Comparison of lipid profiles in normal and hypertensive pregnant women

I. Cüneyt Evrûke, MD; S. Cansun Demir, MD; Ibrahim F. Ürünsak, MD; F. Tuncay Özgünen, MD; Oktay Kadayıfçı, MD

Hypertension during pregnancy is a major health problem. It is one of the leading causes of perinatal morbidity and mortality.¹ Preeclampsia (PE) is a theoretical disease with a pathogenesis that is not clearly understood yet. Lately vascular system pathology and vasoconstriction have been blamed as causes for preeclampsia with growing acceptance. Lipid values in normal pregnancies change with gestational age. In a normotensive pregnancy, serum triglyceride, total and HDL-cholesterol increase during pregnancy, but lipoprotein A levels decrease. These changes are reported to be secondary to hormonal changes during pregnancy.¹⁻³ In this study we aimed to demonstrate the lipid profile of normotensive and hypertensive cases.

Patients and Methods

One hundred fifty-nine pregnant women were included in this study, which lasted from August 2000 to August 2001. The study group included 84 patients who were hypertensive and 75 healthy normotensive (NT) pregnant women in the control group who were randomly selected from patients attending our clinic. Age, parity, number of fetuses, and gestational age of the patients were recorded. Blood pressure and weight was obtained at every follow-up. Hypertension defined as a blood pressure 140/90 mm Hg. Hypertensive patients were divided into subgroups as follows:

1. Gestational hypertension (GHT): Blood pressure 140/90 mm Hg after the 20th week of gestation (n=17).
2. Chronic hypertension (CHT): Hypertension diagnosed before pregnancy (n=16).
3. Preeclampsia (PE): Co-incidence of edema and proteinuria with high blood pressure after 20 weeks of gestation (n=19).
4. Superimposed preeclampsia (SPE): A history of chronic hypertension superimposed with edema and proteinuria (n=15).
5. Eclampsia (E): High blood pressure, findings of preeclampsia plus convulsion or coma (n=17 patients).

Blood was obtained after 8 to 10 hours of fasting at 8:00 am. The blood was sent to Çukurova University Faculty of Medicine Central Laboratory for analysis. The normal range of the tests according to the laboratory are shown in Table 1. Exclusion criteria included a history of familial

From the Department of Obstetrics and Gynecology, Faculty of Medicine, Cukurova University, Adana, Turkey

Correspondence to:

Dr. I. Cüneyt Evrûke

Department of Obstetrics and Gynecology

Faculty of Medicine

Cukurova University

Adana, Turkey

E-mail: evrûke@mail.cu.edu.tr

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hyperlipidemia, and use of statins as anti-hyperlipidemic agents. Statistical analysis was performed with the Chi-square, student *t* test and one-way ANOVA tests.

Results

The mean age was 28.6 ± 4.5 in the control group and 28.5 ± 4.1 in the study group (Table 2). There was no statistically significant difference between the two groups ($P=0.89$). The percentage of hypertensive patients was 32.1% in the second trimester and 64.3% in the third trimester. In the control group, the lipid levels between trimesters were compared with one-way ANOVA. Changes in trimester corresponded with a statistically significant increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL) and triglyceride (TG) levels, but there was not a statistically significant change between trimesters for high-density lipoprotein cholesterol (HDL),

Table 1. The tests used to evaluate lipids levels and the normal ranges used by our laboratory is as follows:

	Test used	Normal values
Total lipid	Turbidimetric method	350-750 mg/dL
Total cholesterol	Enzymatic method	125-250 mg/dL
LDL-Cholesterol	Frieswald formule	80-150 mg/dL
HDL-Cholesterol	Enzymatic method	35-65 mg/dL
Triglyceride	GPO-PAP method	35-165 mg/dL
Apolipoprotein A	Radioimmunoassay	73-169 mg/dL
Apolipoprotein B	Radioimmunoassay	58-138 mg/dL

Table 2. Sociodemographic features of the pregnant women.

		Normal		Hypertensive		P
		N	%	N	%	
Age	20-24	16	21.3	16	19.0	0.924
	25-29	25	33.3	29	34.5	
	30-34	26	34.7	32	38.1	
	35 and above	8	10.7	7	8.3	
Trimester	First	23	30.7	3	3.6	0.00001*
	Second	26	34.7	27	32.1	
	Third	26	34.7	54		
Parity	Primigravida	27	36	16	19	0.026*
	Multigravida	48	64	68	81	

* $P < 0.05$ statistically significant **Figure 1.** Comparison of lipid profiles in the control group according to trimesters (*statistically significant changes by one-way ANOVA).

apolipoprotein A (ApoA) and apolipoprotein B (ApoB) levels (Figure 1). Total cholesterol was lower in the first trimester, but increased with pregnancy and plateaued at the end of the pregnancy. LDL was different between the first and third trimesters but between the first and second and second and third trimesters there was no statistically significant difference. Triglyceride was lower in the first trimester in comparison to the second and third trimesters, but between the second and third trimesters the difference was not statistically significant.

In the hypertensive group, total cholesterol, LDL-cholesterol, triglycerides, and total lipids (TL) were significantly different from the normotensive group but HDL-cholesterol and apolipoprotein A and B were not different between the normotensive and the hypertensive groups (Table 3).

In gestational hypertensive patients only total lipid was different than the control group. ($P=0.0003$) (Figure 2). In

the chronic hypertensive group, LDL and total lipid levels were significantly different than the normotensive group. In the preeclampsia group, total cholesterol, LDL-cholesterol, total lipid and triglyceride levels were statistically different from the control group. In the superimposed preeclampsia group, total cholesterol, LDL-cholesterol, total lipid and triglycerides were significantly different from the normotensive group. In the eclampsia group, total cholesterol, HDL-cholesterol, triglycerides and total lipid and LDL-cholesterol levels were significantly different from the control group.

Discussion

In pregnancy, all lipid fractions increase in parallel to the increase in pregnancy age. This increase is reported to be secondary to the increase in estrogen and progesterone levels during pregnancy.^{1,2,4,5} This increase in lipids is higher in hypertensive pregnant women compared to the normo-

Table 3. Comparison of lipid levels (mg/dL) on normal and hypertensive pregnant women.

	Normal	Hypertensive	
	Mean $\pm$ SD	Mean $\pm$ SD	P Value
Total Cholesterol	209.4 $\pm$ 43.1	237.7 $\pm$ 58.4	0.001*
HDL-Cholesterol	54.8 $\pm$ 13.4	50.2 $\pm$ 15.3	0.5
LDL-Cholesterol	115.4 $\pm$ 33.5	137.1 $\pm$ 42.0	0.0001*
Triglyceride	187.9 $\pm$ 75.5	251.9 $\pm$ 108.7	0.0001*
Total Lipid	831.7 $\pm$ 358.4	1544.4 $\pm$ 773.1	0.0001*
Apolipoprotein A	20.4 $\pm$ 29.6	21.2 $\pm$ 25.1	0.8
Apolipoprotein B	117.7 $\pm$ 81.1	126.5 $\pm$ 76.6	0.4

*P < 0.05 means statistically significant

Figure 2. Comparison of hypertensive study groups with the control group (NT) (*statistically significant difference from control group)

tensive pregnant women, but there is no correlation between lipid levels and the prognosis of disease.

In our study, 64 % of the hypertensive group was in the third trimester, whereas in the control group similar numbers of women were in each trimester. Also, most of the hypertensive patients were multigravida, which could be explained by the higher age of our patients. Triglycerides, total lipid and total cholesterol levels gradually increased from the first to third trimester. Other lipid fractions—HDL, apolipoprotein A and B increased parallel to the gestational age but there was no statistically significant difference between trimesters. Human placental lactogen (HPL) is an important protein for fetus growth which is secreted from the placenta. HPL increases plasma free fatty acids via increasing lipolysis, and increases glucose uptake and inhibits gluconeogenesis. It also has an insulinogenic effect that is related to fetal protein synthesis.

Estradiol, progesterone and HPL are related to plasma lipids levels. Apolipoprotein A1, apolipoprotein A2, apolipoprotein B, LDL and HDL levels (partially) correlate with the level of these hormones through pregnancy. Plasma free fatty acids, triglycerides and phospholipids increase considerably with HPL increase. In our study, LDL, total lipid and cholesterol levels were parallel to each other, which was in agreement with pertinent literature.^{1,6-8} In another study, total cholesterol and HDL were increased.⁹ In our study, total cholesterol was found to be increased during pregnancy but the increase in HDL was not significantly different through pregnancy. Rosing et al reported that especially after the second trimester, levels of ApoA, ApoB, HDL, total cholesterol, and triglycerides were significantly increased.¹⁰ In our study, results were similar for total lipid, triglycerides and LDL, but were different for ApoA, ApoB and HDL levels from Rosing et al's study as the increase was not significant in

those parameters in our study. Potter et al also reported similar results,⁵ but in their study, HDL levels increased during pregnancy, which was different than our study. In a study in chronic hypertensive pregnant, the levels of HDL, LDL and total lipid were lower compared to the normotensive group, but total cholesterol and triglyceride levels were not different in the two groups.¹¹

Endothelial dysfunction is the most important event in the pathogenesis of preeclampsia, and lipids have a role on this event. Free fatty acid flow, triglycerides, LDL, HDL, total lipid, cholesterol and VLDL values are increased during preeclampsia. Beta oxidation is disturbed in the liver and VLDL, LDL and triglycerides are stored in liver. Lipid peroxidase and cytokines increase secondary to an increase at the levels of plasma lipids. Endothelial cells are disturbed directly or indirectly and vasoconstriction occurs all throughout the body.^{8,12}

In the preeclamptic pregnant total cholesterol, LDL, triglycerids, total lipid levels are different from the normal group. Gratacos et al. showed that in all hypertensive and preeclamptic patients, triglycerides, LDL, HDL, total lipid, apoA and apo B were significantly higher especially between 20 to 34 weeks of pregnancy. In our study the results were similar for triglycerides, LDL, and total lipid levels. There was a slight increase of HDL and ApoB levels which were not statistically significant.¹³

In our study, in the superimposed preeclampsia group all lipid fractions were increased except for apoA, apoB and HDL levels. The most significant increases were LDL and total lipid values. This was in accordance with the literature.^{1,2,5} Hubel et al showed in their study that triglyceride and free fatty acids increased two-fold in preeclamptic patients and HDL, LDL and total cholesterol levels were not different from the normotensive pregnant women,

whereas in our study LDL and total cholesterol levels were significantly higher in the preeclamptic patients.¹⁴

Garzetti et al found that lipid fractions increased in preeclamptic patients and plasma lipid peroxidase and free radicals were activated. Also platelet and erythrocyte membrane antioxidant systems were inactivated and this had an important role in etiopathogenesis.¹⁵ In normal pregnancies lipolysis increases but in preeclamptic patients this increase is significantly higher. The changes of lipid metabolism and free fatty acids are not etiological factors but have important role in the pathogenesis.¹⁶

In the eclamptic patients, the levels of total cholesterol, HDL, triglyceride and total lipid levels were higher compared to the patients in the control group, which is in accordance with the pertinent literature. LDL and apoB were higher but the increase was not statistically significant and apoA was lower in the eclamptic group, which is in contradiction with the literature.^{1,10,17}

We conclude that all lipid fractions increase during pregnancy in both normotensive and hypertensive patients. Hyperlipidemia is significant during the second trimester in the normotensive group. The most significant increase is in levels of triglyceride, LDL and total cholesterol. In hypertensive pregnant women, hyperlipidemia is more profound than in the normotensive group. Lipid levels increase parallel to the severity of the disease being improved in normotensive group compared with the gestational hypertensive, chronic hypertensive, preeclamptic, superimposed preeclamptic and worst in the eclamptic group. This is also parallel with the prognosis of the disease. As a result we conclude that lipids have an important role in the etiopathogenesis of preeclampsia, and must not be underestimated during the hypertensive diseases of pregnancy.

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