

LIPID PROFILE OF HEALTHY WOMEN DURING NORMAL PREGNANCY

LIPIDSKI PROFIL ZDRAVIH ŽENA TOKOM NORMALNE TRUDNOĆE

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Summary: The four basic lipid indexes (Chol, Trig, HDL-C and LDL-C) increase during pregnancy, following different rates of increase. Among the four analytes triglycerides show the largest increase and HDL-C the smallest. All analyte values are raised during the 40 weeks of pregnancy, except HDL-C which is stabilized during the second trimester. After delivery the values decrease, except LDL-C which remains steady (for some weeks) before starting to fall following the others. In this study the relations between the four lipid indexes and some predisposing factors (age, gestational age, nationality, body mass index, profession, smoking and diabetes during pregnancy) were investigated. The sample consisted of 413 pregnant women, mainly Greeks and Albanians. After regression analysis it was proved that the only common predisposing factor was the gestational age. Triglycerides and total cholesterol are also influenced by the women's age. The lipid indexes showed no important difference between the pregnant women in the first trimester and the non-pregnant women. On the contrary, there was a statistical difference between the pregnant women in the second and third trimester and between them and the women in the first trimester. The percentages of increase between first and second trimester were: Chol: 38%, Trig: 115%, HDL-C: 30%, LDL-C: 33%. The percentages of increase between first and third trimester were: Chol: 65%, Trig: 208%, HDL-C: 26%, LDL-C: 64%.

Keywords: pregnancy, dyslipidemia, cholesterol, triglycerides, high density lipoprotein, low density lipoprotein

Kratak sadržaj: Vrednosti četiri osnovna lipidska indeksa (Chol, Trig, HDL-C i LDL-C) rastu tokom trudnoće, prateći različite stope rasta. Od ta četiri analita najveći porast pokazuju trigliceridi a najmanji HDL-C. Vrednosti svih analita rastu tokom 40 nedelja trudnoće, osim HDL-C koji je stabilizovan u drugom trimestru. Posle porođaja, vrednosti opadaju, osim LDL-C koji ostaje stabilan (nekoliko nedelja) pre nego što takođe počne da pada. U studiji su proučavani odnosi između četiri lipidska indeksa i određenih faktora predispozicije (starost, gestaciona starost, nacionalnost, indeks telesne mase, profesija, pušenje i dijabetes u trudnoći). Uzorak je činilo 413 trudnih žena, uglavnom Grkinja i Albanci. Regresionom analizom je dokazano da je jedini zajednički faktor predispozicije bila gestaciona starost. Na trigliceride i ukupan holesterol takođe je uticala i starost žena. Nije bilo važne razlike između lipidskih indeksa žena u prvom trimestru i žena koje nisu bile trudne, dok je između žena u drugom i žena u trećem trimestru utvrđena značajna razlika, kao i između njih i žena u prvom trimestru. Porast u procentima između prvog i drugog trimestra bio je: za Chol: 38%, Trig: 115%, HDL-C: 30%, LDL-C: 33%. Porast u procentima između prvog i trećeg trimestra iznosio je: Chol: 65%, Trig: 208%, HDL-C: 26%, LDL-C: 64%.

Ključne reči: trudnoća, dislipidemija, holesterol, trigliceridi, HDL (lipoproteini velike gustine), LDL (lipoproteini male gustine)

Introduction

More than 200 million women become pregnant every year and in most cases the outcome of labour is successful. Because of the hormonal status changes during pregnancy, various adaptive mechanisms are initiated due to sex hormones. Among them, alteration of the energetic metabolism to lipid metabolism is observed. That is, pregnant women

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develop physiological dyslipidemia (1) that can be measured in the laboratory by the lipid indexes: total cholesterol (Chol), triglycerides (Trig), high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C). The alterations of serum lipid indexes are associated with the gestational age.

The increase of the lipid and lipoprotein metabolism reaches the level of cardiovascular risk (2–5) during the second trimester. Especially, the second and third trimester of human pregnancy are characterized by 2–3-fold increases in plasma triglycerides and lesser increases in total cholesterol, HDL-C and LDL-C.

Analytically, the average serum LDL-C concentration increases by about 0.80 mmol/L in the second trimester compared with the first trimester and 0.69 mmol/L in the third trimester compared with the second trimester (6). The major increase of the serum cholesterol concentration occurs in the second trimester (25–50%). The serum triglyceride concentration increases more intensively than the others and its major increase occurs during the third trimester (about 200–300%) (7, 8). Serum HDL-C concentration increases during the second trimester but decreases during the third trimester. Just after delivery the values of all lipid indexes decrease (still remaining above the non-pregnant values) except the LDL-C values which remain constant (3).

Women with an increase in low-density lipoprotein during the second and third trimester show a more marked increase in serum triglycerides. That effect is slightly more evident in the multiparous subjects. The observed changes in low-density lipoprotein patterns during pregnancy may be used to identify those women who later in life will have pathologically high low-density lipoproteins. The pregnant women are affected by a type VI hypertriglyceridemia, according to the Fredrickson/WHO classification of hyperlipoproteinemias, with an increase in chylomicrons and VLDL-lipoproteins. This subtype is characterized by the presence of hypertriglyceridemia associated with hypercholesterolemia.

During early pregnancy there is an increase in body fat accumulation, associated with both hyperphagia and increased lipogenesis. The increased lipid production during pregnancy is necessary as an energy store to fulfill maternal and fetal metabolic needs while maternal hypertriglyceridemia, especially towards late gestation, has an important role as a source of triglycerides for milk formation just before parturition (2). During late pregnancy there is an accelerated breakdown of fat deposits, that plays a key role in fetal development. Moreover, using placental transferred fatty acids the fetus benefits from two other products: glycerol and ketone bodies. Although maternal glucose is quantitatively the main substrate crossing the placenta, glycerol is the preferential substrate for maternal gluconeogenesis. Additionally,

enhanced ketogenesis under fasting conditions and the easy transfer of ketones to the fetus allow maternal ketone bodies to reach the fetus, where they can be used as fuels for oxidative metabolism as well as lipogenic substrates.

Although maternal cholesterol is an important source of cholesterol for the fetus during early gestation, its importance becomes minimal during late pregnancy, due to the high capacity of fetal tissues to synthesize cholesterol. Maternal hypertriglyceridemia is a characteristic feature during pregnancy and corresponds to an accumulation of triglycerides not only in very low-density lipoprotein (VLDL-C) but also in low (LDL-C) and high-density lipoprotein (HDL-C). Although triglycerides do not cross the placental barrier, the presence of lipoprotein receptors in the placenta, together with lipoprotein lipase, phospholipoproteins A2 and intracellular lipase activities, allows the release to the fetus of polyunsaturated fatty acids transported as triglycerides in maternal plasma lipoproteins (9).

The hyperlipidemia of the second half of pregnancy may be a purely physiological response to pregnancy or may be indicative of pathology in some women. It must be investigated whether the hyperlipidemic response to pregnancy is a variable or not and if so, whether it can predict future hyperlipidemia in a manner analogous to that of impaired glucose tolerance during pregnancy, predicting non-insulin dependent diabetes in later life. There is evidence that triglyceride concentration, if measured between 9 and 12 weeks of gestation, has moderate predictive value for subsequent glucose tolerance in pregnancy. For that reason further studies are needed to investigate the role of early measurement in the screening and management of cardiovascular damage (8, 10).

Late pregnancy is associated with the formation of susceptible, oxidisable particles and an increase in oxidative damage. These biochemical changes may be relevant for the long-term cardiovascular health of women, especially those of high parity who are at high risk for cardiovascular disease (e.g. women with diabetes) (6, 11).

The atherogenic lipid profile of human gestation is further enhanced in preeclampsia. This may be a potential contributor to endothelial cell dysfunction. Studies have shown (12–14) that in preeclampsia, plasma lipids climb substantially above levels seen in normal pregnancies. Such lipid changes may play a role in the endothelial damage characteristic of preeclampsia.

The high levels of lipid indexes raise two questions: whether hypercholesterolemia and hypertriglyceridemia of pregnancy must be cured or not, and whether the pregnancy is atherogenic or not. In pregnancy the elevated levels of cholesterol are partially a result of high levels of HDL-C, which theoretically are not associated with increased risk of

coronary heart disease. Furthermore, hypertriglyceridemia is a controversial risk factor for coronary heart disease. In case drugs are necessary, then the statins will be the drugs of choice in hypercholesterolemia along with fibrates for combined hypercholesterolemia and hypertriglyceridemia. There are limited data to suggest that these drugs are not major human teratogens, however it is not recommended to use them during pregnancy (10).

Both cholesterol and triglyceride concentration decrease significantly within 24 hours of delivery and this is reflected in all lipoproteins. However, while triglyceride levels continue to decrease rapidly returning to non-pregnant levels during the puerperium, LDL-C remain elevated for at least six to seven weeks postpartum (9, 15, 16). Hyperlipidemia during pregnancy is not related to nationality (16, 17).

Our study accomplished three different purposes.

Firstly, the study of the alterations of Chol, Trig, LDL-C and HDL-C during the three trimesters of pregnancy. The values of each trimester were compared to the values of non-pregnant women and to the other two trimesters.

Secondly, the estimation of any statistical models which correlate the values of Chol, Trig, LDL-C and HDL-C with a number of predisposing factors such as age, gestational age, nationality, profession, diabetes, smoking and BMI.

Finally, the estimation of reference values for Chol, Trig, LDL-C and HDL-C for each trimester of pregnancy separately.

Material and Methods

The samples of pregnant and non-pregnant women

Our study is based on women who came for prenatal tests in the gynecological offices and laboratories of the local medical centre of the Social Security Institute of Greece¹. We used two samples, one of 413 pregnant women (*Table I*) and another of 102 non-pregnant women (*Table II*). The women of the second sample were the control group in our study. All women were living in the island of Zakynthos. In both samples we got information about Chol, Trig, HDL-C and LDL-C values, age, gestational age, nationality, body mass index (BMI), profession, smoking and diabetes during pregnancy.

According to the nationality, the sample of pregnant women consisted of 386 Greeks, 301 Albanians and ten other nationalities (*Table III*). They had all been living in Greece for many years.

According to the profession, our sample consisted of 219 contemporary clerks (tourist and agricultural jobs), 109 employees, 71 housekeepers, 8 teachers, 2 businesswomen (trade), 2 doctors, 1 gymnast and 2 students. As far as smoking is concerned 348 women

Table I Demographics of pregnant and non-pregnant women. The majority of pregnant women were in the first trimester.

	Population (N)	Mean age (years)	Age range (years)	Mean week of pregnancy
Controls (non-pregnant)	102	28.8 ± 6.2	18–45	–
Pregnant 1 st trimester	355	28.3 ± 5.4	18–43	8
Pregnant 2 nd trimester	189	29.5 ± 5.9	19–45	22
Pregnant 3 rd trimester	223	28.8 ± 5.6	18–46	32

Table II Descriptive statistics of Chol, Trig, HDL-C, LDL-C of non-pregnant women (controls).

	Population	Average & standard deviation (mmol/L)	Range of values (mmol/L)	Median (mmol/L)
Cholesterol	102	4.66 ± 0.54	3.46–5.72	4.63
Triglycerides	102	1.01 ± 0.35	0.41–1.79	0.97
HDL-C	101	1.42 ± 0.30	0.83–2.24	1.37
LDL-C	101	2.75 ± 0.57	0.30–3.95	2.81

¹ Social Security Institute is the largest public insurance organization in Greece. More than half of Greek population are insured in it (about six million people) and the majority of foreign immigrants.

Table III The nationalities of pregnant women.

Greeks	386
Albanians	301
Britons	27
Bulgarians	13
Rumanians	10
Serbs	8
Italians	8
Germans	4
Poles	4
Turks	3
Indians	2
Russians	2

had never smoked, 30 had quit after pregnancy, 27 continued with less smoking and 8 continued to smoke regularly. From the 413 pregnant women only 5 had diabetes during pregnancy.

On the other hand, the sample of the 102 non-pregnant women (controls) consisted of 62 Greeks, 35 Albanians and 5 other women of three different nationalities. The majority were working as contemporary clerks (51), employees (23), students (2) and businesswomen (1). The majority were non-smokers and their body mass index varied from 19 to 24.

Chemical analysis

For each woman we determined the values of cholesterol, triglycerides, HDL-C and LDL-C. Sampling was done in the morning after a twelve-hour fast. Cholesterol was measured by the enzymatic end point method CHOD-POD, triglycerides were measured by the enzymatic glycerol phosphate oxidase/peroxidase method, HDL-C by a homogenous enzymatic direct assay and LDL-C by Friedewald calculation: $LDL-C = Chol - [HDL-C - Chol] - Trig/5$ (18, 19).

Statistical analysis

Data were gathered in Excel sheets and analyzed in the Minitab statistical software package. The statistic analysis included descriptive statistics (e.g. medians, ranges, percentiles), non-parametric statistics (Mann-Whitney and Kruskal-Wallis test), normality test (Kolmogorov-Smirnov) and regression methods (stepwise method, backward elimination method and forward elimination method) (20).

Results and Discussion

The comparison of Chol/Trig/HDL-C/LDL-C between the three trimesters of pregnancy

We studied statistically the differences in Chol/Trig/HDL-C/LDL-C between pregnant and non-pregnant women for each trimester separately. We also compared the lipid values between the three trimesters. According to the *Tables IV–VII* the values of the four analytes increased during pregnancy very intensely. The percentages of increase between first and second trimester were: Chol: 38%, Trig: 115%, HDL-C: 30%, LDL-C: 33%. The increase between second and third trimester was even higher: Chol: 65%, Trig: 208%, HDL-C: 26%, LDL-C: 64%. Triglycerides were proved to show the largest increase during pregnancy.

The medians of Chol/Trig/HDL-C/LDL-C of pregnant (separately in three trimesters) and the non-pregnant women were compared with the non-parametric test statistics »Mann Whitney« and »Kruskal-Wallis«. Both tests compare the medians of the two or more groups of values.

The mean value of total cholesterol increased in each trimester (*Table IV, Figure 1*). In the first trimester there was no statistical difference between the values of pregnant and non-pregnant women ($P = 0.31$). On the contrary, between non-pregnant and pregnant women of the second and third trimester there was a large statistical difference ($P < 0.0001$). There was also a statistical difference between pregnant women of the second and third trimester ($P < 0.0001$). Cholesterol values climbed over the upper reference value (5.69 mmol/L) in the 15th week of pregnancy (*Figure 1*).

The mean value of triglycerides also increased in each trimester (*Table V, Figure 2*). The medians of each trimester values differed (statistically important difference) from the median of the non-pregnant women. There was also a statistically important difference between the three trimesters. Triglyceride values were going over the upper reference value (2.28 mmol/L) in 27th week of pregnancy (*Figure 2*).

High density lipoprotein had a similar attitude with cholesterol (*Table VI, Figure 3*). The trimester medians were increasing gradually. There was no statistical difference between the median of the first trimester the median of the non-pregnant women ($P = 0.084$). On the contrary, the second and third trimester were statistically different from the non-pregnant women ($P < 0.0001$). Between the third and second trimester there was no statistical difference ($P = 0.7140$) but there was a statistical difference between them and the first trimester. According to *Figure 3*, all HDL-C values were over the upper reference value (0.90 mmoles/l).

Low density lipoprotein had a similar attitude with cholesterol (*Table VII, Figure 4*). Its values increased in relation to the week of pregnancy but they remained

within the reference range (< 5.18 mmol/L). The median of the first trimester statistically different from the median of the non-pregnant women ($P = 0.07$). The values in the other two trimesters were statistically diffe-

rent from those of the non-pregnant women ($P < 0.0001$). There was also a large statistical difference between the three trimesters ($P < 0.0001$). All LDL-C values were below the upper reference value (5,2 mmol/L).

Table IV Descriptive statistics of cholesterol versus the trimester of pregnancy. The percentage of increase has been calculated against the first trimester.

Cholesterol	Population (mmol/L)	Mean (mmol/L)	Median (mmol/L)	Range	Percentage of increase
1st Trimester	158	4.55 ± 0.78	4.45	3.22–7.02	–
2nd Trimester	111	6.19 ± 1.35	6.14	3.17–10.22	38%
3rd Trimester	144	7.25 ± 1.27	7.33	4.08–10.92	65%

Table V Descriptive statistics of triglycerides versus the trimester of pregnancy. The percentage of increase has been calculated against the first trimester.

Triglycerides	Population	Mean (mmol/L)	Median (mmol/L)	Range (mmol/L)	Percentage of increase
1st Trimester	150	0.88 ± 0.36	0.75	0.41–2.18	–
2nd Trimester	100	1.67 ± 0.59	1.62	0.46–3.71	115%
3rd Trimester	82	2.40 ± 0.84	2.31	0.5–5.48	208%

Table VI Descriptive statistics of HDL-C versus the trimester of pregnancy. The percentage of increase has been calculated against the first trimester.

Triglycerides	Population	Mean (mmol/L)	Median (mmol/L)	Range (mmol/L)	Percentage of increase
1st Trimester	150	0.88 ± 0.36	0.75	0.41–2.18	–
2nd Trimester	100	1.67 ± 0.59	1.62	0.46–3.71	115%
3rd Trimester	82	2.40 ± 0.84	2.31	0.5–5.48	208%

Table VII Descriptive statistics of LDL-C versus the trimester of pregnancy. The percentage of increase has been calculated against the first trimester.

LDL-C	Population	Mean (mmol/L)	Median (mmol/L)	Range	Percentage of increase
1st Trimester	158	2.65 ± 0.68	2.6	0.83–4.94	–
2nd Trimester	111	3.53 ± 1.01	3.48	1.48–3.48	33%
3rd Trimester	144	4.26 ± 1.09	4.26	2.03–7.51	64%

Table VIII Reference values for Chol, Trig, HDL-C and LDL-C separately for the three trimesters of pregnancy.

	Cholesterol (mmol/L)	Triglycerides (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
1st Trimester	3.98–6.52	0.62–1.78	1.25–2.34	2.23–4.29
2nd Trimester	5.22–8.97	1.33–2.77	1.58–2.65	2.78–5.80
3rd Trimester	6.37–9.83	1.89–4.38	1.58–2.60	3.43–6.68

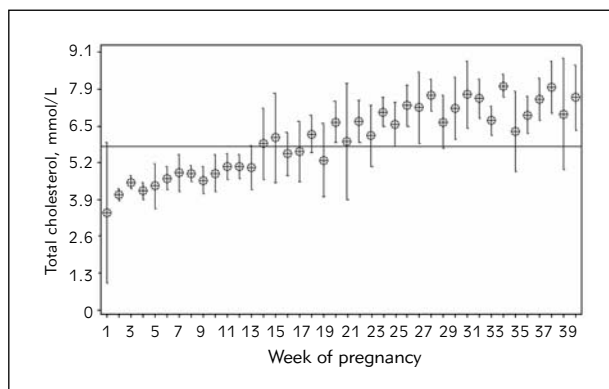


Figure 1 Interval plots of total cholesterol versus the week of pregnancy. The upper reference limit for total cholesterol has also been plotted (5.69 mmol/L). Total cholesterol is going over the upper reference limit after the 13th week.

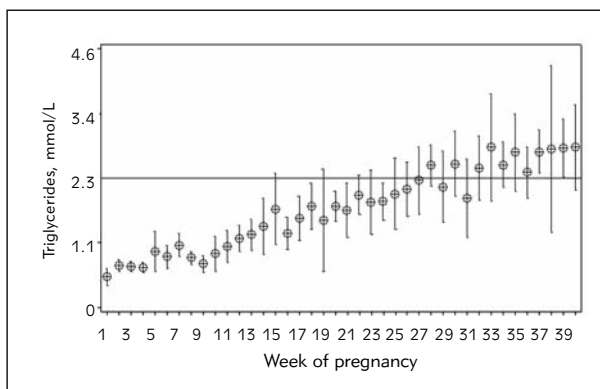


Figure 2 Interval plots of triglycerides versus the week of pregnancy. The upper reference limit for triglycerides has also been plotted (2.28 mmol/L). Triglycerides are going over the upper reference limit after the 27th week.

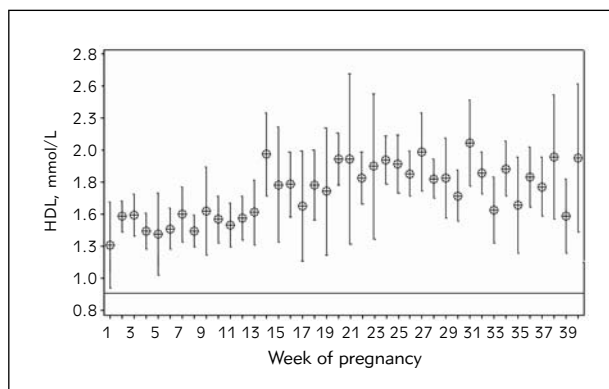


Figure 3 Interval plots of high density lipoprotein (HDL-C) versus the week of pregnancy. The lower reference limit for HDL-C has also been plotted (0.90 mmol/L). HDL-C values are always above the lower reference limit.

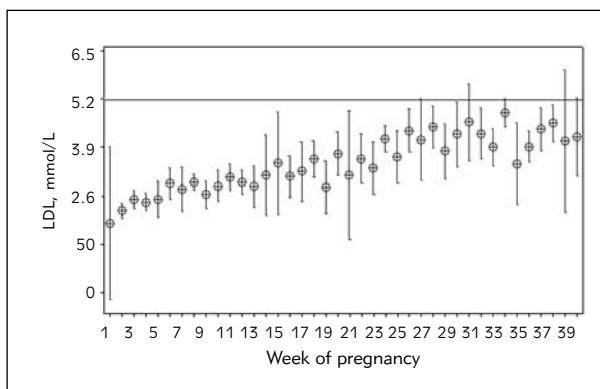


Figure 4 Interval plots of low density lipoprotein (LDL-C) versus the week of pregnancy. The upper reference limit for LDL-C has also been plotted (5.18 mmol/L). LDL-C values are always below the upper reference limit.

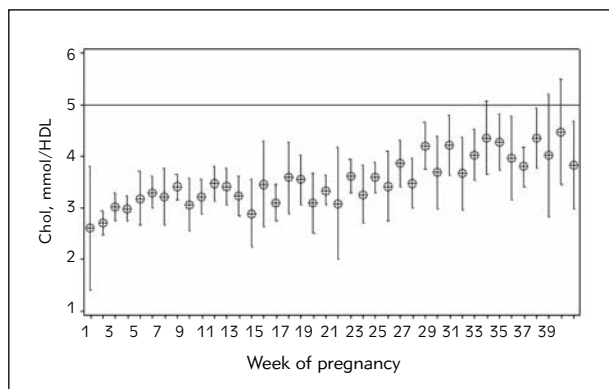


Figure 5 Interval plots of the atheromatic index Chol/HDL-C versus the week of pregnancy. All values are below the upper limit which is equal to 5.

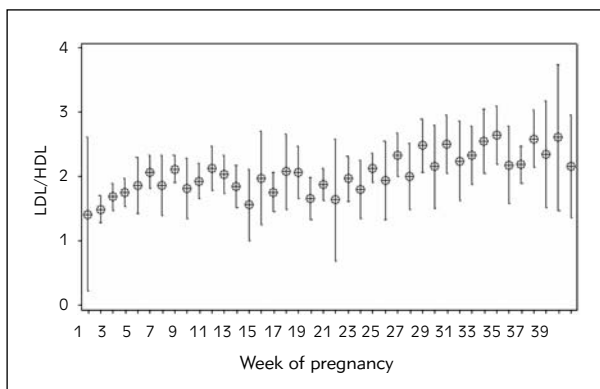


Figure 6 Interval plots of the atheromatic index LDL-C/HDL-C versus the week of pregnancy. All values are below the upper limit which is equal to 4.

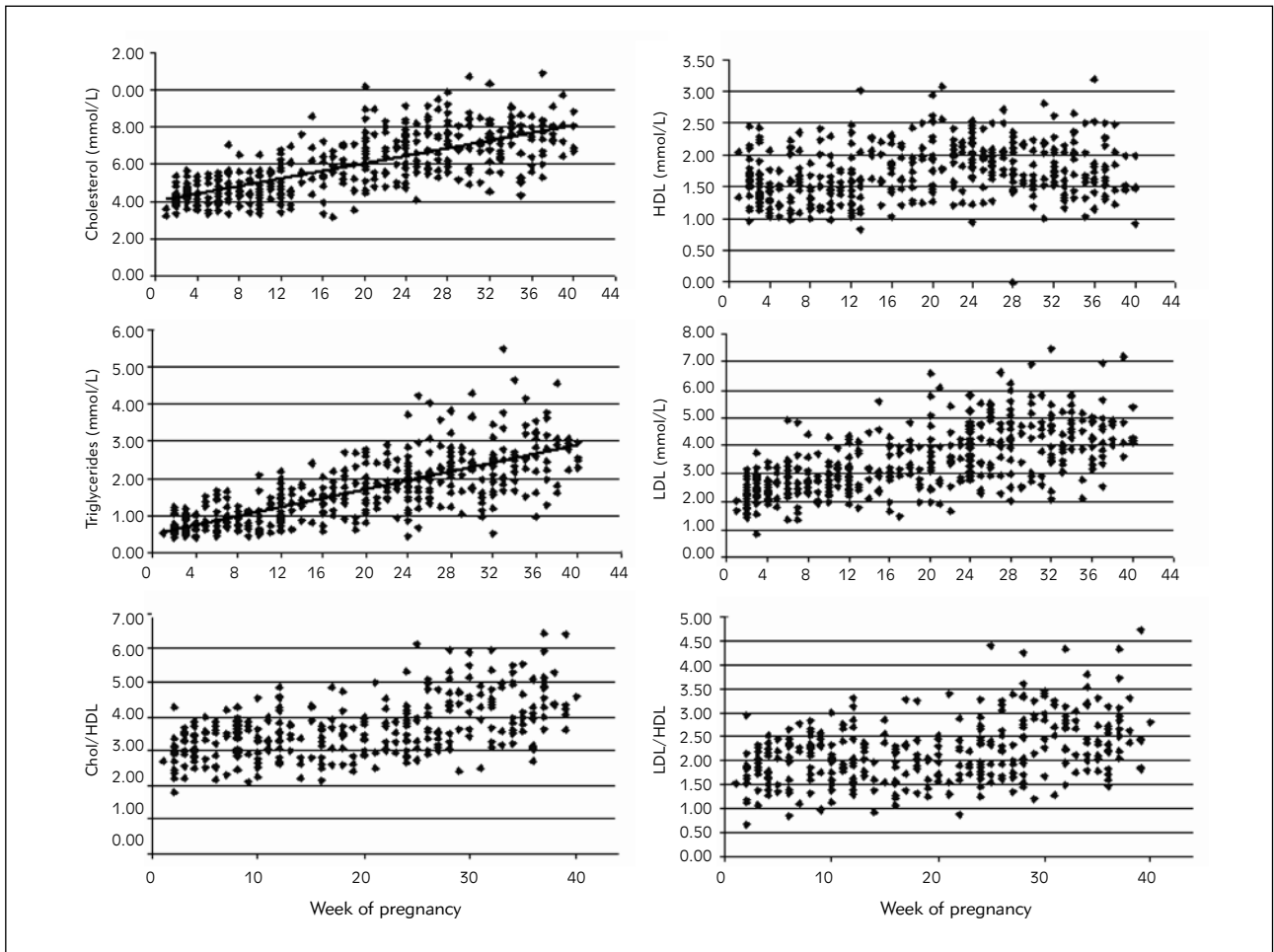


Figure 7 Scatter plots of all the lipid indexes versus the week of pregnancy. Although all lipid indexes show positive correlation, only triglycerides have r^2 larger than 50% (59%).

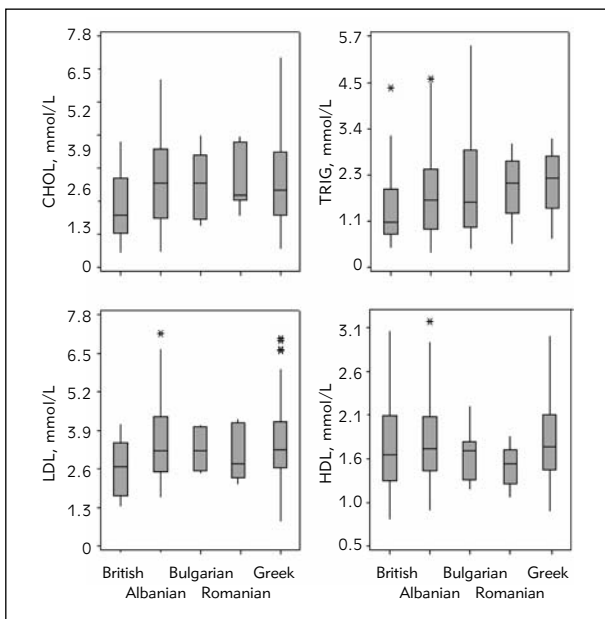


Figure 8 Box-plots of Chol/Trig/HDL-C/LDL-C versus the nationality of the pregnant women.

We also studied separately the atheromatic indexes Chol/HDL-C (Figure 5) and LDL-C/HDL-C (Figure 6). Both increase during pregnancy but their values remain below the upper limit of their reference range (5 for Chol/HDL-C and 4 for LDL-C/HDL-C).

In Figure 7, there are the scatter plots of all lipid indexes versus the week of pregnancy. All lipid indexes have positive correlation, although it is very week. The statistic r^2 (coefficient of determination) is always under 50% except for triglycerides which have the coefficient of determination r^2 equal to 59%.

Parameters and models that explain the values of Chol/Tri/HDL-C/LDL-C during pregnancy

The second purpose of our study was to find out which of the predisposing factors influence the values of Chol, Trig, HDL-C και LDL-C (except, of course, the gestational age). The predisposing factors considered were: age, gestational age, nationality, body mass index (BMI), profession, smoking and diabetes during pregnancy.

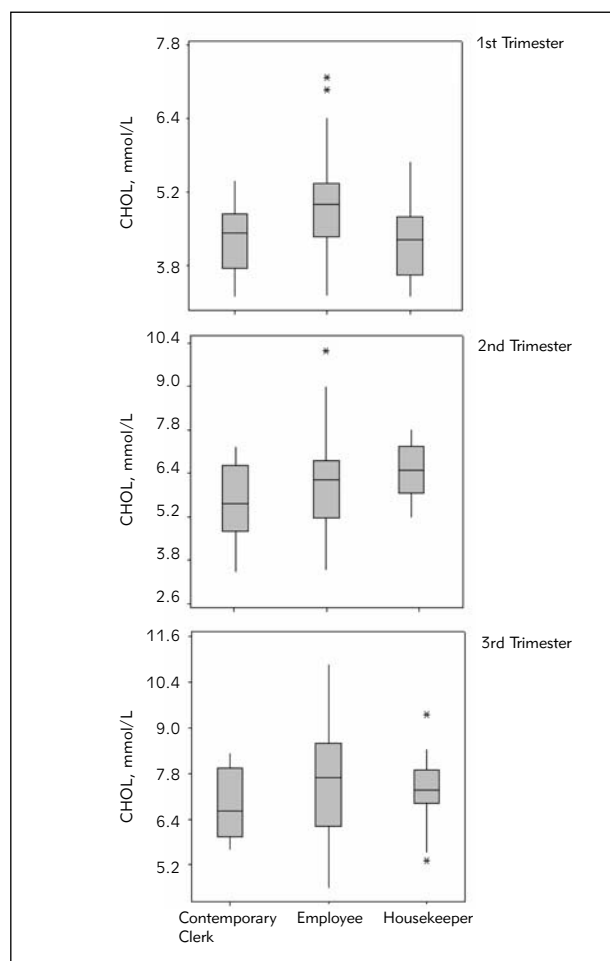


Figure 9 Box-plots of total cholesterol versus the three professions with the larger frequency. All subjects are Greeks.

The first approach in this study was the estimation of the descriptive statistics of the lipid indexes. Their descriptive statistics, especially box-plot graphs, gave an idea about the relations between large groups of pregnant women.

For instance, the influence of the nationality on the lipid indexes is displayed in *Figure 8*. As shown, there was no important difference between the larger national groups of our sample (Greek, Albanian, Bulgarian, Rumanian, British). Because of the graphs in *Figure 7* that include all the pregnancy trimesters, we analyzed our data further with another block of box plot graphs (*Figure 9*). In these three box-plots, the total cholesterol values of the three trimesters have been pictured. As shown, there was no important difference between the three professions. However, the median value of the employees was larger than the median of the contemporary clerks.

To find out exactly the parameters which influence the values of Chol, Trig, HDL-C and LDL-C we tried to estimate the statistical models which involve them with some predisposing factors. The following statistical models were investigated by three different

regression methods (stepwise method, backward elimination, forward elimination method). The final model includes the most common predisposing factors of the three.

Total cholesterol. The common predisposing factors in the three regression methods were chronic age and gestational age, so they must be considered as the most reliable predisposing factors for the explanation of cholesterol values. The regression model between cholesterol and age/gestational age was: $\text{cholesterol} = 5 \text{ age} + 4.4 \text{ gestational age}$. This model shows that cholesterol values are influenced by age and gestational age in the same percentage. However, the coefficient of determination (r^2) of the model was too low (only 13.7%). As a result the model was not considered reliable.

Triglycerides. The three regression models we used proved that only two predisposing factors were common to all of them, chronic age and gestational age. The best model which explained triglyceride values was: $\text{Trig} = 1.59 \text{ age} + 5.9 \text{ gestational age}$. The coefficients of this model (1.59 and 5.9) showed that triglycerides are more influenced by gestational age. The r^2 of the model was only 55.6%, which means that only 55% of the triglyceride values can be explained by chronic age and age of pregnancy.

High density lipoprotein. From the three regression methods we used, only one predisposing factor appeared in all three models, gestational age. The most suitable statistical model was: $\text{HDL-C} = 56.9 + 0.53 \text{ gestational age}$. The r^2 was too low (only 13.7%). As a result, the model was not considered reliable.

Low density lipoprotein. Regression analysis showed that LDL-C like HDL-C depended only on one of the studied predisposing factors, the gestational age. The most suitable statistical model was: $\text{LDL-C} = 87.9 + 2.40 \text{ gestational age}$. The model is not reliable since the r^2 was just 38.1%.

Reference values per trimester

We tried to find out the reference values for Chol, Trig, HDL-C and LDL-C separately for each trimester. Firstly, the distribution of values was checked by using the statistical test Kolmogorov-Smirnov. It proved that all lipid index values differed a lot from the normal distribution. For that reason the calculation of reference values was based on non-parametric methods (percentiles 2.5 and 97.5). The results are synopsised in the *Table VIII*. In order to calculate them all subjects that had a pathological predisposing factor were excluded.

Generally, our results confirmed previous references. Lipid indexes were increasing during pregnancy, although in the first trimester there was no important difference between pregnant and non-pregnant women for the majority of indexes. Triglycerides

proved to have the largest increase. Triglycerides were the only lipid index that showed a statistically important difference between the women in the first trimester and the non-pregnant women. On the other hand, HDL-C had a profile different from the others. It increased during the first and second trimester but remained steady during the third trimester. It must be underlined that the relation between the lipid index values and the week of pregnancy was too weak, although they had an apparently positive correlation. The positive correlations had very small coefficient determinations (under 50%).

Regression analysis showed that the predisposing factors studied (age, gestational age, nationality, body mass index, profession, smoking and diabetes during pregnancy) had no important influence on the lipid index values. Except gestational age, only

total cholesterol and triglycerides were influenced also by the chronic age. However, all these relations were not strong (under 50% except triglycerides). As a result all the models we manufactured were not reliable. Additionally, nationality and profession had no important influence on the lipid index values. Considering the foreign nationalities in the sample, it may be assumed that their long stay in Greece (for many years) conducted them to adopt the way of life of the locals.

The last scope of our study was to calculate the reference values for each trimester separately. Although all subjects with pathological predisposing factors were excluded from the calculations, the results must be considered absolutely reliable only after prior execution of further studies with larger samples from different populations of women.

References

- Merabishvili V, Kambladze O, Sulaberidze T. Peculiarities of lipid metabolism during pregnancy. *Georgian Med News* 2006; 138: 86–9.
- Lippi G, Albiero A, Montagnana M, Salvagno GL, Scavarolli S, Franchi M, Guidi GC. Lipid and lipoprotein profile in physiological pregnancy. *Clin Lab* 2007; 53 (3–4): 173–7.
- Loke DF, Viegas OA, Kek LP, Rauff M, Thai AC, Ratnam SS. Lipid profiles during and after pregnancy. *Gynecol Obstet Invest* 1991; 32 (3): 144–7.
- Chiang AN, Yang ML, Hung JH, Chou P, Shyn SK, Nq HT. Alterations of serum lipid levels and their biological relevancies during and after pregnancy. *Life Sci* 1995; 56 (26): 2367–75.
- Oureshi IA, Xi XR, Limbu YR, Bin HY, Chen MI. Hyperlipidaemia during pregnancy. *Ann Acad Med Singapore* 1999; 28 (2): 217–21.
- Martin U, Davies C, Hayavi S, Hartland A, Dunne F. Is normal pregnancy atherogenic? *Clin Sci (Lond)* 1999 April; 96 (4): 421–5.
- Sattar N, Greer IA, Loudon J, Lindsay G, McConnell M, Shepherd J, Packard CJ. Lipoprotein subfraction changes in normal pregnancy: threshold effect of plasma triglyceride on appearance of small, dense low density lipoprotein. *J Clin Endocrinol Metab* 1997; 82 (8): 2483–91.
- Brizzi P, Tonolo G, Esposito F, Puddu L, Dessole S, Malolo M, Milla S. Lipoprotein metabolism during normal pregnancy. *Am J Obstet Gynecol* 1999; 181 (2): 430–4.
- Hillman L, Schonfeld G, Miller JP, Wulff G. Apolipoproteins in human pregnancy. *Metabolism* 1975; 24 (8): 943–52.
- Sattar N, Greer IA, Galloway PJ, Packard CJ, Shepherd J, Mathers A. Lipid and lipoprotein concentrations in pregnancies complicated by intrauterine growth restriction. *J Clin Endocrinol Metab* 1999; 84 (1): 128–30.
- Toescu V, Nutall SL, Martin U, Kentall MJ, Dunne F. Oxidative stress and normal pregnancy. *Clin Endocrinol (Oxf)* 2002; 57(5): 609–13.
- Mazurkiewicz JC, Watts GF, Warburton FG, Slavin BM, Lowy C, Koukkou E. Serum lipids, lipoproteins and apolipoproteins during pregnancy. *Clin Pathol* 1994; 47 (8): 728–31.
- Belo L, Caslake M, Gaffney D, Santow-Silva A, Pereira-Leite L, Quintanilla A, Rebelo I. Changes in LDL size and HDL concentration in normal and preeclamptic pregnancies. *Atherosclerosis* 2002; 162 (2): 425–32.
- Bodnar M, Ness B, Hanger F, Roberts M. Inflammation and triglycerides partially mediate the effect of pre-pregnancy body mass index on the risk of preeclampsia. *Am J Epidemiol* 2005; 162 (12): 1198–206.
- Van Stiphout W, Hofman A, Buijn A. Serum lipids in young women before, during and after pregnancy. *American Journal of Epidemiology* 1987; 126 (5): 922–8.
- Udoh AE, Ndem ED, Itam EH, Odigwe CO, Archibong E. Serum cholesterol profile of some Nigerian pregnant women. *Acta Med Hung* 1994; 50 (1–2): 75–81.
- Ojule AC, Akani CI, Oporum HC. Plasma lipids during pregnancy in Nigerian women. *Niger J Med* 2005; 14 (2): 155–60.
- Tietz W. *Clinical Guide to Laboratory Tests*. W.B. Saunders Company, Philadelphia, 1990, 2nd edition.
- Tietz W. *Textbook of Clinical Chemistry*. W.B. Saunders Company, Philadelphia, 1986.

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