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To Evaluate the Role of Lipid Profile in the Etiopathogenesis of Mild and Severe Preeclampsia

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Abstract

Objective: To evaluate the role of lipid profile in the etiopathogenesis of mild and severe preeclampsia.

Methods: Fifty-nine preeclamptic pregnant and 66 normotensive pregnants who applied to our clinic between January 2005 – December 2006 were included into the study. Preeclampsia patients were divided into two groups as mild preeclampsia (Group:1, n: 27) and severe preeclampsia (Group: 2, n: 32). Sixty-six normotensive pregnants composed the control group (Grup: 3). In cases, triglyceride, cholesterol, high-density lipoprotein, cholesterol, low-density lipoprotein and very low-density lipoprotein levels were measured. Correlation between lipid profile and markers of preeclampsia was investigated.

Results: Median triglyceride and VLDL levels of group 1 and 2 were higher than group 3, but only difference between group 2 and group 3 was statistically sigificant ($p<0.05$). Median cholesterol in group 2 was significantly higher than in group 1 and 3 ($p<0.05$). LDL and HDL levels were determined similar in all groups ($p>0.05$) ($p>0.05$). There was a significantly positive correlation between the amount of proteinuria and cholesterol, LDL, TG and VLDL levels (respectively, r: + 0.216 ($p<0.05$), + 0.194 ($p<0.05$), + 0.194 ($p<0.05$), + 0.208 ($p<0.05$). A significant negative correlation between proteinuria and HDL levels was determined (r:-0,202), $p<0.05$). There were significant positive correlations between systolic tension and cholesterol, TG, VLDL levels (respectively, r: +0.235 ($p<0.01$), + 0.311 ($p<0.01$), + 0.311 ($p<0.01$); and between diastolic tension and with LDL, TG, VLDL levels (respectively, r: +0.242 ($p<0.05$), + 0.280 ($p<0.05$), + 0.280 ($p<0.05$).

Conclusion: The changes in lipid profile was related with preeclampsia and especially severe preeclampsia.

Keywords: Preeclampsia, hypertension, pregnancy, lipid, dyslipidemia.

Hafif ve ağır preeklampsi olgularında maternal serum lipid profilinin değerlendirilmesi

Amaç: Lipid profilinin hafif ve ağır preeklampsi etiyopatogenezindeki rolünü araştırmak.

Yöntem: Ocak 2005 – Aralık 2006 tarihleri arasında, kliniğimize müracaat eden 59 preeklamptik gebe çalışmaya alındı. Preeklamptik olgular; hafif (Grup 1, n:27) ve ağır (Grup 2, n:32) olmak üzere 2 gruba ayrıldı. Kontrol grubu için de 66 sağlıklı gebe (Grup 3) alındı. Tüm olgularda trigliserid (TG), kolesterol, yüksek dansiteli lipoprotein (HDL), düşük dansiteli lipoprotein (LDL) ve çok düşük dansiteli lipoprotein (VLDL) düzeyleri ölçüldü. Lipid profili ile preeklampsi belirteçleri arasında korelasyonlar araştırıldı.

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Bulgular: Kolesterol düzeyi grup 2' de diğer iki gruptan anlamlı olarak yüksek idi ($p<0.05$). TG ve VLDL düzeyleri grup 1 ve 2' de grup 3' e göre yüksekti, fakat sadece grup 2 ile arasındaki fark anlamlıydı ($p<0.05$). LDL and HDL düzeyleri tüm gruplarda benzer bulundu ($p>0.05$; $p>0.05$). Proteinüri miktarı ile kolesterol, LDL, TG ve VLDL seviyesi arasında pozitif yönde bir korelasyon tespit edildi (sırasıyla, r: + 0.216 ($p<0.05$), +0.194 ($p<0.05$), +0.194 ($p<0.05$), + 0.208 ($p<0.05$). Proteinüri ile HDL arasında ise negatif yönde bir korelasyon tespit edildi (r: -0,202; $p<0.05$). Sistolik kan basıncı ile kolesterol, TG, VLDL arasında (sırasıyla, r: +0.235 ($p<0.01$), + 0.311($p<0.01$), +0.311 ($p<0.01$) ve diastolik kan basıncı ile LDL, TG ve VLDL arasında pozitif yönde korelasyonlar bulundu (sırasıyla, r: +0.242 ($p<0.01$), +0.280 ($p<0.01$), +0.280 ($p<0.01$).

Sonuç: Lipid profilindeki değişikler preeklampsi ve özellikle ağır preeklampsi ile ilişkili bulundu.

Anahtar Sözcükler: Preeklampsi, hipertansiyon, gebelik, lipid, dislipidemi.

Introduction

The relationship between essential hypertension and serum lipid profile was found in many trials.[1-3] Anormal lipid profile is strongly related with atherosclerotic cardiovascular diseases and causes endothelial dysfunction directly. The most important feature of pregnancy induced hypertension is hypertension via vasospasm in kidneys, uterus, placenta, and brain.[4] Primary source of prostacyclin and tromboxane are endothelial cells and thrombocytes, respectively. In normal pregnant woman endothelial prostacycline reaches 8-10 times more than a non pregnant woman. But in preeclamptic women this rising is only 1-2 times more. Besides in preeclamptic women thromboxane rises more than normal pregnant women.[5] Because prostocyclin is a vasodilator and thromboxane is vasoconstrictor, endothelial cell destruction causes rising in the thromboxane / prostacyclin rate which makes vasospasm.[6] Increasing lipid synthesis causes rising in the thromboxane / prostacyclin rate and takes a role in the pathogenesis of pregnancy induced hypertension.[7] That's why abnormal lipid profile may be an important marker for pregnancy toxemia. In this study, we aimed to evaluate the role of the alterations of lipid profile in the etiopathogenesis of mild and severe preeclampsia.

Methods

Fifty-nine preeclampsia patients, with no history of chronic HT, thyroid disease, renal disease, dislipidemi or diabetes mellitus (DM), and 66 healthy pregnant women who applied to Kahramanmaraş Sütçü Imam University Medical Faculty Obstetrics and Gynecology Clinic between January 2005 – December 2006 were included into the study. Research ethics approval from KSU Medical Faculty Ethics Committee was obtained before the initiation of the study.Preeclampsia patients were divided into two groups as mild preeclampsia (Group:1, n: 27) and severe preeclampsia (Group: 2, n: 32) according to the bulletin of American College of Obstetricians and Gynecologists (ACOG) named as 'Preeclampsia and Eclampsia Diagnose and Management'.[8] Sixty-six healthy pregnant women composed the control group (Grup: 3). From all cases after 12 hour fasting 8-10 ml blood samples were taken from antecubital vein.. The blood samples were centrifuged for 4 minutes at 4.000 rpm (Eppendorf santrifuge 5810) after waiting 30 minutes in room temperature to seperate the serum for study. In these serums, triglyceride (TG), cholesterol, HDL (High density lipoprotein), LDL (Low density lipoprotein) and VLDL (Very low density lipoprotein) levels were measured with kinetic method using ready kit at Dade Behring RXL (USA) machine. Results of 3 groups were evaluated. Correlations between

lipid profile and preeclampsia markers were investigated one by one . For statistical analysis SPSS 11.0 package program was used. Variables evaluated with One Way Anova test. Pearson correlation analysis was applied between laboratory parameters of preeclampsia.

Results

Demographic data as age, gravida, and parity was similar in all groups (p>0.05). Body mass index (BMI) was higher in group 2 than other groups. The difference from group 1 was not significant (p>0.05), but the difference from group 3 was significant (p<0.05). We thought that could be a relation between severe preeclampsia and obesity (Table 1). PT and PTT were similar in all groups (p>0.05) (Table 2). Cholesterol level in group 2 was significantly higher than other 2 groups (p<0.05)(Table 2). Triglyceride and VLDL levels in group 1 and 2

Table 1. Dissociation of demographic characteristics in groups (Median ± Standard erro)r.

	Mild preeclampsia (Group: 1) (n: 27)	Severe preeclampsia (Group: 2) (n:32)	Control (Group: 3) (n: 66)	P value
Age	29.7 ± 1.5	29.2 ± 1.2	28.8 ± 0.5	*, **, ***: p>0.05
BMI	23.3 ± 3.0	23.2 ± 3.2	23.3 ± 2.7	*, **, ***: p>0.05
Gravida	3.9 ± 0.6	3.8 ± 0.5	2.8 ± 0.2	*, ***: p>0.05 **: p<0.05
Parity	3.1 ± 0.5	3.3 ± 05	2.3 ± 0.2,	*, **, ***: p>0.05

*: Comparison between Group 1 and Group 2
**: Comparison between Group 2 and Group 3
***: Comparison between Group 1 and Group 3

Table 2. Dissociation of preeclampsia indicators and lipid profile among groups.

	Mild preeclampsia (Group: 1) (n: 27)	Severe preeclampsia (Group: 2) (n:32)	Control (Group: 3) (n: 66)	P value
Systolic TA(mmHg)	154.9 ± 2.5	182.6 ± 4.5	110.9 ± 1.5	
Diastolic TA(mmHg)	100.9 ± 1.5	108.8 ± 2.4	67.9 ± 1.1	
Amount of proteinuria at urine sample (mg/dL)	116.1 ± 15.9	211.7 ± 14.6	2.3 ± 10.2	
Platelet (K/uL)	265.5 ± 18.1	178.6 ± 16.4	240.1 ± 7.9	
AST(U/L)	32.4 ± 2.5	133.6 ± 22.8	20.5 ± 0.7	
ALT(U/L)	34.0 ± 2.1	96.1 ± 15.0	29.6 ± 0.9	
LDH(U/L)	243.1 ±12.6	526.8 ± 56.2	170.2 ± 5.3	
PT (second)	12.3 ± 0.2	12.6 ± 0.2	12.3 ± 0.2	*,**,***:(p > 0.05)
PTT (second)	28.2 ± 0.8	27.9 ± 0.7	29.5 ± 0.4	*,**,***:(p > 0.05)
Cholesterol (mg/dL)	234.9 ± 9.7	270.3 ± 15.1	240.8 ± 4.5	*,**:(p< 0.05); ***:(p> 0.05)
Triglyseride (mg/dL)	292.9 ± 23.0	306.1 ±22.8	266.8 ± 6.4	**:(p< 0.05); *,***:(p> 0.05)
VLDL (mg/dL)	58.9 ± 4.6	61.2 ± 4.6	53.4 ± 1.3	**:(p< 0.05); *,***:(p> 0.05)
LDL (mg/dL)	119.9 ± 6.4	137.4 ± 9.1	123.0 ± 3.7	*,**,***:(p> 0.05).
HDL (mg/dL)	59.4 ± 3.3	60.5 ± 3.5	68.8 ± 2.3	*,**,***:(p> 0.05).

*: Comparison between Group 1 and Group 2
**: Comparison between Group 2 and Group 3
***: Comparison between Group 1 and Group 3

were increased due to group 3. Only the difference between group 2 and 3 was significant (p<0.05). Group 2 LDL level was higher than other groups, but difference was not significant (p>0.05). HDL level was highest in group 3 but the differences were not significant (p>0.05) (Table 2). Gestational week at labour in group 1 and 2 was very low than group 3 (p<0.01) (Table 3). Cesarean section (C/S) ratio in group 1 and 2 (56%, 62%) was higher than group 3 (p<0.05) (Table 3). Birth weight, 1-minute and 5-minute Apgar scores in group 1 and 2 were very low than group 3 (p<0.01) (Table 3). Pearson correlation analysis was made between some parameters evaluated in our study (Table 4). Positive correlation was determined between amount of proteinuria and cholesterol, TG, VLDL, and LDL (respectively, r: + 0.216, + 0.194, + 0.194, + 0.208; p<0.05). On the other hand there was an inverse correlation between amount of proteinuria and HDL (r: - 0,202; p<0.05). Systolic tension correlated with cholesterol,TG, VLDL (respectively, r: +0.235, +0.311, +0.311; p<0.01) and diastolic tension correlated

Table 3. Dissociation of neonatal results among groups.

	Mild preeclampsia (Group: 1) (n: 27)	Severe preeclampsia (Group: 2) (n:32)	Control (Group: 3) (n: 66)	P value
Birth week	34.9 ± 0.9	35.4 ± 0.7	38.4 ± 0.3	*,**,***:(p< 0.001).
Vaginal delivery	12 (% 44)	12 (% 37.5)	48 (% 73)	
C/S	15 (% 56)	20 (% 62.5)	18 (% 27)	*,**:(p< 0.05); ***:(p> 0.05)
Birth Weight (g)	2403.7 ± 167.2	2381.6 ± 179.1	3399.3 ± 77.9	*,**: (p< 0.01); ***:(p> 0.05)
1-minute Apgar score	5.4 ± 0.6	5.6 ± 0.5	8.0 ± 0.1	*,**: (p< 0.01); ***:(p> 0.05)
5-minute Apgar score	6.9 ± 0.7	7.1 ± 0.6	9.5 ± 0.1	*,**: (p< 0.01); ***:(p> 0.05)

*: Comparison between Group 1 and Group 2
**: Comparison between Group 2 and Group 3
***: Comparison between Group 1 and Group 3

Table 4. Correlation values between lipid profile and other parameters (r values).

	Cholesterol	TG	VLDL	LDL	HDL
Proteinuria	+ 0.216*	+ 0.194*	+ 0.194*	+ 0.208*	- 0.202*
Sys. Tension	+ 0.235**	+ 0.311**	+ 0.311**	+ 0.091	- 0.044
Dia. Tension	+ 0.076	+ 0.280**	+ 0.280**	+ 0.242**	- 0.123
Fetal Weight	- 0.105	- 0.087	- 0.023	- 0.012	+ 0.034
1-minute. Apgar score	- 0.115	- 0.137	- 0.023	- 0.112	+ 0.134
5-minute Apgar score	- 0.127	+ 0.107	+ 0.025	- 0.123	+ 0.131
AST	+ 0.076	+ 0.128	+ 0.028	+ 0.124	- 0.124
ALT	+ 0.126	+ 0.125	+ 0.078	+ 0.129	- 0.144
LDH	+ 0.137	+ 0.108	+ 0.092	+ 0.122	- 0.196*
Platelet	- 0.124	+ 0.127	+ 0.035	- 0.126	+ 0.101
PT	- 0.228*	- 0.127	- 0.023	+ 0.124	+ 0.103
aPTT	- 0.344**	- 0.285**	- 0.285**	- 0.111	+ 0.103

* p < 0.05
** p < 0.01

with LDL, TG, VLDL (r respectively +0.242, +0.280, +0.280; p < 0.01). Hypertension and proteinuria, the most important two diagnostic criteria for preeclampsia, were found to be effected significantly in relation with lipid profile. No relation was found between 1 and 5 minute Apgar scores and lipid profile. At correlation analysis between AST, ALT, LDH and lipid profile, no other relation except negative correlation between LDH and HDL (r: -0.196; p< 0.05) was found. No relation was present between thrombocyte number and lipid profile. Between systolic, diastolic tension and birth weight, 1 and 5 minute Apgar scores negative relation was determined (respectively, r: -0.466, -0.458, -0.409; p< 0.01; respectively, r: -0.476, -0.466, -0.418; p< 0.01). At the correlation between coagulation parameters and lipid profile, there was an inverse correlation between PT and cholesterol levels (r:-0.228; p< 0.05), and no other relation was determined with other lipid parameters. But there was an inverse relation between PTT and cholesterol, TG, VLDL (respectively, r: -0.344, -0.285, -0.288; p< 0.01).

Discussion

At recent times there is a great interest about the role of lipid metabolism on the development of preeclampsia. The previous studies reported that plasma lipid levels were higher in preeclamptic pregnant women than healthy pregnant women.[9,10] It is thought that this lipid changes has a role at endothelial cell damage which is a characteristic symptom of preeclampsia. Oxidized LDL inhibits endotelial prostocycline syntesis and inactivates endothelial derived relaxing factor (EDRF) and also stimulates synthesis and release of endothelin hormone which has vascular smooth muscle contracting effect.[2,3] This changes cause thrombocyte activation that results in thromboxane releasing. In previous studies it has been shown that maternal obesity is an independent risk factor at preeclampsia development.[11] Again in a recent study Bodnar et al asserted BMI as a strong and independent risk factor for preeclampsia development.[12] In our study BMI was the highest in group 2 and the difference with group 3 was significant (p<0.05). Like the studied mentioned above, our result also supports that obesity is a risk factor for preeclampsia (especially severe preeclampsia). In two studies performed previously serum TG levels were found significantly high in early pregnancy in preeclamptic patients.[13,14] Both Ware-Jauregui et al and both Rossing et al reported high TG and low HDL levels in preeclamptic patients compared to control groups in their study.[15,16] Again other studies have also showed that TG rich lipoproteins increased significantly in preeclamptic patients[17,18] James T et al reported that maternal BMI, TG and fatty acids increase significantly in preeclamptic patients.[19] Parallel to this study, we determined increased TG, cholesterol, LDL and VLDL levels in severe preeclampsia cases . Ray et al, in a meta analysis including 19 case-control and 3 prospective cohort study comparing preeclamptic patients to normotensive pregnants, determined TG level high in 14 study, similar in 7 study.[20] Mikhail et al determined TG level high in mild preeclampsia group, but similar in severe preeclampsia group compared to control group and defended that no direct relation exists between TG level and severity of preeclampsia.[21] While Baksu et al found total cholesterol and LDL levels similar in preeclampsia and control groups; they found TG and VLDL levels high and HDL levels low in preeclampsia group.[22] In our study cholesterol level was similar in group 1 and 3, but was high-

er in goup 2 from both groups($p< 0.05$). TG and VLDL levels were the lowest in group 3 and highest in group 2. The difference of group 2 from group 3 was significant ($p<0.05$), the difference from group 1 was not significant. While group 1 level was higher than group 3, the difference was not significant. Although LDL level was the highest in group 2, differences from other groups were not significant HDL level was the highest in group 3, the differences were not significant ($p> 0.05$). As in many studies,[23, 24] 1 and 5th minute Apgar scores were obviously low in preeclamptic patients in our study. Fall et al have shown that fetal growth is in relation with blood pressure, serum lipid, plasma glucose and insulin levels, which are the risk factors for cardiovascular diseases[25] Sattar et al reported that LDL level was decreased in blood samples of mothers who has IUGR fetuses and this can be the reason of IUGR.[26] In our study, birth weight was determined very low in mild and severe preeclampsia group due to control group($p<0.01$). But in correlation analysis we couldn't show any significant relationship between lipid profile and fetal weight. It was claimed that abnormal lipid profile can be in relation with impaired liver function.[27] But we couldn't determined any significant relation between liver function tests (AST, ALT and LDH) and lipid profile. It is thought that increased lipid synthesis is effective at pathogenesis of pregnancy induced hypertension with increasing Thromboxane A2: Prostoglandine I2 (TXA2/PGI2) ratio.[7] Because hypertriglyceridemia causes hypercoagulability in this way.[28] In our study there was a negative correlation between cholesterol level and PT ($p< 0.05$). No relation was determined between other lipid levels and PT. But there was a negative relation between cholesterol, TG, VLDL and PTT ($p< 0.01$).

Conclusion

The changes in lipid profile was related with preeclampsia and especially severe preeclampsia. In correlation analysis hypertension and proteinuria which are the most important two diagnostic criteria for preeclampsia, were found in relation with lipid profile. Previously, in studies performed at early pregnancy period, preeclampsia risk was higher in patients with dyslipidemia.[13,14] When our results interpreted with literature, it must be thought that dyslipidemia could be important cofactor in preeclampsia etiopathogenesis that couldn't been explained up to present.

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