Assessment of serum lipids in pregnant women aged over 35 years and their relation with pre-eclampsia

Avaliação do perfil lipídico em gestantes acima de 35 anos e sua relação com pré-eclâmpsia

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ABSTRACT

Objective: To assess serum total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, very low density lipoprotein cholesterol and triglyceride levels in pregnant women aged over 35 years during the first and second trimesters of pregnancy, and to relate these values with the diagnosis of pre-eclampsia in the 3rd trimester of pregnancy. Methods: Fifty-three pregnant women were divided into two groups, one with no pre-eclampsia and another diagnosed with pre-eclampsia. Five pregnant women were excluded due to miscarriages. Serum total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, very low density lipoprotein cholesterol and triglyceride levels were measured in all pregnant women during the first and second trimesters of pregnancy. Results: Thirty-nine pregnant women had no pre-eclampsia and nine were diagnosed with pre-eclampsia. Serum total cholesterol, low density lipoprotein cholesterol and triglyceride levels were similar in both groups during the first and second trimesters of pregnancy (p = 0.25, p = 0.71 and p = 0.30, respectively). However, serum total cholesterol, low density lipoprotein cholesterol and triglyceride levels were significantly higher during the second trimester compared to the first trimester in both groups (p < 0.001, p < 0.005 and p < 0.001, respectively). Serum high density lipoprotein cholesterol and very low density lipoprotein cholesterol levels were similar in both groups during the first trimester (p = 0.21 and p = 0.38, respectively); during the second trimester, however, these levels were significantly higher in the pre-eclampsia group compared to the group with no pre-eclampsia (p = 0.005 and p = 0.003, respectively). Furthermore, serum high density lipoprotein cholesterol levels in the pre-eclampsia group were significantly higher during the second trimester compared to the first trimester in the same groups, and serum very low density lipoprotein cholesterol levels in both groups were significantly higher during the second trimester compared to the first trimester (p = 0.016 and p < 0.001, respectively). Conclusions: Serum total cholesterol, low density lipoprotein cholesterol, very low density lipoprotein cholesterol and triglyceride levels raised from the first to the second trimester of pregnancy. Serum high density lipoprotein cholesterol levels increased only in pregnant women with pre-eclampsia during the second trimester of pregnancy. Pregnant women with pre-eclampsia had higher serum high density lipoprotein cholesterol and very low density lipoprotein cholesterol levels compared with pregnant women with no pre-eclampsia.

Keywords: Dyslipidemias; Pregnancy; Pre-eclampsia

RESUMO

Objetivo: Avaliar os níveis séricos de colesterol total, colesterol da lipoproteína de baixa densidade, lipoproteína de alta densidade, lipoproteína de muito baixa densidade e triglicérides em mulheres acima de 35 anos no primeiro e segundo trimestres de gestação e relacionar os valores obtidos com o diagnóstico de pré-eclâmpsia no terceiro trimestre de gestação. Métodos: Foram estudadas 53 gestantes que foram divididas em dois grupos. Um grupo com e outro sem o diagnóstico de pré-eclâmpsia. Cinco gestantes foram excluídas devido a abortamento. Dosaram-se os níveis séricos de colesterol total, colesterol da lipoproteína de baixa densidade, lipoproteína de alta densidade, lipoproteína de muito baixa densidade e triglicérides em todas as gestantes no primeiro e segundo trimestres. Resultados: Trinta e nove gestantes não tiveram pré-eclâmpsia e nove gestantes tiveram pré-eclâmpsia. Os níveis séricos de colesterol total, colesterol da lipoproteína de baixa densidade e triglicérides foram semelhantes nos dois grupos no primeiro e segundo trimestres de gestação.
In the course of normal gestation, serum lipid and lipoprotein levels undergo variations, and triglycerides (TG), cholesterol and phospholipids are elevated. These changes are considered a reflection of increased metabolic demands by the mother’s organism(1-2).

Serum low-density lipoprotein cholesterol (LDL) levels increase as gestation progresses, peaking at 36-week gestation, probably due to the hepatic effects of estradiol and progesterone. High-density lipoprotein cholesterol (HDL) levels increase until reaching a peak at 25 weeks, decreasing thereafter until the 32nd week, after which values remain constant until birth. It is thought that estrogen is responsible for elevating HDL levels during the first half of gestation(3). Maternal progesterone-induced lipoprotein lipase activity leads to hypertriglyceridemia(3).

Pre-eclampsia (PE), a non-convulsive form of pregnancy-induced hypertension, occurs in 5 to 10% of gestations. It accounts for a significant proportion of maternal and fetal morbidity and mortality(4).

PE is more frequent in first-gestation young women and in older multiparous women. It is defined as the development of elevated arterial blood pressure, significant proteinuria and edema occurring from 20 weeks gestation onwards(5).

Endothelial injury is a key event in the pathogenesis of PE, occurring due to multiple factors. The typical uteroplacental bed lesion in PE is necrotizing arteriopathy. It has been shown that lipids accumulate in arterial intima cells and in macrophages(6).

The similarity between lesions in PE and in atherosclerosis has raised speculation about a common pathophysiological pathway. Recent papers have suggested that a maternal predisposition to PE may be explained by abnormal lipid metabolism. An altered lipid profile is associated with atherosclerotic cardiovascular disease and with endothelial dysfunction. The true influence of an altered lipid profile in the pathophysiology of PE has raised interest(7). Although data are scarce and inconsistent, marked hyperlipidemia has been observed in PE patients compared to women with normal pregnancies.

PE is thus characterized by profound lipid changes similar to those found in atherosclerosis, including hypertriglyceridemia and relatively increased LDL levels, both of which play a role in endothelial injury and dysfunction. Decreased HDL serum levels were also related to PE. There are, however, few studies assessing lipid profile changes early in pregnancy and the progression to PE.

The purpose of this study was to evaluate serum TC, TG, LDL, HDL and VLDL levels in pregnant women aged over 35 years during the first and second trimesters of pregnancy, and to relate these levels to diagnosis of PE during the third trimester of pregnancy.

METHODS

The study included 53 pregnant patients from the Prenatal Outpatient Unit of the Hospital do Servidor Público Estadual “Francisco Morato de Oliveira” (HSPE-FMO), in the city of São Paulo, Brazil. All had a systolic blood pressure below 140 mmHg and a diastolic blood pressure below 90 mmHg; none had a history of cardiovascular or kidney disease, and/or diabetes mellitus. Ongoing gestations were of single fetuses with gestational ages equal to or below 13 weeks. Maternal age was over 35 years. Calculation of the gestational age was based on the first day of the last menstrual period and confirmed by ultrasound by the 20th week. The subjects signed a free informed consent form and participated in a predefined protocol.

In the first trimester (T1, until the 13th week of pregnancy), the body mass index (BMI) was assessed, arterial blood pressure was checked, and serum TC, TG, LDL, HDL and VLDL were measured. In the second trimester (T2, between the 23rd and 27th week of pregnancy), these procedures (except for the BMI) were repeated, and proteinuria was investigated in a single sample. A diagnosis of PE was made according to the following criteria: arterial blood pressure $\geq 140/90$
mmHg and proteinuria > 1 g/l, in a single urine sample during the third trimester\(^4\).

Five of 53 subjects that had been enrolled in the study were excluded due to spontaneous abortion. The remaining sample, therefore, was composed of 48 subjects. The analysis was made after separating the sample into two groups, as follows: one group contained 39 subjects with no PE, and another group contained nine subjects that developed PE.

Two subjects were smokers, one in each group. Age ranged from 36 to 43 years; the mean age was 39 years in both groups, and the standard deviation was ± 1.79 years in the group of subjects with no PE and ± 2.40 years in the PE group.

The BMI mean and standard deviation was 26.58 ± 5.07 kg/m\(^2\) (group with no PE) and 27.81 ± 2.66 kg/m\(^2\) (PE group). The p value was 0.49. Eleven (22.9\%) subjects were primigestas and three (27.3\%) of them developed PE. The mean systolic arterial blood pressures and the standard deviation in the first trimester were 112.82 ± 9.99 mmHg (group with no PE) and 116.67 ± 7.07 mmHg (PE group). The mean diastolic arterial blood pressures and the standard deviation in the first trimester were 72.05 ± 6.95 mmHg (group with no PE) and 73.33 ± 5.0 mmHg (PE group).

The mean systolic arterial blood pressures and the standard deviation in the second trimester were 111.79 ± 10.23 mmHg (group with no PE) and 131.11 ± 20.28 mmHg (PE group). The mean diastolic arterial blood pressures and the standard deviation in the first trimester were 70.51 ± 8.26 mmHg (group with no PE) and 64.56 ± 32.62 mmHg (PE group).

The measurement of serum TC, TG, LDL, HDL and VLDL was done using the enzymatic colorimetric method on an Advia\(^\circledast\) 1650 (Bayer\(^\circledast\)) device.

Differences between groups according to the analysis of variance model (ANOVA) for repeated measurements and qualitative variables (TC, TG, LDL, HDL and VLDL) across time (T1 and T2) were assessed. In this analysis, group and time effects, and the interaction between group and time were studied. The time effect and the group effect were assessed when the interaction was deemed not significant. Comparisons between both groups were made separately for each time period when interaction effects were significant, and the time effect was tested separately for each group.

Data were recorded in MS Office Excel, version 2000. The Statistical Package for the Social Science (SPSS) for Windows, version 10.0, was used for statistical analysis.

The HSPE-FMO Research Ethics Committee analyzed and approved the research protocol.

### RESULTS

Serum TC, TG, LDL, HDL and VLDL levels in both groups across time (T1 and T2) are shown on Table 1 and Figure 1. Serum TC levels were similar in both groups during the first and second trimesters (p = 0.245). These values, however, increased significantly from the first to the second trimesters of pregnancy in both groups (p < 0.001).

Serum HDL levels during the first trimester were similar in both groups (p = 0.210); during the second trimester, serum HDL was significantly higher in the PE group (p = 0.005). Furthermore, serum HDL increased significantly only from the first to the second trimesters in pregnant patients that developed PE (p = 0.016). Serum LDL levels were similar in the first and second trimesters in pregnant patients that did not develop PE (p = 0.85). Serum LDL levels were similar in both groups during the first and second trimesters (p = 0.71). Serum LDL increased significantly from the first to the second trimester in both groups (p = 0.01). Serum VLDL levels were also similar in both groups during the first trimester (p = 0.38). During the second trimester, however, pregnant patients that developed PE had significantly higher serum VLDL levels (p = 0.034). Serum VLDL levels increased significantly in both groups from the first to the second trimester (p < 0.001). Serum TG levels were similar in both groups during the first and second trimesters.
trimesters (p = 0.30), and increased significantly from the first to the second trimester in both groups (p < 0.001).

**DISCUSSION**

Some studies showed that older pregnant women are at a higher morbidity risk, the most common complications being hypertensive disorders\(^8\). Other studies showed that pregnant patients that develop PE are not more overweight compared to pregnant women that do not develop PE, although they might gain more weight during the third trimester\(^7\). In our study, both groups (with and with no PE) had similar initial BMI.

The literature describes lipid alterations along pregnancy\(^9\). We also found significantly elevated TC, TG, LDL and VLDL levels as pregnancy progressed. Serum TC, TG, LDL and HDL and VLDL levels during the second trimester were higher in pregnant patients that developed PE, compared to the groups with no PE, although only serum VLDL and HDL levels were significantly elevated.

Enquobahrie et al. assessed serum lipid levels in 57 patients that developed PE and in 510 pregnant patients in the control group during the first trimester\(^10\). These authors found a significant relation between PE and elevated serum TC, TG and LDL levels, as well as decreased serum HDL levels. The conclusion was that early dyslipidemia in pregnancy increased the risk of PE.

Clausen, Djurovic and Henriksen demonstrated a significant relation between hypertriglyceridemia before 20 weeks of gestation and the development of early PE\(^11\). These authors found no significant changes in serum HDL and TC levels. Ziaei, Bonab and Kazemnejad analyzed 470 primigestas between 28 and 32 weeks of gestation, and also found hypertriglyceridemia in the PE group\(^12\).

Elzen et al. assessed 393 pregnant women during the first trimester and 351 pregnant women during the second trimester, all aged 36 years or over, and concluded that an altered lipid profile during the first trimester, especially an altered serum TC, increased the risk of PE\(^8\).

Chappell et al. analyzed 65 patients at 20 to 36 weeks of gestation\(^13\). Twenty-one of these patients developed PE, 17 patients presented restricted fetal growth, and 27 had uncomplicated pregnancies. They found that serum TG levels increased as pregnancy progressed; the elevation was higher in the PE group. Serum HDL levels were lower in the PE group; no difference was found in serum TC and LDL levels.

Contrary to the literature, we found no decrease in serum HDL levels during the second trimester in the PE group. Bayhan et al. assessed 25 pregnant women that developed mild PE, 28 pregnant women that developed severe PE, and 25 pregnant women in a control group, during the third trimester, and found a significant decrease in serum HDL levels in patients that developed PE\(^14\). Similarly, Kocyiigit et al. found significantly decreased serum HDL levels in a study that analyzed 45 patients that developed PE during the third trimester, compared to 30 control patients\(^7\).

**CONCLUSIONS**

The present study concluded that serum TC, LDL, VLDL and TG levels increased from the first to the second trimester of pregnancy, that serum HDL levels increased only in pregnant patients with PE from the first to the second trimester, and that pregnant women that developed PE presented higher serum HDL and VLDL levels during the second trimester compared to those who did not develop PE.

No clear relation was found between early changes in the lipid profile and the development of PE. This divergence with the international literature is hard to explain, since the population, racial and socioeconomic diversity may have a significant role in the genesis or PE. We expect that this study may pave the way for further research, and that, in future, our results may be compared with other Brazilian studies. Investigation of the methods that may best select those women at risk for PE is significantly useful, and may offer the possibility of improved care and decreased PE-related morbidity and mortality.

**REFERENCES**

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