Original Paper

Maternal Lipid Profile as a Risk Factor for Gestational Diabetes Mellitus in Obese Women

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ABSTRACT: As dyslipidemia is frequently associated with gestational diabetes mellitus, the aim of this study was to establish a correlation between the evolution of the maternal lipid profile evaluated in the first and third pregnancy trimester for a series of parameters: triglycerides, cholesterol, high-density lipoprotein cholesterol (HDL-C), blood sugar fasting (BSF), triglyceride-glucose index (TyG index), TG/HDL-C ratio, leptin and the risk of gestational diabetes mellitus occurrence. The results were statistically interpreted, establishing the mean value of the obtained results and the standard deviation. From the studied parameters, only HDL-C and Tyg were statistically significant different in the first trimester for the two study groups, while in the third trimester statistically significant differences were observed also for triglycerides, blood sugar fasting and the TG/HDL-C ratio.

KEYWORDS: *Gestational diabetes mellitus, lipid profile, obesity.*

Introduction

Pregnancy is characterized by a number of important changes in the physiology of the pregnant woman, changes that play a fundamental role in meeting the basic needs of the mother and the requirements of the fetus [1].

Among maternal physiological adaptations, changes in lipid metabolism are among the most characteristic [2].

Estimation of maternal lipid profile is recommended during pregnancy because dyslipidemia is frequently associated with gestational diabetes mellitus [3].

The average blood concentrations of the most investigated lipids, TG, TC and LDL, increase from the first trimester to the third trimester.

The increase in triglycerides right from the beginning of pregnancy seems to be associated with insulin resistance and implicitly with gestational diabetes, one of the important complications of pregnancy [4].

The aim of this study was to establish a correlation between the evolution of the maternal lipid profile evaluated in the first and third pregnancy trimester and the risk of gestational diabetes mellitus occurrence.

Materials and Methods

This prospective study included a group of 99 patients, studied between October 2016 and May 2020, in the Obstetrics and Gynecology Clinic of the Craiova Municipal Hospital Filantropia.

During the mentioned research period, the informed consent was obtained from the women who agreed to participate in this study, subjected to an investigation protocol establishing the set of quantifiable, specific, case-tracking parameters.

The study was conducted in full compliance with the ethical principles contained in the "Declaration of Human Rights" adopted in Helsinki, which are in accordance with the Rules of Good Practice in Clinical Trials and legal regulations and with the approval of the Ethics Committee of our institution.

The statistical analysis was performed in the Biostatistics department of University of Medicine and Pharmacy Craiova.

The statistical assessment was carried out in part in Excel (Microsoft, USA) and in part in Matlab (Mathworks, USA).

The variables were presented as mean±standard deviation. For statistical significance between variables we used the Chi-square test.

A p-values <0.05 were considered as statistically significant.

The screening for gestational diabetes was performed in the second trimester of pregnancy at 22-24 weeks, after which the patients were divided into two study groups:

- GDM+, with gestational diabetes mellitus (16 patients)
- GDM-, without gestational diabetes mellitus (83 patients)

The maternal lipid profile was evaluated by blood analyses performed in the first trimester,

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at 11-14 weeks of pregnancy and in the third trimester, at 28-32 weeks of pregnancy for a series of parameters: triglycerides, cholesterol, high-density lipoprotein cholesterol (HDL-C), blood sugar fasting (BSF), triglyceride- glucose index (TyG index), TG/HDL-C ratio, leptin.

Results

In our study population the maternal age in the GDM group was 30.06±4.35 years, while in the group without GDM maternal age was 28.06±4.70 years. The distribution of cases by age groups is presented in Figure 1.

The pre-pregnancy BMI was 32.35±6.81 kg/m^2 in the GDM group, higher value than in the group without GDM of 27.30±6.70kg/m^2 (Figure 2).

We found that in cases that developed gestational diabetes, the mean triglycerides value was 144.57mg/dl±69.04 SD, while in the rest of the cases without GD, the mean triglycerides value was 115.14mg/dl±57.33 SD.

So, the increase was higher in cases that developed diabetes, but within normal values. We did not notice a statistically significant correlation between blood triglycerides and GD in the first trimester of pregnancy ($p>0.05$) (Table 1, Figure 3).

The determination of triglycerides at 28-32 weeks of pregnancy showed a large increase, with an average of 324.6mg/dl±132.88 SD, so a doubling of values compared to the first trimester. In comparison, in the rest of the cases, without GD, the mean triglycerides value was 186.48mg/dl±65.75 DS. We noticed a statistically significant significance between blood triglycerides and DG, in the third trimester of pregnancy ($p<0.05$) (Table 2, Figure 3).

The mean cholesterol values at 11-14 weeks of pregnancy showed slightly higher mean values in cases that later developed GD, 205.62 mg/dl±40.74 SD, compared to cases without GD, 187.68mg/dl±27.29 SD (Table 1, Figure 4).

At 28-32 weeks of pregnancy the average cholesterol value was 248.89±54.55 SD in the cases that developed GD, compared to the cases without GD, where the mean value was 232.12±41.27 DS, so relatively similar (Table 2, Figure 4).

The resulting data do not indicate any statistical significance observed between serum cholesterol and GD, both in the first and third trimesters ($p>0.05$).

The mean level of HDL-C at 11-14 weeks of pregnancy in cases that later developed GD was 56.32mg/dl±16.54 SD, lower than in cases without DG, 66.18 mg/dl±14.34 DS, but in the normal range.

However, the difference was statistically significant between blood HDL-C levels in the first trimester for GD+cases and GD-ones ($p<0.05$) (Table 1, Figure 5).

At 28-32 weeks of pregnancy in cases that developed DG, the mean HDL-C values were 63.18 mg/dl±19.38 SD, compared to 69.46 mg/dl±14.52 SD, in cases without GD.

No statistically significant significance was observed between the blood levels of the 2 groups in the third trimester ($p>0.05$) (Table 2, Figure 5).

The mean value of fasting blood sugar at 11-14 weeks of pregnancy in cases that developed GD was higher, 82.77mg/dl±17.26 SD, compared to 75.51mg/dl±10.85 SD in cases without GD, but in normal range. No statistically significant differences in blood glucose levels were observed between the 2 groups ($p>0.05$) (Table 1, Figure 6).

At 28-32 weeks of gestation in the cases that developed DG, the mean blood glucose values were higher than in the first trimester, 91.33mg/dl±6.94 SD, and a statistically significant difference was observed between the 2 study groups ($p<0.05$) (Table 2, Figure 6).

The TyG index at 11-14 weeks of gestation in cases that developed GD was 4.65±0.24 SD, slightly higher than the mean values in cases without DG, 4.49±0.21SD, with a statistically significant difference between the 2 groups in the first trimester ($p<0.05$) (Table1, Figure 7).

At 28-32 weeks of gestation in the cases that developed GD, the mean values of the TyG index were higher than in the first trimester, 4.99±0.17 SD and higher than the mean values from the cases without DG, 4.76±0.21 SD.

Again, the difference between the 2 groups was statistically significant in the third trimester ($p<0.05$) (Table 2, Figure 7).

The TG/HDL-C ratio at 11-14 weeks of pregnancy in the cases that developed GD, was 2.86±2.05 SD, much higher than the mean value from the cases without GD of 1.86±1.2 SD (Table 1, Figure 8).

At 28-32 weeks of pregnancy in cases that developed GD, the mean value of the TG-G index was higher than in the first trimester, 5.58±2.66 SD and higher than the mean value in cases without GD, of 2.84±1.33 SD.

We also noticed a statistically significant difference between the 2 groups in the third trimester ($p<0.05$), but not in the first trimester ($p>0.05$) (Table 2, Figure 8).

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The mean leptin value at 11-14 weeks of pregnancy was the same in pregnant women who developed GDM and in those without GDM, 38.05±24.66 SD and 38.35±30.13 SD, respectively, so no statistically significant difference was observed between those 2 groups (p> 0.05) (Table 1, Figure 9).

Mean leptin values at 28-32 weeks of pregnancy were higher in pregnant women who developed GDM than in those without GDM, 73.25±41.03 SD and 66.03±38.91 SD, respectively, but no statistically significant difference was observed between the 2 groups (p>0.05) (Table2, Figure 9).

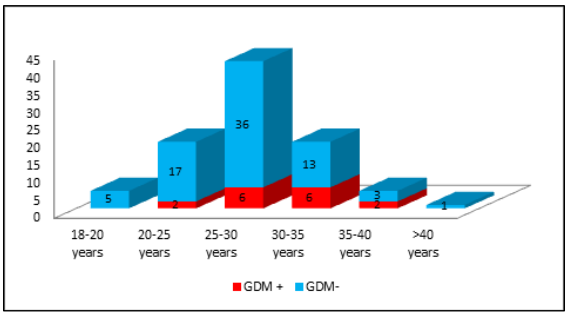

Figure 1. Distribution of cases by age groups.

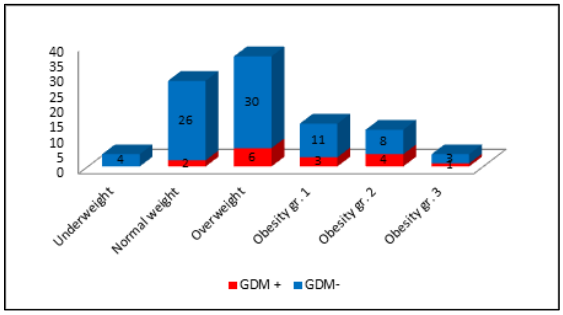

Figure 2. Distribution of cases according to BMI.

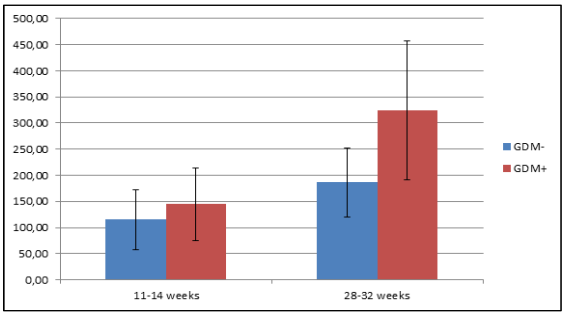

Figure 3. Triglycerides mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

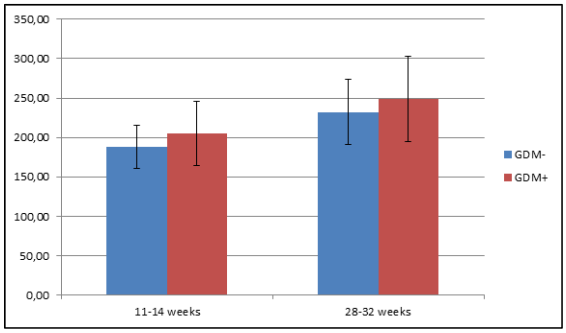

Figure 4. Cholesterol mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

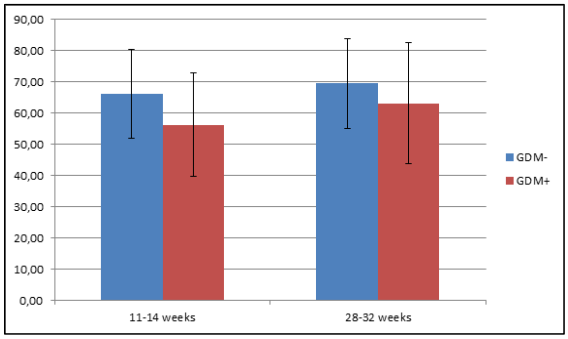

Figure 5. HDL-C mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

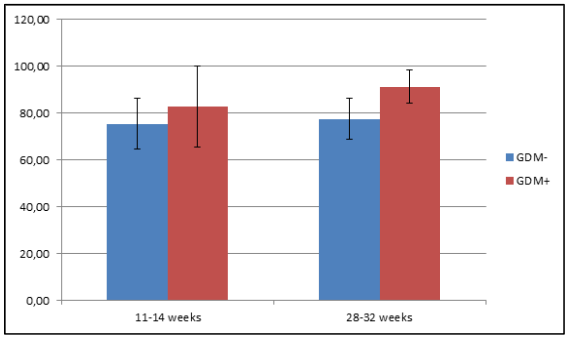

Figure 6. Fasting Blood Sugar mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

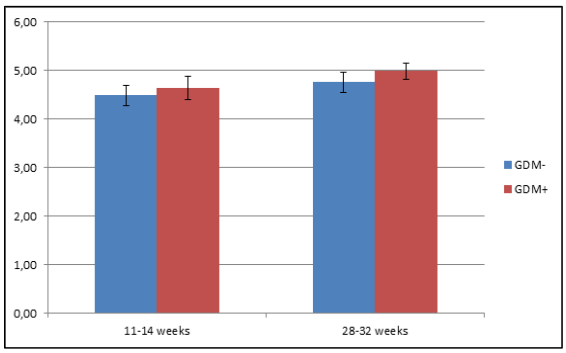

Figure 7. The TG-G index mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

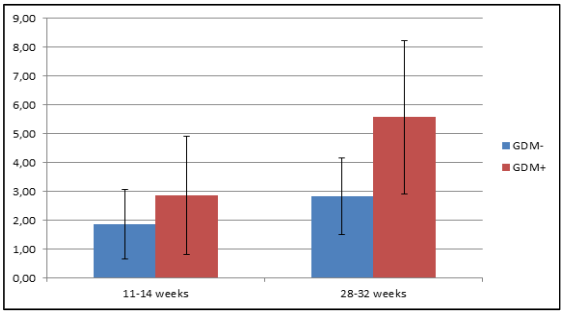

Figure 8. The TG / HDL-C ratio mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

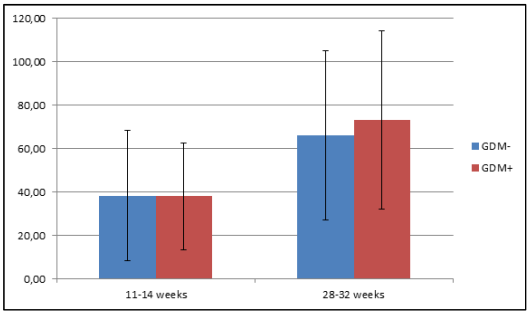

Figure 9. Leptin mean values and their standard deviations for the two study groups in the 1-st and 3-rd trimesters.

Table 1. The relationship between the maternal lipid profile and the gestational diabetes at 11-14 weeks of pregnancy.

11-14 weeks	GD Yes	GD No	p value
n=	16	83	
Triglycerides	144.57±69.04	115.14±57.33	0.125
Cholesterol	205.62±40.74	187.68±27.29	0.109
HDL-C	56.32±16.54	66.18±14.34	0.038
Fasting blood glucose	82.77±17.26	75.51±10.85	0.123
TyG Index	4.65±0.24	4.49±0.21	0.019
TG/HDL ratio	2.86±2.05	1.86±1.2	0.077
Leptin	38.05±24.66	38.35±30.13	0.966

Table 2. The relationship between the maternal lipid profile and the gestational diabetes at 28-32 weeks of pregnancy.

28-32 weeks	GD Yes	GD No	p value
n=	16	83	
Triglycerides	324.6±132.88	186.49±65.75	0.001
Cholesterol	248.89±54.55	232.12±41.27	0.258
HDL-C	63.18±19.38	69.46±14.52	0.234
BSF	91.33±6.94	77.51±8.81	0.000
TyG Index	4.99±0.17	4.76±0.21	0.000
TG/HDL	5.58±2.66	2.84±1.33	0.001
Leptin	73.25±41.03	66.03±38.91	0.523

Discussions

Maternal dyslipidemia has become a common phenomenon in pregnancy, especially in obese women.

Hyperlipidemia is usually found in the second half of pregnancy and can be considered a necessary physiological mechanism for providing energy and nutrients to the fetus [5].

It has been found that in early pregnancy, the lipid level is slightly increased, but in a late pregnancy the lipid level increases significantly [6].

Shen et al. found that lipid levels, including TyG, CT and LDL-C, gradually increased during pregnancy and peaked before birth, while HDL-C levels increased from the first trimester to the second trimester, then showing a slight decrease in the third trimester [7].

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In our study we found a correlation between plasma triglycerides and GDM, but statistically significant only in the third trimester, showing that only their dynamic determination can give us reports about a possible risk, which is consistent with data from other studies [8,9].

It is known that hypercholesterolemia causes excessive peroxidation of lipids, coexisting with a reduction in antioxidant activity leading to oxidative stress.

The association between atherogenic index growth, oxidative stress and endothelial cell dysfunction during pregnancy may influence the occurrence of preeclampsia [10].

Thus in our study we wanted to see if it had the same influence on gestational diabetes mellitus, but our results did not indicate any statistical significant difference observed between the two study groups ($p>0.05$).

The dosing of fasting blood glucose on the first prenatal visit is related to glycemic metabolism in the middle of the gestational period.

Obesity and increased fasting blood glucose in the first trimester of pregnancy is independently associated with the further development of GDM [11].

But in our study, no statistically significant significance was observed between fasting blood glucose and GDM in the first trimester ($p>0.05$), but in the third trimester a statistical significant difference was observed between the two study groups ($p<0.05$).

Increased insulin resistance during pregnancy is present in order to limit maternal glucose use, in order to provide an adequate amount of glucose necessary for fetal development [12].

Insulin resistance is not the same over time during pregnancy, in the last half of pregnancy, insulin resistance increases significantly, mainly in women with gestational diabetes and type 2 diabetes [13].

Although the mechanisms of insulin resistance are complex and still incompletely elucidated, it has been found that a number of factors such as placental hormones, obesity, diet and genetic influence can affect insulin resistance in pregnancy [14].

One of the parameters of the research in this study was to evaluate the triglyceride and glucose index (TyG-G) as a marker of insulin resistance in pregnant obese women, knowing that the basis of GDM pathophysiology is increased insulin resistance.

The TyG-G index is a screening method for insulin resistance that requires only two laboratory determinations: triglycerides and blood glucose.

The TyG index has been shown to reflect the metabolic status of the pregnant woman and may predict the onset of gestational diabetes mellitus [15,16].

Hypertriglyceridemia and low HDL-C levels are two important metabolic abnormalities associated with insulin resistance [17,18] and so with GDM.

The cases that developed DG later, presented at 11-14 weeks of pregnancy, average values of the TG/HDL-C index similar to those found in the cases without DG in the third trimester, 2.86±2.05 SD, and at 28-32 weeks, the mean value was 5.58±2.65 SD. Some studies show an increase in the TG/HDL-C ratio with mean values over 4.24 [19], which is consistent with the results of this study.

Also, some researchers confirmed a high level of serum lipid profile, including TG/HDL-C ratio concentrations in mothers with GDM compared to pregnancies without GDM.

Thus, the TG/HDL-C ratio may be a good indicator of insulin resistance and may play an important role in the incidence of GDM [20,21].

A recent study [9] noted that women who developed GDM from early pregnancy began to show an increase in the TyG/HDL-C ratio and TyG-G values compared to the control group.

Regarding plasma leptin values, although some studies have shown that hyperleptinemia in early pregnancy may be a good predictive index for GDM [22,23], in our study we did not observe a statistically significant difference.

Conclusions

Our results show that a dynamic determination of the lipide profile may give important data about a possible risk for gestational diabetes mellitus.

From the studied parameters, only HDL-C and Tyg were statistically significant different in the first trimester for the two study groups, while in the third trimester statistically significant differences were observed also for triglycerides, blood sugar fasting and the TG / HDL-C ratio.

The data obtained may be the basis for future studies to determine a specific set of risk assessment tests for gestational diabetes mellitus in obese women.

Conflict of interests

None to declare.

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