably related to the peculiar dietary pattern of these ages, and in terms of sex, a predominance in the female group, although in this case, the differences were significant between the ages of 6 and 12.[39,44,115,116,117]

The overall prevalence of low HDL (<35 mg/dL) was 3,3 %, which was much higher than that reported in other studies, with a value of 1,84 %, or that reported by a study, with a value of 1,13 %. This alteration was significantly greater in the group of adolescent males (6,64 %) than in the group of younger children (1,78 %), a situation already described in the literature[59] and possibly related to hormonal changes during puberty, with no differences between males and females aged 13-16 years, despite the lower number of cases in the latter (3,75 %). When hyperlipidemia was defined on the basis of these risk ratios (TC/HDL>3,5 and LDL/HDL>2,2), the prevalence rates were 36,18 % and 39,86 %, respectively; other studies, such as that by Galarregui et al.[88] with 14,51 % and 15,7 %, respectively, or that of a cohort in a study with 21,8 % and 24,16 %, respectively, the prevalence was lower.

According to the first ratio, the prevalence is much higher in girls during childhood (38 % versus 29 %), with the relationship being reversed when the adolescent group is studied (35 % versus 46 % in boys). In terms of age group, adolescent boys had a much higher prevalence than younger age groups did; in girls, the opposite was true, although the differences were not significant.[118,119]

In conclusion, we found a high prevalence of lipid disorders in our children, which was

greater than that reported in previous national studies, and these results are consistent with those obtained in the adult population of Extremadura;[113] moreover, CVD, the leading cause of mortality in our region, accounts for 46,78 %[13] of the overall decreasing trend.[106] All of these findings seem to point to the need to introduce dietary changes at an early age and early screening for hyperlipidemia (either opportunistic or selective), promoting healthy lifestyles, measures that are perfectly accessible in our primary care consultations.

Overweight and obesity are highly prevalent among children and adolescents in developed countries, and since the 1990s, a variable increase has been reported in developing countries, with interest in their associations with adult obesity, high blood pressure, cardiovascular disease, and elevated plasma insulin and lipid levels.[24,29,120,121]

A study conducted at the Tomás Romay Polyclinic reported that there are coronary risk factors for great importance in relation to the genesis and development of atherosclerotic disease. A total of 22,5 % were overweight, 10 % were obese, 76,6 % were passive smokers, 23,3 % were active smokers, 66 % had a family history of hypertension, 43,3 % had ischemic heart disease, 33 % had high cholesterol, and 8,3 % had high blood pressure. The coronary risk of these patients was high.

With respect to the analysis of the race-age relationship in our study, a predominance of black and mestizo races was found in all the age groups. The literature reviewed corresponds with the findings of the study.[122] This study reports a predominance of females and black individuals among adolescents. They consider this race to have a genetic predisposition to developing cardiovascular disease, although more recent studies from after 2000 in European countries and the United States revealed an increase in white and mixed-race adolescents.[113] In our country, as there is no ethnic difference, race is not significant.[30]

In recent years, obesity has been considered one of the main risk factors for CHD, along with smoking, hypercholesterolemia, high blood pressure, a sedentary lifestyle, and other nonmodifiable factors, such as advanced age. Obesity is not considered a clinical manifestation but rather a trigger or even a cause of lipid disorders, with increased triglycerides being the most common disorder.[92]

A study evaluated a group of children in the northern part of the state of Valencia, Venezuela. The low HDL and high triglyceride profiles suggest a greater risk of cardiovascular disease in these obese children, with a greater impact on males. A high proportion of these individuals meet three defining criteria for metabolic syndrome, so dietary control and modifications in eating patterns and physical activity are recommended.[112]

The literature reviewed presents these toxic habits, with a relatively high incidence accompanied by alcoholism and drug addiction, which were not found in our study.[123,124,125]

Research on heart attack and other circulatory problems indicates that certain forms of these diseases are caused in part by excessive consumption of foods rich in fats, including lipids and sterols. Studies also show that the likelihood of heart attack decreases when saturated fat intake is reduced.[106,126,127]

In Latin America, obesity has increased considerably, becoming a public health problem in almost all countries in the region.[128] In Venezuela, as in other countries in the area, a nutritional epidemiological transition is observed. According to the latest reports on the nutritional status

of children aged 2 to 6 years and 7 to 14 years, issued by the Food and Nutrition Surveillance System of the National Institute of Nutrition,[112] 10,67 % and 14,60 %, respectively, suffer from malnutrition due to excess nutrition. This highlights the existence of a public health problem that needs to be addressed, especially when there is evidence that childhood obesity increases the risk of obesity in adulthood and is associated with risk factors for chronic diseases common at that age.[92,129,129,130,131] Furthermore, it is the leading cause of chronic disease worldwide, as it induces multiple metabolic abnormalities that contribute to the development of this disease.[44]

Studies conducted in Venezuela on 121 children between the ages of 2 and 17 (average age 8,8 ± 3,34 years) who were overweight during childhood revealed that 41,3 % (n=50) were male and that 58,7 % (n=71) were female. Among these children, 8,3 % were overweight (n=10), and 91,7 % were obese (n=111), according to a BMI of 90 or more, which corresponds to our research where obesity associated with poor eating habits corroborates the risk of atherosclerosis that begins in childhood and predominates in adulthood.[44]

A family history of disease is a predisposing factor for this disease related to sex, with 106 patients having a family history of hypercholesterolemia (80 %) and 92 patients having ischemic heart disease (69 %). A higher incidence was observed in females, with a total of 124 cases (93 %), and 78 cases were in males (59 %).

The family history collected was familial hypercholesterolemia followed by ischemic heart disease, which coincided with studies conducted by authors such as Duque et al.[69]. These findings suggest that these diseases are genetically determined, providing great value to family history. Various factors contribute to the onset of hyperlipidemia. These include genetic factors, with polygenic transmission being the most important; environmental factors, such as a diet rich in saturated fats; and alcohol, which can induce a large increase.[58,132,133]

Risk factors include a family history of high cholesterol and early coronary artery disease.[134] It is important to study the family history of hyperlipidemia or early ischemic heart disease in men under 55 years of age and women under 65 years of age. Similarly, it is necessary to study the personal history of cardiovascular disease and its risk factors, as well as to analyze the personal pathological history to detect secondary hyperlipidemia.[135]

The literature reviewed suggests that the primary causes are genetically determined, such as familial hypercholesterolemia, whereas the secondary causes originate in various pathologies that alter blood lipid levels, such as diabetes mellitus.[15,136,137,138,139]

In a family study, two brothers were found to be asymptomatic with low glucose intolerance and obesity. In both cases, the lipid disorder improved with a low-carbohydrate diet, and the father was found to have hypercholesterolemia of 312 mg/dl with a type IIa electrophoretic pattern. The mother was normal, and the parents were first cousins.

Familial combined hyperlipidemia is the most common disorder associated with increased blood fat content and can cause early heart attack. It is a genetic disorder, which means it is caused by a problem with genes. However, researchers have not yet identified the specific genes responsible. People with familial combined hyperlipidemia have a higher rate of obesity and glucose intolerance.[44]

In this study, the risk factors that appeared first were poor eating habits, followed by obesity, a sedentary lifestyle, and high blood pressure. The number of hypertensive adolescents included

in this study is shown below. The average SBP values obtained in Ocaña are somewhat lower than those reported in other Cuban studies,[22,29,30,120] although the study by Álvarez Gómez et al. included children from younger age groups. A greater prevalence of HTN was found than in studies published by other authors from Latin American countries,[21,23] although these differences may be related both to the different age groups of the children studied and to possible differences in the technique used to measure blood pressure. The study by Delgadillo et al.[61] included children and adolescents aged 4-17 years.

Several studies indicate that children with first- or second-degree relatives with hypertension are at greater risk of developing hypertension.[5,29,30,91] Several studies have indicated that the mean SBP and DBP values are significantly greater in children with a history of hypertension in their parents.[30,58,120] This means that hypertension runs in families and that BP readings in children and adolescents with a hypertensive parent are more likely to be higher than those without a history of HTN, as has been demonstrated in other studies.[5,21,22,23,30,120] All of these findings support the need for more frequent BP monitoring, especially in children and adolescents with a family history of HTN.

The results of this study reveal a high-risk profile among adolescents overall. One hundred percent of the patients included in the study had at least one of the four major cardiovascular risk factors. These results coincide with data published by González Santiesteban et al.[95] and Bonet-Gorbea et al.[30], who reported that 80 % to 90 % of people who develop heart disease in adolescence have at least one cardiovascular risk factor. A research studied the prevalence of cardiovascular risk factors in 14 544 children with both personal and family histories of hypertension or obesity, reported that 94,3 % of them had much more severe hypertension in adulthood.

Similarly, a study reported that at least 80 % of the first major episodes of CHD could be attributed to hypercholesterolemia, hypertension, or a sedentary lifestyle. These data contrast with claims that only 50 % of cases of coronary heart disease in children can be attributed to conventional risk factors. Despite this, it is necessary to continue researching the role of new cardiovascular risk factors, but we must not forget that there are possibilities for controlling conventional risk factors, such as the prevention of atherosclerotic disease.

These data coincide with the reviewed literature, where authors such as Machado de Ponte et al.[116] and Acosta-García et al.[126] include these data in their studies. Most patients evolve without symptoms or signs for a period of time until early symptoms of atherosclerosis appear.

Atherosclerosis rarely occurs in pediatric patients as a clinical manifestation, except in the homozygous form of type II disease. Importantly, the nonspecific clinical manifestations, asthenia, and digestive manifestations are discomforts that, on other occasions, have no other causes, only lipid disorders. Physicians may look for other diseases and overlook them.[140,141,142,143] The literature from other countries, except France, does not usually include these manifestations, and in our clinical practice, they are part of the questioning of patients with hyperlipoproteinaemia. These symptoms disappear with effective antilipemic treatment and are more common in hypertriglyceridemia patients.[11,38,137,140,144]

In a study of 158 patients in a clinic dedicated exclusively to lipid disorders, dyspeptic disorders were found in 13 patients, and asthenia was present in 65 % of patients.[111,145,46,47]

This scarcity of clinical manifestations has also been noted by a study, who reported that

7 of their series of 9 patients were asymptomatic. This finding is consistent with the reviewed literature,[141,142,143,148,19,150] which suggests that hyperlipidemia is the onset of cardiovascular damage and a predisposition to future hypertension and ischemic heart disease.[144,145,151,152,153]

A wide variety of epidemiological studies have shown that plasma cholesterol levels are a risk factor for ischemic heart disease.[154,155,156,157,158] The Framingham study, a must-read reference, was conducted in that city on a total of 5000 people over 44 years of age and demonstrated a linear relationship between cholesterol levels and the risk of ischemic heart disease.[6,18,146,147,159,160]

People with this condition develop high triglyceride or cholesterol levels during adolescence, and these levels remain high throughout their lives.[161,162,163,164,165] These individuals are at increased risk for early coronary heart disease and, therefore, heart attack.[43,109,166,167,168]

In a study conducted in 2015 at Dr. Enrique Cabrera Teaching Hospital, which reviewed the autopsy protocols of diabetic patients from 2004-2008, with a total of 423 deaths (257 females and 166 males), the leading causes of death were atherosclerotic heart disease (20,3 %), peripheral artery disease (14 %), pulmonary thromboembolism (9,4 %), and stroke (9,2 %). Importantly, 80 % of diabetic patients die from one of the complications of atherosclerosis.[148,169,170]

Many researchers point to the correlation between the quality of metabolic control and virtually all lipid levels as a proportional correlation. These studies highlighted the interrelationship between duration of evolution, age, completed puberty, and female sex as factors that increase the risk of HLP.[138,149,150,151]