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Serum oxidized low density lipoprotein levels in preeclamptic and normotensive pregnants

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Summary

Backgrounds/Aim: The aim of the study was to determine serum lipids and oxidized low density lipoprotein (ox-LDL) levels in preeclamptic pregnants and compare with those of normotensives. *Materials and Methods:* Ox-LDL levels were determined by enzyme linked immunosorbent assay (ELISA); total cholesterol, hight density lipoprotein (HDL)-cholesterol and triglyceride levels were measured by enzymatic colorimetric assay in 26 normotensive and 27 preeclamptic pregnants. LDL and very low density lipoprotein (VLDL) cholesterol was calculated by Friedwald formula. *Results:* Serum levels of Ox-LDL (U/L), total-cholesterol (mg/dL), HDL-cholesterol (mg/dL), LDL-cholesterol (mg/dL), triglyceride (mg/dL), and VLDL-cholesterol (mg/dL) in normotensive and preeclamptic pregnants were found as 130±60 and 133±69; 248±49 and 248±81; 67±14 and 61±16; 147±61 and 135±59; 207±76 and 256±87; 41±15 and 50±17, respectively. Mean values of Ox-LDL and other lipid parameters were higher than the upper limits of their reference ranges in both of groups. However no significant differences were found in Ox-LDL, total, HDL and LDL-cholesterol levels between two groups. However, the levels of triglyceride and VLDL-cholesterol were significantly higher in preeclampsia group. *Conclusions:* The present results suggest that the levels of serum Ox-LDL and other lipid parameters rise as a result of pregnancy rather than as a result of preeclampsia.

Key words: Low density lipoprotein; Preeclampsia; Pregnancy.

Introduction

Low density lipoprotein (LDL)-cholesterol elevation is closely related to endothelial damage and increased inflammatory response. After infiltrating the arterial endothelium LDL enters into intima, where it undergoes oxidative modification that leads to the accumulation of cholesterol and migration of macrophages [1, 2]. Macro-phages that phagocytose ox-LDL, are transformed into foam cells and contribute to the maintenance of this process. Oxidation of LDL lipids is associated with many clinical conditions [3-6]. In particular, the study of atherosclerosis has gained importance in recent years [7]. It was determined that inflammation in atherosclerosis plays an important role in tissue damage and oxidative stress, and in these patients increased LDL oxidation is associated with end products of lipid peroxidation [2, 7].

Preeclampsia is a hypertensive disorder leading to abnormalities like proteinuria, coagulation disorders, and various systemic symptoms [8-10]. Although preeclampsia is the most common complication of pregnancy that causes maternal and perinatal morbidity and mortality, very little information is available about its etiology [10]. Increased oxidative stress and endothelial disfunction have been suggested as the reason of poor placentation [11] and the presence of oxidative stress are shown in both of maternal circulation and placenta [12, 13]. Villar *et al.* [14] have reported high levels of oxidatively modified forms of proteins and lipoprotein particles in the serum of pregnant women with preeclampsia.

Ox-LDL plays a key role in the development of atherosclerotic cardiovascular disease [15]. Because of the similarities between the pathogenesis of atherosclerosis and preeclampsia, the interest of researchers has concentrated on this issue in recent years; however, conflicting results have been found [16-18].

The aim of this study was to measure and compare serum Ox-LDL, total cholesterol, LDL-cholesterol and high density lipoprotein (HDL)-cholesterol and triglyceride (TG) levels in preeclamptic and normotensive pregnant groups and to investigate their possible roles in the etiopathogenesis of preeclampsia.

Materials and Methods

Twenty-seven preeclamptic and 26 normotensive pregnant women in their third trimester, were included in the study. The aim of the study was explained to the pregnant women and those who accepted were enrolled into the study. Blood pressure measurements were taken on the left arm at the heart level in a seated position, after a ten-minute rest period. Those with blood pressures under 140/90 mmHg were considered normotensive, and

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Table 1. — *Comparison of Ox-LDL and lipid parameters.*

Parameter	Group	Mean ± standard deviation (SD)	*p* value
Ox-LDL (U/L)	Control	130.08 ± 60.04	0.878
	Preeclampsia	132.81 ± 68.81	
LDL-cholesterol (mg/dL)	Control	147.00 ± 61.25	0.501
	Preeclampsia	135.81 ± 59.03	
VLDL-cholesterol (mg/dL)	Control	41.42 ± 15.26	0.040
	Preeclampsia	50.81 ± 17.55	
HDL-cholesterol (mg/dL)	Control	67.46 ± 14.30	0.156
	Preeclampsia	61.41 ± 16.69	
Total cholesterol (mg/dL)	Control	248.19 ± 49.37	0.990
	Preeclampsia	248.04 ± 81.50	
TG (mg/dL)	Control	207.08 ± 76.90	0.033
	Preeclampsia	256.74 ± 87.86	

those with blood pressures equal to or higher than 140/90 were considered as hypertensive. Following criteria were used in the diagnosis of preeclampsia: two blood pressure values measured at least six hours being 140/90 or higher; > 75 mg/dL urine protein levels; > +1 edema after 24 hours bed rest. The blood samples were taken into ten-ml vacuum glass tubes from antecubital vein for Ox-LDL and lipid profiles. Samples were centrifuged at 4,000 rpms for 15 minutes and sera were stored at -80 °C for a maximum six months until the time of the study. Ox-LDL levels were determined by enzyme linked immunosorbent assay (ELISA) (solid phase bidirectional enzyme immunoassay). Total-cholesterol, HDL-cholesterol, and TG levels were measured by colorimetric method in an autoanalyzer. LDL-cholesterol levels were calculated using the Friedwald formula. VLDL cholesterol levels were calculated by dividing the TG values by 5. Statistical evaluation was performed by SPSS, and comparisons were made using Student's t test. A $p < 0.05$ was considered significant.

Results

The ages and gestational weeks of normotensive and preeclamptic women were 27.9±5.7 (minimum 19, maximum 39) and 28.7±5.5 years (minimum 18, maximum 40); 30.9±3.0 (minimum 26, maximum 36), and 32.3±2.7 weeks (minimum 27, maximum 36), respectively. Age and gestational week distributions did not differ significantly between the two groups. Diastolic and systolic blood pressures of normotensive and preeclamptic pregnant women were 71±5 mmHg and 96±8 mmHg; 110±8 mmHg and 147±8 mmHg, respectively. Statistically significant difference was observed between diastolic and systolic blood pressures of the two groups ($p < 0.01$). Ox-LDL levels of normotensive and preeclamptic women were 130±60 U/L and 133±69 U/L, respectively, and there was no significant difference between these values. LDL-cholesterol, HDL-cholesterol and total cholesterol levels measured in normotensive and preeclamptic pregnant women were 147±61 mg/dL and 136±59 mg/dL; 68±14 mg/dL and 61±16 mg/dL; 248±49 mg/dL and 248±82 mg/dL, respectively. There was no significant difference between two groups' total cholesterol, LDL-cholesterol, and HDL-cholesterol levels (Table 1). TG and VLDL-cholesterol levels of normotensive and preeclamptic women were 207±77 mg/dL and 257±88 mg/dL; 41±15 mg/dL and 51±18 mg/dL, respectively. TG and VLDL-cholesterol levels were significantly higher in the preeclamptic pregnant group ($p < 0.05$) (Table 1).

Discussion

Hyperlipidemia predisposes to the development of atherosclerotic disease by impairing endothelial function [19]. Physiological hyperlipidemia in pregnancy have been reported [20]. Sattar *et al.* reported that high levels of TG in normal pregnancy is accompanied by an increase in small dense LDL [21]. According to a study made by Belo *et al.* [22], TG, VLDL-cholesterol, and small dense LDL levels were high in normal pregnant women. In this study, 77% of normal pregnant women's total cholesterol, TG and VLDL-cholesterol, 53% of their Ox-LDL, 58% of their LDL-cholesterol, and 69% of their HDL-cholesterol levels were higher than upper reference values, and these findings are supportive of the results of Belo *et al.* [22].

In preeclampsia, contradictory results have been found regarding the levels of serum lipid parameters. Although there is a study which has reported that abnormal lipid profiles in preeclampsia play a role in the progression of vascular dysfunction and oxidative stress [23]. Kim *et al.* [16] reported low serum total and HDL-cholesterol levels in preeclamptic women when compared to normotensive ones. Uzun *et al.* [17] have found higher serum total cholesterol, LDL-cholesterol and VLDL-cholesterol, and TG levels in preeclamptic women than in normotensive pregnant women. According to Roberts *et al.* [24], impairment of oxidant-antioxidant balance against antioxidants causes a 'defense' dysfunction of vascular endothelial vasodilator and antiplatelet activity by increasing the lipid peroxidation and lipid peroxides show a higher degree of circulation in preeclamptic women than in normal pregnant women. Oxidative degradation products of modified polyunsaturated fatty acids, malondialdehyde (MDA), and 4-hidroxynonenal (4-HNE), are covalently bound to apoB lysine residue [25]. In the present study, total cholesterol levels in 74%, TG and VLDL-cholesterol levels in 85%, Ox-LDL levels in 48%, and LDL-cholesterol and HDL-cholesterol levels in 59% of preeclamptic women were higher than upper reference values, unlike some of the results of some researches [16, 17, 23-25], no significant difference was observed between the values of total, LDL- cholesterol and HDL-cholesterol in preeclamptic and normotensive pregnant women. However, compatible with the study of Uzun *et al.* [17], TG and VLDL-cholesterol levels were significantly higher in the preeclamptic group than in the normotensive group.

Different and conflicting results have been reported concerning Ox-LDL levels in preeclamptic women. While Raijmakers *et al.* [18] have reported that in preeclamptic women ox-LDL levels are lower than the Ox-LDL levels in the sim-

ilar gestational age control group and low ox-LDL levels could be an indicator of preeclampsia; in contrast, Kim *et al.* [16] reported that high serum ox-LDL levels in preeclamptic women is important in endothelial dysfunction, and Uzun *et al.* [17] emphasized that pre-eclampsia is associated with high ox-LDL, leading to vascular endothelial damage by contributing to the patho- genesis of preeclampsia. Pavan *et al.* [11] have reported that in-vivo human trophoblast invasion can be modulated by ox-LDL and this defective trophoblast invasion could shed light on the pathogenesis of preeclampsia. According to Hörkö *et al.* [26], antibodies against MDA-LDL are very important in pathogenity of ox-LDL. In a study conducted by Branch *et al.* [27], MDA-LDL auto-antibody titer remained quite high in preeclampsia compared to healthy pregnant women. Pecks *et al.* [15] found no difference between preeclamptic and normotensive pregnant womens' placental ox-LDL levels, whereas Açıkgöz *et al.* [28] reported that they found lower placental ox-LDL levels in preeclamptic women than in normotensive ones. In the present study, although the mean serum ox-LDL levels were found above the upper reference range, no significant difference was found between the two groups.

As a result, high VLDL-cholesterol and TG levels in preeclamptic women suggesting dyslipidemia associated with high TG, may contribute to the pathogenesis of preeclampsia despite the lack of significant difference between ox-LDL, total cholesterol, LDL-cholesterol, and HDL-cholesterol levels in normotensive and preeclamptic women, who have similar distribution of age and gestational week. Even though the ox-LDL levels were above the upper reference limit in preeclamptic and normotensive women, still there was no significant difference between the levels of these two groups. The present results show that these parameters are not suitable for use as diagnostic markers.

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