REVIEW ARTICLE

Obesity and postprandial lipemia in adolescents: Risk factors for cardiovascular disease

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KEYWORDS
Obesity; Postprandial lipemia; Adolescents; Heart disease

Abstract In the last 50 years, obesity has become a global epidemic and is one of the main public health problems in many parts of the world. Adolescence is a critical period regarding weight control. The factors determining obesity include a complex group of interrelated biological, behavioral and environmental factors which reinforce each other. In children and adolescents, obesity is associated with premature cardiovascular diseases, diabetes mellitus type 2, acanthosis nigricans, respiratory and skeletal muscle problems, as well as psychological problems. The clinical manifestations of cardiovascular disease begin in middle age. Nevertheless, studies indicate that the atherosclerotic process begins to develop during childhood. Postprandial hyperlipemia is a physiological process that occurs several times a day after the complete absorption of a diet including lipids and has been suggested as a risk factor for coronary heart disease (CHD). New study areas include the effects of different fatty acids, lipid sources (endogenous and exogenous), and the effect ingesting alcoholic beverages during meals. Given the evidence that postprandial lipemia is an independent risk factor for CHD, it is vital to establish normative values for children and adolescents such that more effective and efficient preventive and therapeutic measures can be adopted.

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PALABRAS CLAVE
Obesidad; Lipemia postprandial; Adolescentes; Enfermedad cardiovascular

Resumen En los últimos cincuenta años, la obesidad se ha transformado en una epidemia global y figura en la lista de los principales problemas de salud pública en varios países del mundo. La adolescencia representa un periodo crítico para el control del peso. Los factores determinantes de la obesidad incluyen un complejo conjunto de factores biológicos, comportamentales y ambientales que se interrelacionan y que potencializan mutuamente. En niños y adolescentes, la obesidad se asocia a la aparición precoz de enfermedades cardiovasculares, diabetes mellitus tipo 2, acanthosis nigricans, complicaciones respiratorías.

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Introduction

The World Health Organization defines obesity as a disease in which the excess of body fat causes serious health problems to the individual.1

In the last fifty years, obesity has become a global epidemic and it is in the list of the main problems of public health in many parts of the world. It is estimated that there is 1.6 billion of individuals with current excess of body weight and, at least, out of these, four hundred million of them are obese. Until 2015, approximately 2.3 billion people will show overweight and more than seven hundred million people will be obese.1

Adolescence represents a critical period for the control of weight. In this stage of growth, the individual acquires approximately twenty-five percent of the final stature and fifty percent of body weight. Besides, the risk of an adolescent who is overweight to be obese in adulthood as well, is of approximately 80%.2 During adolescence, besides the physiological transformations, the individual passes through important psychosocial changes that contribute to the vulnerability of this population group.

The increase of overweight and obesity in even more precocious ages has arisen important issues related with the harms and grievance to health provoked by the excess of weight, such as hypertension, cardiopathies, diabetes and hyperlipemia among other pathologies.3

In this review of literature the main risk factors for cardiovascular diseases in adolescents, the alterations in the lipoprotein metabolism and the role of post-prandial lipemia will be analyzed.

Epidemiology of overweight and obesity in children and adolescents

The prevalence of obesity in youths has been dramatically increasing in the three last decades, not only in developed countries but also in developing ones.3

Obesity represents, in the United States, the most prevalent disease among children and adolescents that affects one in each seven Americans.4

A multicenter study held by Wang et al.5 in countries in different phases of social and economic development observed an important increment of obesity: in the United States, from 15.4 to 25.6%; Brazil, from 4.1% to 13.9% and China, from 6.4% to 7.7%. On the other hand, in Russia there was a reduction in its prevalence from 15.5% to 9.0% and an increase of underweight from 6.9 to 8.1%. The annual increase of the obesity rates was of 5% in Brazil, 2% in China, 1% in Russia and 6% in the United States. A possible explanation for the reduction of obesity in Russia was the economical recession, a period in which the country suffered serious socioeconomical difficulties.5

In Canada, in 1981, only 11% of the boys and 13% of the girls were overweight or obese while in 1996 these numbers reached 33% and 27%, respectively.6

In Chile7 two important studies held with children showed a notable increase in the excess of weight in childhood between 1987 and 2000, from 12% to 26% for boys and from 14% to 27% for girls. In Bolivia,8 the prevalence of overweight in pre-scholar children increased from 15.9% in 1989 to 22.7% in 1997 and in the Dominican Republic9 it varied from 12.3% to 15.3% between 1986 and 1996. On the other hand, the prevalence of obesity in pre-scholar children was reduced in Colombia7 from 4.6% to 2.6% between 1986 and 1995.

The highest prevalence rates of obesity are observed in European countries. A recent survey found that 36% of 9-year-olds in mainland Italy and Sicily10 were overweight or obese (IOTF criteria). In Spain,11 27% of children and adolescents were overweight or obese (IOTF criteria).

Table 1 presents the comparison of the variable prevalences of obesity in children and adolescents in different regions worldwide.

Risk factors for cardiovascular diseases

Obesity that starts before adulthood seems to have an important connection with diverse factors: genetics, life style, food habits, practice of physical activity, among others.

Longitudinal studies have identified that obesity in childhood and adolescence, particularly during the second decade in life, is an important predictor of obesity in adulthood, especially in children with severe obesity whose
parents are obese. Deshmukh-Taskar et al. analyzed data on weight and height of children from Bogalusa Heart Study, initially during childhood from nine to eleven years old and later, again, from 19 to 35 years old. It was observed that out of 841 individuals in the last quartile of Body Mass Index (BMI) 61.9% remained in this same position during adulthood.

The determinant factors of obesity are part of a complex group of biological, behavioral and environmental factors interrelated and able to potentize one another. For children and adolescents, examples of these factors are present in the school environment, into the family nucleus and in the neighborhood. Some characteristics as nutritional maternal status, tobacco smoking during pregnancy and nutritional status during childhood are highlighted because they are present during pregnancy and in the beginning of life. Epidemiological studies suggest that there can be an inverse relation between birth weight and risk of obesity and cardiovascular diseases in adulthood. Barker et al. and Osmond et al. described an association of high mortality rates due to coronary heart disease and stroke in adults with lower birth weight.

The changes in patterns of nutrition and physical activity described in many societies are, admittedly, the determinants that most contribute for the increase in overweight. Oliveira et al. highlight the role of the economical development and the process of urbanization on changes in the population's lifestyle, translated by inadequate nutrition patterns and sedentary models of occupation. The high technology available in the contemporary societies such as TVs, wireless telephones, videogames, computers, and remote controls, have favored the reduction of energetic waste. The changes in the nutrition habits, with the easy access to and the low cost of food rich in fattening and sugar, have been associated with an increased risk for atherosclerotic disease.

Nowadays, the characteristic nutrition pattern of adolescents include the excessive consumption of soft drinks, sugar and junk food, as well as the reduced ingestion of fruits and vegetables, the adoption of monotonous diets or alimentary fads, and the skip of breakfast.

Studies that were held in Sweden demonstrated low consumption of fruits and vegetables by adolescents, as only 40% of those aged 15 years have fruits and vegetables on a daily basis. In Australia, it was also observed the low consumption of fruits and vegetables among 1.656 children (limits 5–15 years), not only in the school environment but also outside it as well. In the United States, the Continuing Survey of Food Intake by Individuals – CSF, held in 1989–1991 (CSFII) and in 1994–1996 (CSFII), showed a little tendency of increase in the consumption of fruits and vegetables. Nevertheless, it was observed that the consumption of these foods reached only the minimum number of professed portions. According to CSFII the children and adolescents that had been evaluated (n=5.144) consumed, in average, 1.6 portion of fruits and 2.7 portions of vegetables per day.

In many parts of the world as in the United States, Norway and Finland high taxes of fat in the adolescents’ diet were identified. Similar findings have been described in the south of Europe, in countries like Spain, Greece, Italy and Portugal showing that healthy aspects which are characteristics from the Mediterranean Diet, probably are not being used anymore.

Hyperinsulinemia, on the basis of cardiovascular risk factor, is strongly associated with the intra-abdominal adipose tissue. As demonstrated in a longitudinal study, hyperinsulinemia can be the main abnormality in obese children and adolescents, what contributes for dyslipidemia. The pathophysiological mechanism, involved in this process, suggests that the intra-abdominal fat with a high and intense metabolic activity allows the deposits of triglycerides, which are concentrated in this region, to be easily mobilized into the bloodstream, causing an increase in the hepatic production of free fatty acids and LDL cholesterol.

### Table 1  Prevalence of obesity and low weight in children and adolescents from four countries.

<table>
<thead>
<tr>
<th></th>
<th>Brazil (n = 56 295)</th>
<th>China (n = 4875)</th>
<th>Russia (n = 688)</th>
<th>United States (n = 6108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>4.1 ± 0.10</td>
<td>13.9 ± 0.66</td>
<td>6.4 ± 0.44</td>
<td>7.7 ± 0.51</td>
</tr>
<tr>
<td>Children</td>
<td>4.9 ± 0.18</td>
<td>17.4 ± 1.35</td>
<td>10.5 ± 1.00</td>
<td>11.3 ± 1.11</td>
</tr>
<tr>
<td>Adolescents</td>
<td>3.7 ± 0.11</td>
<td>12.6 ± 0.76</td>
<td>4.5 ± 0.46</td>
<td>6.2 ± 0.56</td>
</tr>
<tr>
<td>Low weight (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>14.8 ± 0.17</td>
<td>8.6 ± 0.52</td>
<td>14.0 ± 0.64</td>
<td>13.1 ± 0.65</td>
</tr>
<tr>
<td>Children</td>
<td>12.3 ± 0.27</td>
<td>6.1 ± 0.79</td>
<td>12.5 ± 1.08</td>
<td>9.4 ± 1.03</td>
</tr>
<tr>
<td>Adolescents</td>
<td>16.1 ± 0.26</td>
<td>9.6 ± 0.65</td>
<td>15.4 ± 0.79</td>
<td>14.7 ± 0.82</td>
</tr>
</tbody>
</table>

Obesity and its consequences

Obesity is one of the main factors that contribute for the arising of cardiovascular diseases in adolescence, beyond type 2 diabetes mellitus, *acanthosis nigricans*, respiratory and skeletal muscle dysfunctions and psychological problems.

The *Bogalusa Heart Study*, held with 9.167 individuals with ages varying from 5 to 17 years old, between 1973 and 1994, aimed to evaluate risk factors for cardiovascular diseases in the first decades of life. It was found that, among obese children and adolescents 58% (n=813)
The described events, including the progression of fat streaks to fibrous plaques from the age of fifteen, was also observed. Atherosclerosis then moved gradually, from a model of chronic-degenerative disease and exclusively from older individuals, to a model of a subclinical chronic inflammatory disease that has been present since childhood. Obese children seem to have higher levels of LDL cholesterol, pattern B (smaller and denser particles) than eutrophic peers. It has been documented that obese children with normal levels of LDL cholesterol, can present a less favorable lipidic profile, depending on the subclasses of their lipoproteins.

The increased lipoproteins that are rich in triglycerides do not depend only on their quantitative elevation, but also on the qualitative characteristics of the diet (saturated, polyunsaturated and monounsaturated fats). The saturated fatty acids increase the LDL cholesterol levels through the reduction of its depuration. LDL cholesterol favors the lipidic deposit in the walls of blood vessels, promoting the arising of atheromatosis plaques. The cholesterol that is in the alimentation has a lower deleterious effect over plasmatic cholesteroloma than saturated fats.

**Postprandial lipoproteic metabolism**

The term postprandial lipemia refers to a series of metabolic events that are related to the increase in lipoproteins (LP) concentrations that are rich in triglycerides (TG)–chylomicron and their remainders, very low density protein (VLDL) and their remainders, after the ingestion of fat.

Under normal conditions, the plasmatic levels of postprandial triglycerides and the conversion of the particles of very low density protein (VLDL) in LDL cholesterol is controlled by a dynamic metabolic process that involves lipoproteic enzymes and hepatic lipase.

The basic function of the plasmatic lipoproteins is the transportation of lipids to the peripheral tissues and liver, where they are metabolized. There are three (03) systems of lipidic transportation that act in the plasma simultaneously: the lipids that are originated from the diet, those that are synthesized by the liver and from the system of reversal transportation. The first two systems transport the lipids from intestine and liver to the peripheral tissues and the other mainly carries the cholesterol from the tissues to the liver. The lipoproteic lipase enzyme (LPL) hydrolizes the triglycerides in free fatty acids, monoglycerides and diglycerides which allow the supply of free fatty acids to the peripheral tissues. The hepatic lipase, in its turn, removes triglycerides and phospholipids from kilomicrons and remainders of very low density protein (VLDL). After some food ingestion, the content of triglycerides present in the food, is hydrolized, absorbed and transformed in big particles of kilomicrons that contain apolipoproteins A-I, A-IV, and B-48. In the lymph and in the blood, the kilomicrons acquire apolipoproteins C-II, C-III and E. In the capillaries of the adipose and muscular tissues, the kilomicrons interact with lipase lipoprotein (LPL) and its nucleus (that contain triglycerides) is hydrolyzed.

The products of the hydrolysed triglycerides – the free fatty acids – through lipase lipoprotein (LPL) can be stored.

**Atherosclerosis in adolescents**

The clinical manifestations of cardiovascular diseases start from middle age onwards. However, a recent study indicates that the atherosclerotic process starts in childhood.

Fatty streaks – that are precursors of atherosclerotic plaques – appear in the inside layer of the aorta at three years of age and in the coronary layers during adolescence.

Cresanta et al. cite the report from Monckberg, in which it is described how atheromatosis of the inside layer of the aorta was found in children who had died in the First World War. Enos et al. described atherosclerotic disease in young soldiers dead during the Korea war and, in 1958 Holman et al. confirmed that children over three years old presented fatty streaks in the coronary arteries.

Studies from autopsies after sudden death in children and young adults demonstrated that the presence and severity of atherosclerotic lesions were correlated with the presence of cardiovascular risk factors. The progression of the fat streaks to fibrous plaques from the age of fifteen was also observed. Atherosclerosis then moved gradually, from a model of chronic-degenerative disease and exclusively from older individuals, to a model of a subclinical chronic inflammatory disease that has been present since childhood. Obese children seem to have higher levels of LDL cholesterol, pattern B (smaller and denser particles) than eutrophic peers. It has been documented that obese children with normal levels of LDL cholesterol, can present a less favorable lipidic profile, depending on the subclasses of their lipoproteins. The increased lipoproteins that are rich in triglycerides do not depend only on their quantitative elevation, but also on the qualitative characteristics of the diet (saturated, polyunsaturated and monounsaturated fats). The saturated fatty acids increase the LDL cholesterol levels through the reduction of its depuration. LDL cholesterol favors the lipidic deposit in the walls of blood vessels, promoting the arising of atheromatosis plaques. The cholesterol that is in the alimentation has a lower deleterious effect over plasmatic cholesteroloma than saturated fats.

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in the adipocytes or used by the muscular cells as a source of energy.\textsuperscript{47}

\textbf{Post-prandial lipemia, inflammation and atherogenic state}

Post-prandial lipemia has been suggested as a risk factor for coronary heart disease.\textsuperscript{44} Post-prandial hyperlipemia is a physiological process that occurs many times a day after the complete absorption of a diet that contains lipids. The absorbed lipids are incorporated in chylomicron for the distribution of triglycerides (TG) in the adipose tissue (storing) or muscular cells. In some circumstances the process of triglycerides removal is not efficient which results in an excess of triglycerides (TG) in the postprandial period, leading to the formation of lipoproteins rich in triglycerides (LpRT) and potentially atherogenic.\textsuperscript{48,49}

Until now, the number of studies is not sufficient to allow estimative of the normal bands of blood concentrations of triacylglycerol (TAG) that occur after the consumption of a standardized meal by healthy individuals. The blood concentrations of triacylglycerol (TAG) in fastening can broadly vary up to 10% overnight,\textsuperscript{50} and the values of 60–150 mg/dl are considered normal in healthy individuals, with the average concentration of triacylglycerol (TAG) in the population of 100 mg/dl.\textsuperscript{51}

In the post-prandial state, the persistent elevation of lipoproteins, rich in triglycerides, can cause endothelial dysfunction,\textsuperscript{52} less availability of nitric oxide and increase of oxidative stress, which are alterations involved in the genesis of atherosclerosis.\textsuperscript{53}

The oral fat load has been widely used to evaluate the postprandial fat load effect on single markers of inflammation mainly in small samples of healthy subjects or in patients affected by metabolic diseases.\textsuperscript{54}

Laugerette et al.\textsuperscript{55} investigated the impact of a mixed meal containing dispersed lipids on postprandial endotoxemia and inflammation. They observed that postprandial endotoxemia increased early after the meal. Moreover, they evidenced that the endotoxin receptors CD14 increased during digestion and that chylomicrons could contribute to absorbed endotoxin transport. This is the first study in healthy humans that, mixed meal containing lipids, evidenced a positive association between endotoxemia and CD14 and a peak of IL-6.

Neri et al.\textsuperscript{56} analyzed the changes in the oxidation–reduction balance and endothelial function before and after meal in patients with type 2 diabetes or impaired glucose tolerance (IGT) and determine the effects of standard antioxidant supplementation. They observed that in diabetic subjects, altered glycemia and lipemia are closely correlated with markers of systemic oxidative stress. Supplementation with a pool of antioxidants can reduce oxidative stress and inflammation in healthy subjects and, more importantly, in IGT patients.

In a randomized, cross-over trial\textsuperscript{57} including ten healthy subjects, plasma TAG and the inflammatory cytokines, C-reactive protein, TNF-a and IL-6 before and after eating 100 g of kangaroo (4% fat on average, with, 1% of this saturated), or a ‘new’ form of hybridized beef (fat: 25–30%, of which about 40% is saturated) separated by about one week were compared. They observed that postprandial levels for 1 and 2 h of TAG, IL-6 and TNF-a were significantly higher after eating hybridized beef compared with kangaroo.

Alvarez et al.\textsuperscript{58} evaluated the associations of fasting and postprandial markers of inflammation (MOI) with total and regional adiposity and insulin sensitivity in 59 children aged 7–12 years. They observed that central adipose measures were not independently associated with fasting MOI, although they were independently and inversely associated with the postprandial TNF-R2 response. Insulin sensitivity was not associated with fasting or postprandial CRP or TNF-R2. The authors concluded that excess adiposity is associated with both fasting and postprandial MOI and the postprandial MOI response may be influenced by central adiposity in children.

To investigate the degree of endothelial activation and inflammation in prepubertal obese children and to determine the relationship between the markers of endothelial activation, inflammation, and cardiovascular risk factors 30 obese and 28 healthy prepubertal children were studied. The authors\textsuperscript{59} observed that endothelial inflammation is present in obese prepubertal children and is mainly associated with insulin resistance and lipid levels as well as BMI.

The main protocols of investigation and policies in dyslipemias do not consider postprandial lipemia as a risk factor and they purpose dosages performed after a 12-hour fasting.\textsuperscript{60} However, the postprandial triglycerides that have been measured in healthy individuals, is associated, separately from other risk factors, with the highest thickness of the intimate-average of the carotid.\textsuperscript{61}

Two studies compare the association between triglycerides levels – in fastening and postprandial conditions – and cardiovascular events in adults. The first study arose from the cohort of the Women’s Health Study, where 26.509 healthy American women were monitored during 11 years for the occurrence of acute myocardial infarction, cerebrovascular accident, coronary revascularization and death due to cardiovascular disease.\textsuperscript{52} It was observed that the postprandial triglyceride (TG) levels was independently associated with future cardiovascular events.

The second study arose from a prospective cohort with 7587 women and 6394 men in Copenhagen, with followed-up for 26 years.\textsuperscript{63} In this study, the levels of postprandial triglycerides (TG) showed to be an important predictor of future cardiovascular events, regarding both sexes.

Another factor that seems to have influence in the postprandial lipemia is aging. Issa et al.\textsuperscript{64} investigated the behavior of postprandial lipemia – it was held through repeated measurements of triglycerides (fastening, 02 h and 06 h after standardized meal with 40 g of fat) in healthy individuals aged 20–50 years. The authors observed distinct behavior of the age groups throughout the 06 h. The younger participants (20–30 yr.) showed a reduction in the triglycerides levels, the older participants (41–50 yr.) showed ascending values and those from the intermediary age group (31–40 yr.) maintained the level of triglycerides at the sixth hour.

The oral triglyceride tolerance test (OTTT) offers a mechanism of analysis of the metabolic answer to the overload of fat, but its standardization is controversial.\textsuperscript{65} The protocols of OTTT that are available are based on the ingestion of fat according to body weight (1.0 g of fat/kg weight) or on
the ingestion of a preparation that contains 50 g of carbohydrate and 50 g of fat. Table 2 shows the main factors that affect the postprandial answer of triglycerides to a meal test.

<table>
<thead>
<tr>
<th>Characteristics of the meal test</th>
<th>Effect on the answer of triglycerides</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase of fat in the meal</td>
<td>The area under the curve increases for triglycerides</td>
<td>71</td>
</tr>
<tr>
<td>Consumption of alcohol before and during meals</td>
<td>The area under the curve increases for triglycerides</td>
<td>72,73</td>
</tr>
<tr>
<td>Addition of fibers</td>
<td>Reduction in the answer of triglycerides</td>
<td>74</td>
</tr>
<tr>
<td>Proportion of fat in relation to protein and carbohydrate</td>
<td>Addition of carbohydrate to meal increases the area on the curve for triglycerides</td>
<td>75,76</td>
</tr>
<tr>
<td>Characteristics of the patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of last session of physical activities</td>
<td>The recent practice of physical activities reduces the postprandial answer</td>
<td>75,76</td>
</tr>
</tbody>
</table>

Postprandial lipemia in children and adolescents

Data on postprandial lipemia in children and adolescents are scarce. Couch et al. evaluated the postprandial TG response to a fat load in children and their mothers from families with or without history of premature coronary heart disease (Columbia University Biomarkers Study). They found that a profile of low HDL-C and high TG levels is associated with impaired postprandial TG response in children (the highest TG values postprandially were 200 mg/dl at 3 h) after post-prandial lipemia. Moreno et al. studied 24 adolescents, obese (n = 12) or not (n = 12) and they observed that the triglyceride levels after the oral tolerance test to lipids, positively correlated with the accumulation of fat in the abdominal region. Umpaichitra et al. studied 15 obese adolescents with no associated disease, 12 obese with DM2 and 12 healthy controls. After the lipidic overload, the authors observed that the obese and diabetic adolescents presented hypertriglyceridemia (at fastening and postprandial periods) that was associated with the presence of insulin resistance. Reiber et al. evaluated postprandial TG levels in familial combined hyperlipidemic subjects and their relatives (16 children, aged 22 ± 5 years). They found that children of parents with familial combined hyperlipemia although normolipidemic in the fasting state already have abnormal postprandial status. On the other hand, Tiret et al. in the European Atherosclerosis Research Study (EARS) compared the postprandial TG response of offsprings whose fathers had suffered a myocardial infarction before the age of 55 with controls from different populations in Europe (including Greece with Kolovou as one of 53 collaborators of EARS group). They did not find any difference between cases and controls in the TG response postprandially [TG values at 4 h after OFT were <200 mg/dl (<2.3 mmol/l)]. It seems that the exaggerated postprandial lipemia in children and adolescents only concerns those with underlying lipid metabolic disorders.

Final considerations

Postprandial lipemia can be considered a useful tool in the evaluation of the risk for coronary heart disease in adolescents. The establishment of normative values for
postprandial lipemia in children and adolescents may allow the adoption of preventive and/or therapeutic measures. So, we suggest that cohort studies are implemented in adolescents, in order to evaluate the real role of the lipidic changes in fasting, and in the postprandial state and its impact on the atherosclerotic process.

Conflict of interest
The authors declare no conflict of interests.

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