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A study of serum Apo A-1 and Apo B-100 levels in women with preeclampsia

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ABSTRACT

Objective: To investigate Apo A-1 and Apo B-100 levels and Apo B-100/Apo A-1 ratios in preeclamptic (PE) patients.

Materials and methods: Forty-eight PE and 48 without PE patients (healthy pregnancies) matched for gestational age were included. Maternal age, parity, gestational age at delivery, obstetrical complications including intrauterine growth restriction (IUGR) and gestational diabetes mellitus (GDM), serum Apo A-1 and Apo B-100 levels, and the Apo B-100/Apo A-1 ratio were compared.

Results: Preeclamptic patients had significantly lower Apo A-1 levels (167.07 mg/dl ± 14.61 mg/dl vs. 244.37 mg/dl ± 20.84 mg/dl, $p < 0.001$), higher Apo B-100/Apo A-1 ratio (0.63 ± 0.07 vs. 0.42 ± 0.05, $p < 0.001$), but similar Apo B-100 levels (104.84 mg/dl ± 7.05 mg/dl vs. 102.39 mg/dl ± 8.08 mg/dl, $p = 0.118$). Mean Apo A-1 and Apo B-100 levels and the Apo B-100/Apo A-1 ratio were similar in patients with severe PE, HELLP syndrome, IUGR, and patients requiring antihypertensive therapy compared to PE patients who did not have these complications ($p > 0.05$). Apo A-1 levels had the best accuracy followed by the Apo B-100/Apo A-1 ratio in patients with PE.

Conclusion: Apo A-1 and the Apo B-100/Apo A-1 ratio may be useful markers in patients with PE. Further studies are required to elucidate this issue.

1. Introduction

Preeclampsia (PE) is characterized by hypertension with signs of systemic endothelial activation that begins after the 20th week of gestation [1]. PE is a multi systemic disorder and affects 2–8% of pregnancies [2]. However, the underlying pathogenic mechanisms of PE remain uncertain. Early onset PE is associated with failure of spiral artery remodeling and consequent inadequate placentation and angiogenic imbalance [3]. Late onset PE is mostly related with increased maternal susceptibility to the inflammatory state of pregnancy [4].

Apolipoprotein (Apo) A-1, the major structural protein component of high-density lipoprotein (HDL) particles, has pleiotropic biological functions as well as anti-inflammatory properties. These functions include the inhibition of low-density lipoprotein (LDL) oxidation and scavenging toxic phospholipids [5,6]. Apo B represents the total amount of potentially atherogenic circulating lipoproteins, including LDL, intermediate density lipoprotein, very low-density lipoprotein, and lipoprotein (a) [7–9]. Two main isoforms of Apo B exist: Apo B100 and Apo B-48. Apo B-100 is synthesized in the liver and represents the circulating Apo B particles [10]. The Apo B-100/Apo A-1 ratio has been proposed as a reliable parameter that reflects lipid disturbances and the potential to develop atherosclerosis [7]. Moreover, it may predict cardiovascular risk better than any cholesterol index [9]. It has been previously shown that PE patients possess a future risk for cardiovascular disease. Moreover, both conditions share common risk factors as well as etiopathogenetic mechanisms such as endothelial dysfunction and metabolic abnormalities [11,12]. However, despite these similarities, only a few studies with somewhat conflicting results have investigated Apo B-100 and Apo A-1 levels in PE.

In the present study, we aimed to compare the levels of Apo A-1 and Apo B-100 and the Apo B100/Apo A-1 ratio in PE patients and healthy controls.

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2. Material and methods

The present study was a case-control study conducted at the maternal fetal medicine clinic of Dr. Zekai Tahir Burak Women's Health, Training and Research Hospital between June 2014 and June 2015. This study was approved by the Institutional Ethics Review Board (reference number: 2014/31) and written informed consent was obtained from all patients. Forty-eight patients who were admitted to the Perinatology Unit with a diagnosis of PE were included in the study. The control group consisted of forty-eight patients without PE (healthy pregnancies) who were matched for gestational age to deliver after each patient. The PE diagnosis was made when systolic blood pressure (BP) was ⩾ 140 mmHg or when diastolic BP was ⩾90 mmHg after 20 weeks of gestation with at least one of the following: proteinuria with urinary excretion of ⩾0.3 g protein in a 24-h urine specimen; thrombocytopenia (platelet count <100,000/μL); impaired liver function (increase in serum transaminases to twice the normal concentration); renal insufficiency (serum creatinine >1.1 mg/dL or doubling of serum creatinine in the absence of other renal diseases); pulmonary edema; and new-onset cerebral or visual disturbances (1). PE patients with systolic BP above 160 mmHg or diastolic BP above 110 mmHg, or having any of the above-mentioned criteria except for proteinuria, was considered severe PE (1).

Maternal serum was obtained from the antecubital vein on the day of admission to determine plasma Apo B-100 and Apo A-1 levels. Biochemical tests were carried out in the laboratories of Intergen, Ankara. Commercially available human ELISA kits for Apo A-1 (Cusabio Biotechnology Company, China) and Apo B-100 (Cusabio Biotechnology Company, China) were used on a single analyzer. The standard ELISA procedures were followed per the manufacturer's instructions. The sensitivity of the Apo A-1 and Apo B-100 assays was 1.95 and 19.5 mg/ml, respectively. Intraassay coefficients of variations were 8% for both Apo A-1 and Apo B-100, and the interassay coefficients of variations were 10% for both Apo A-1 and Apo B-100.

The following clinical and demographic data were obtained by reviewing the patients' medical records: maternal age, parity, gestational age at delivery, and the presence of obstetrical complications such as intrauterine growth restriction (IUGR) and gestational diabetes mellitus (GDM). Also included were the evaluated biochemical values including serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum creatinine, lactate dehydrogenase, fibrinogen, and complete blood counts. Serum laboratory tests were typically obtained at the time of presentation in both groups of patients and daily thereafter until delivery in PE patients. Neonatal data reviewed for analysis included: neonatal birth weight, Apgar scores for the first and fifth minutes, the Neonatal Intensive Care Unit (NICU) admission, and perinatal mortality.

The IUGR was defined as the estimated fetal weight below the 10th percentile associated with fetal Doppler abnormalities. Deliveries occurring prior to 37 weeks of gestation were recorded as preterm deliveries. GDM was defined as one abnormal result in a 75 g, or two abnormal results in a 100 g, oral glucose tolerance test that exceeded the threshold for diagnosis (13,14).

We used the SPSS 15 package program (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) for statistical analyses. The distributions of all continuous variables for normal or abnormal distributions were tested. The variables with normal distributions were compared between groups by independent samples *t*-tests. The MannWhitney *U* test was applied for non-normally distributed variables. For the categorical variables, the Pearson chisquare analysis and Fisher's exact tests were used. Receiver operating characteristic (ROC) analysis was used to evaluate the diagnostic performance of Apo B-100/Apo A-1for PE. A p value of <0.05 was considered statistically significant.

3. Results

Demographic and clinical characteristics of the groups are shown in Table 1. Age, parity, body mass index (BMI), and the rates of smoking and gestational diabetes were similar between the groups ($p > 0.05$). However, compared to the control group, PE patients had significantly higher systolic BP (median = 160, min = 140, and max = 199 mmHg vs. median = 110, min = 90, and max = 120 mmHg, for PE and controls, respectively, $p < 0.001$) and diastolic BP (median = 100, min = 88, and max = 139 mmHg vs. median = 70, min = 60, and max = 80 mmHg, for PE and controls, respectively, $p < 0.001$).

Laboratory characteristics from the PE patients and the control group are compared in Table 2. PE patients had significantly lower Apo A-1 levels (167.07 mg/dl ± 14.61 mg/dl vs. 244.37 mg/dl ± 20.84 mg/dl, for PE and controls, respectively, $p < 0.001$) but similar Apo B-100 levels (104.84 mg/dl ± 7.05 mg/dl vs. 102.39 mg/dl ± 8.08 mg/dl, for PE and controls, respectively, $p = 0.118$) in

Table 1
Clinical and demographic data of patients with preeclampsia and control group.

	Preeclampsia (n = 48) (%)	Control (n = 48) (%)	p
Maternal age (years)	28.70 ± 4.49	28.04 ± 5.19	0.503
<19	1 (2.1)	1 (2.1)	1.0
19–35	45 (93.8)	44 (93.8)	
>35	2 (4.2)	2 (4.2)	
Parity			
0	18 (37.5)	20 (41.7)	0.835
1–3	30 (62.5)	28 (58.3)	
Body Mass Index (kg/m^2)	28.44 (23.23–37.78)	27.81 (24.15–35.70)	0.076
20–25	2 (4.2)	3 (6.3)	0.853
25–30	24 (50)	25 (52.1)	
>30	22 (45.8)	20 (41.6)	
Smoking	7 (14.6)	5 (10.4)	0.759
Gestational diabetes	4 (8.4)	2 (4.2)	0.677
Systolic BP (mm Hg)	160 (140–199)	110 (90–120)	<0.001*
Diastolic BP (mm Hg)	100 (88–139)	70 (60–80)	<0.001*

Data are expressed as mean ± standard deviation, median (min-max), and number (%). BP: Blood Pressure.
* Statistically significant.

Table 2
Comparison of laboratory parameters in preeclamptic patients and control group.

	Preeclampsia (n: 48) (%)	Control (n:48) (%)	p
Apo A-1(mg/dl)	167.07 ± 14.61	244.37 ± 20.84	<0.001*
Apo B-100 (mg/dl)	104.84 ± 7.05	102.39 ± 8.08	0.118
Apo B-100 /ApoA-1	0.63 ± 0.07	0.42 ± 0.05	<0.001*
Serum creatinine (mg/dl)	0.84 ± 0.19	0.50 ± 0.12	<0.001*
Serum creatinine > 1.1 mg/dl	3 (6.3)	0	0.039*
ALT (IU/L)	53.16 ± 52.46	28.25 ± 3.20	0.002*
AST (IU/L)	53.18 ± 52.74	29.29 ± 3.42	0.003*
Elevated liver enzymes	7 (14.6)	0	0.012*
Serum LDH (IU/L)	379.73 ± 283.24	228.52 ± 63.74	0.001*
Serum Fibrinogen (mg/dl)	313.46 ± 65.64	291.73 ± 68.64	0.116
Platelet count (x10^3/mm^3)	194.52 ± 65.67	268.50 ± 35.33	<0.001*
LDL (mg/dl)	157.90 ± 32.99	131.74 ± 16.05	<0.001*
HDL (mg/dl)	46.74 ± 9.22	58.19 ± 8.09	<0.001*
Urinary dipstick protein			
Negative	1 (2.1)	48 (100)	<0.001*
+	9 (18.7)	0	<0.001*
++	23 (47.9)	0	<0.001*
+++	15 (31.3)	0	<0.001*

Data are expressed as mean ± standard deviation and number (%). Apo: Apolipoprotein; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; LDH: Lactate Dehydrogenase; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein.
* Statistically significant.