

Familial Hypercholesterolemia and Familial Chylomicronemia May be Enhanced by Lipid Alterations During Pregnancy

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Abstract

Pregnancy by itself occurs with alterations in most of the metabolic aspects of the body. In relation to lipids, total cholesterol, triglycerides and all the spectrum of lipoproteins tend to present a trend for increase in atherogenic risk. Lipoprotein fractions also show qualitative changes, so that high-density lipoprotein cholesterol (HDL-c) and Low-Density Lipoprotein cholesterol (LDL-c) have an increased number of triglycerides. HDL-c has a slightly different behavior from total cholesterol and triglycerides, as it presents a progressive increase, reaching its maximum in the twenty-fourth week, with an increase of 50% in the values when compared with the non-pregnant period. Then, it presents a drop equivalent to 15% above the values before pregnancy until the term period. LDL-c levels increase in synchrony with those of total cholesterol; however, they present a more delayed decrease, and the fall may occur after the eighth week of puerperium. These differences are mainly explained by sexual hormonal variations during the condition. It may be an opportunity to raise the awareness for serious genetic lipid disorders such as Familial Hypercholesterolemia with its risks for atherosclerotic lesions as well as for Familial Chylomicronemia Syndrome and the high risk for pancreatitis.

Keywords: Pregnancy; Lipoproteins; Familial Hypercholesterolemia; Familial Chylomicronemia Syndrome; Cholesterol; Triglycerides

Abbreviations: HDL: high-density lipoprotein; LDL: low-density lipoprotein

Lipid Changes

During pregnancy, there is a substantial increase in the plasma concentration of lipoproteins, consequent to the elevation of circulating estrogen and progesterone. Triglycerides increase two to three times in relation to the pre-gestational value, reaching the peak at the end of pregnancy, with a progressive return to baseline at the end of the puerperium. In the same way, there is a progressive increase in total cholesterol levels, which corresponds to two to five times the values prior to pregnancy, with a decrease a little slower than the levels of triglycerides with normalization, which can extend beyond six weeks after delivery [1].

Lipoprotein fractions also show qualitative changes, so that high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) have an increased number of triglycerides. HDL-c has a slightly different behavior from total cholesterol and triglycerides, as it presents a progressive in-

crease, reaching its maximum in the twenty-fourth week, with an increase of 50% in the values when compared with the non-pregnant period. Then, it presents a drop equivalent to 15% above the values before pregnancy until the term period [1]. LDL-c levels increase in synchrony with those of total cholesterol; however, they present a more delayed decrease, and the fall may occur after the eighth week of puerperium.

The factor responsible for these lipoprotein changes is the hormone estrogen. The decrease in HDL-c after the twenty-fourth week is explained by the increase in plasma insulin concentration, which represents an increase in insulin resistance. It is concluded, therefore, that HDL-c levels are more related to estrogen level in the first phase and insulin in the second phase of pregnancy.

It is recommended that the dosage of a lipid profile be postponed at least 4 or 6 weeks after pregnancy, especially in those women without previous changes.

In the update of the Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis, recommendations for dyslipidemic women of childbearing age include dietary guidance and adoption of a healthy lifestyle, as well as body weight control, physical activity, and smoking cessation [2]. Statin therapy should be avoided in women of childbearing age planning pregnancy (class II-A; C).

Gestational hypertriglyceridemia occurs to meet maternal energy demands, as a precursor of hormones to the placenta and to provide cholesterol and essential fatty acids to the fetus. In pregnant women in the second and third trimesters and in lactating women, statin therapy should not be indicated (class III-C). The contraindication is due to reports of teratogenicity, although the information available in the literature is inconclusive [3].

Fibrates, ezetimib, niacin, cholesterolamine and omega-3 are considered drugs with no absolute contraindication, but cholestyramine is the only one with defined safety. Fibrates can be used in cases of very severe hypertriglyceridemia (plasma triglyceride level > 1,000 mg/dl), under the risk/benefit analysis for pregnant women (high mortality for mother and fetus due to acute pancreatitis). However, dietary control should be the treatment of choice in pregnant women (class IIA; C); in extreme cases, apheresis may be recommended [4].

As for omega-3 fatty acids, pregnant and lactating women should be advised to introduce mineral-rich, deep-water fish with low mercury levels into their diet. The recommended ones are salmon, mackerel, herring, sardines, tuna and trout. There are no studies on supplementation (capsules) and phytosterols during pregnancy.

Genetic dyslipidemias, both hypertriglyceridemia with frequent pancreatic complications and familial hypercholesterolemia, deserve consideration. The special therapeutic approach in these severe circumstances is apheresis, and in cases of familial hypercholesterolemia, apheresis is selective LDL-apheresis [5].

It was assumed that dyslipidemia in pregnancy should be con-

sidered physiological, so much so that the study of the lipid profile is not part of the prenatal routine. However, recently, fatty striae have been described in the aorta of fetuses of dyslipidemic mothers. From these observations, it has been suggested that maternal cardiometabolic dysfunction may not only contribute to long-term maternal effects, but also cause a risk of atherosclerosis in future generations. These considerations suggest that the diagnosis and treatment of dyslipidemias should be performed before conception and have a continuity during pregnancy and postpartum [6].

Key points

- Increased triglycerides and cholesterol occur in pregnancy;
- The use of statins has not been recommended, although there is controversy about their teratogenic effects;
- Maternal dyslipidemia can induce fetal atherosclerosis and also in future generations.

Conflicts of interest: No conflict of interest.

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