The Relationship of Paraoxonase 1 Activity With Lipid Metabolism In Obese Women

Obez Kadınlarda Paraoksonaz 1 Aktivitesinin Lipit Metabolizması ile İlişkisi

Fatih Özcan[1], Güler Bugdayci[2], Erdinç Serin[3], Mehmet Tosun[2]

[1] Department of Medical Biochemistry, Elbistan State Hospital, Kahramanmaraş, Turkey
[2] Department of Medical Biochemistry, School of Medicine, Abant İzzet Baysal University, Bolu, Turkey
[3] Department of Medical Biochemistry, İstanbul Education and Research Hospital, İstanbul, Turkey

ABSTRACT

Objective: The aim of this study was to identify the effects of serum lipids, apolipoprotein (apo) A-I, apo B and paraoxonase/arylesterase (PON1) activity on obesity in women.
Methods: The study was conducted on 90 subjects categorized into three groups; there were 30 women in each group with an age range of 18-48 years. Group 1 had 30 abdominal obese patients, group 2 had 30 gynoid obeses and group 3 included 30 healthy control subjects.
Results: There was a statistically significant difference between the triglyceride, high-density lipoprotein cholesterol (HDL-C), apo B, direct low-density lipoprotein cholesterol (D-LDL-C), high sensitive-CRP (hsCRP), homeostasis model insulin resistance (HOMA-IR) levels of group 1 and 2 (p=0.001, p<0.0001, p=0.016, p=0.001, p<0.0001, p<0.0001, respectively). For HDL-C, D-LDL-C, hsCRP and HOMA-IR levels, there were statistically significant differences between group 1 and 3 (p=0.023, p=0.023, p<0.0001, p=0.001, respectively). Triglyceride, apo B, HDL-C, D-LDL-C parameters differed significantly in abdominal obesity, whereas there was no difference among the groups for PON1 activity.
Conclusion: Our results indicate that lipid metabolism is altered in obesity, but PON1 activity appears not to be affected.

Key Words: Lipid metabolism, obesity, paraoxonase 1

Received: 02.06.2014 **Accepted:** 02.20.2014

ÖZET

Giriş: Bu çalışmanın amacı serum lipitleri, apolipoprotein (apo) A-I, apo B, paraoksonaz 1 (PON 1) aktivitesinin kadınlarda obeziteye etkilerini saptamaktır.
Yöntemler: Çalışmaya toplam 90 kadından oluşan, yaşları 18-48 yaş arası değişen, 30 abdominal obez (grup 1), 30 jinoid obez (grup 2), 30 sağlıklı kontrol (grup 3) olmak üzere üç grup alındı.
Bulgular: Yüksek dansiteli lipoprotein kolesterol **(**HDL-K), apo B, direk düşük dansiteli lipoprotein kolesterol (D-LDL-K), yüksek duyarlılıklı-CRP (hsCRP), "homeostasis model insulin resistance" (HOMA-IR) testlerinde, grup 1 ve 2 arasında istatistiksel anlamlı fark saptandı (p=0,001, p<0,0001, p=0,016, p=0,001, p<0,0001, p<0,0001, sırasıyla). HDL-K, D-LDL-K, hsCRP ve HOMA-IR testlerinde grup 1 ve 3 arasında anlamlı fark saptandı (p=0,023, p=0,023, p<0,0001, p=0,001, sırasıyla). Trigliserit, apo B, HDL-K, D-LDL-K parametrelerinde abdominal obezitede belirgin olmak üzere fark saptanırken, PON 1 düzeylerinde gruplar arası fark olmadığı ortaya kondu.
Sonuç: Sonuçlarımız obezite de lipit metabolizmasının değiştiğini gösterirken, PON1 aktivitesinde değişiklik olmadığını ortaya koymuştur.

Anahtar Sözcükler: Lipit metabolizması, obezite, paraoksonaz 1

Geliş Tarihi: 06.02.2014 **Kabul Tarihi:** 20.02.2014

Address for Correspondence / Yazışma Adresi: Guler Bugdayci, MD, Department of Biochemistry School of Medicine Abant Izzet Baysal University 14280 BOLU Tel: +90374 253 46 56 -3064 Fax: +90372 253 46 15 E-mail: gbugdayci@gmail.com

doi: http://dx.doi.org/10.12996/gmj.2014.03

INTRODUCTION

Increasing prevalence of obesity all around the world causes great concerns both for individual health and for the national health prevention systems (1). Obesity has been shown to predispose individuals to several chronic diseases like atherosclerosis, arterial hypertension, glomerulopathies that go together with proteinuria, diabetes mellitus and osteoarthritis (2).

In obese patients, changes have been demonstrated in lipid levels and lipoprotein metabolism (3). Changes in the levels and components of lipoproteins are thought to have a connection with the generation of cardiovascular disease (CVD) risk that accompanies obesity. Obese patients experience increased oxidative stress. When obese patients were compared to healthy individuals, low-density lipoprotein cholesterol (LDL-C) was shown to have undergone lipid peroxidation. Increases in oxidative damage could be related to the decreases in the antioxidant defense. There is strong evidence in support of the fact that oxidative stress, resulting from metabolic changes secondary to insulin resistance, contributes to the complications of obesity. The decrease in the activity of PON1, which is an antioxidant enzyme related to high density lipoprotein cholesterol (HDL-C), is found to be related to dyslipidemia, diabetes mellitus, advanced age and increased oxidative stress (4).

Paraoxonase/arylesterase (PON1) enzymes have a glycoprotein structure synthesized by the liver. It hydrolyzes aromatic esters of carboxylic acid and is an esterase firmly bound to HDL-C. PON1 is an enzyme with important roles in the prevention of atherosclerosis and the detoxification of organophosphates (5). In 1970s, among the scientific circles, toxicologists were the first to focus on the protective effects of PON1 in organophosphate poisoning. PON1 is an enzyme that accompanies HDL, while it metabolizes lipid hydroperoxides (6). The studies performed in this field have demonstrated that PON1, an antioxidant enzyme found in the structure of HDL, hydrolyzes lipid peroxides and protects them against the oxidation of LDL-C. PON1 stimulates the flow of cholesterol from macrophages through the inhibition of LDL oxidation. PON1 is associated to apolipoprotein (apo) A-I and apo J proteins of HDL-C (6). Several studies in recent years concentrated on the role of PON1 in instances of CVD, diabetes, neurological diseases, HIV and some other bacterial infections, chronic liver diseases and the use of alcohol (7).

Oxidation of LDL on the arterial wall is an important step in the generation of atherosclerosis. PON1 breaks down the active lipid found in oxidized LDL and prevents the inflammatory response on the arterial cell wall (8). In this study, the measurement of PON1 levels, lipid profile and apoprotein levels and the determination of the relationships between them in obese women, aims to contribute to the literature by delineating the mechanisms underlying atherosclerotic vascular disease that develops in obesity.

METHODS

This study was conducted in Abant Izzet Baysal University, School of Medicine, Bolu Research and Implementation Center. Among the patients or relatives who come to the Blood Sampling Unit for routine control purposes, 60 obese women without any systemic diseases were selected (android, n=30 and gynoid, n=30) and 30 individuals were chosen as the control group to yield a population of 90 individuals. Obesity group was determined based on the National Institute of Health (NIH) Criteria (9). Individuals with BMI of > 30 kg/m^2 were qualified as obese, among these, those with a waist-to-hip (WTH) ratio of larger than 0.85 were classified as android obese and those with a WTH ratio smaller than 0.85 as gynoid obese. Among the individuals participating in the study, the following were determined as the exclusion criteria: a history of cerebrovascular disease within the last three months, significant weight loss, giving birth within the last six months, hypertension, diabetes mellitus, previous myocard infarction, history of anorexia/bulimia, medication use (aspirin, anti-inflammatory drugs, oral contraceptive medications, hypolipemic drugs etc.), vitamins, antioxidants, smoking, pregnancy, menopausal-postmenopausal state, hepatic, renal, thyroid or atherosclerotic diseases, pituitary disease or dysfunction.

The individuals participating in the study provided venous blood samples at 9:00 am in the morning following a 12-hour fast, the samples were obtained while they were sitting. Tubes used for serum separation were either dry tubes with gel separators containing clot activators (Vacuette, Greiner Bio-one GmbH, Kremsmünster, Austria) or those with K_3EDTA (Vacuette, Greiner Bio-one GmbH, Kremsmünster, Austria); 8 ml. of sample was placed in the first, 2 ml in the second. For the clotting to take place, the obtained blood samples were kept at room temperature for 30 minutes. They were then centrifuged at +4 °C at 1250 g for 15 minutes to separate the plasma and the serum. Serum samples were stored at -80°C until the day of the analyses. Frozen samples were sequentiallythawed immediately before the analysis. We refrained from repetitive thawing and freezing.

Measurement of biochemical parameters

Serum paraoxonase activity was measured by utilizing Rel Assay Diagnostics commercial kit (Catalog no: 5D43, Gaziantep, Turkey). CV% values of the test were reported as 4.1, 1.7 and 1.5 for the low, medium and high serum pools by the manufacturer, respectively. The absorbance produced in a minute by p-nitrophenol generated as a result of the reaction was measured by spectrophotometry at 412 nm. Molar absorption coefficient for p-nitrophenol was ϵ_{412}= 18290 M^{-1} cm^{-1}. One unit of paraoxonase activity was defined as the amount of enzyme hydrolyzing one µmole of paraoxone under these conditions and enzyme activity was expressed as U/L.

Serum arylesterase (ARE) activity was measured by using Rel Assay Diagnostics arylesterase activity measurement kit (Catalog no: 4D23. Gaziantep, Turkey). CV% values of the test were reported as 4.0, 3.3 and 3.1 for the high, medium and low serum pools by the manufacturer, respectively. The method is based on the colorimetric measurement of the phenol produced as a result of the enzymatic hydrolysis of the phenylasetate used as a substrate. The absorbance produced in a minute by the phenol generated as a result of the reaction was measured by a spectrophotometer at 548 nm. Molar absorption coefficient for phenol was ϵ_{548}= 4000 M^{-1} cm^{-1}. Under these conditions, one unit of arylesterase activity was defined as the amount of enzyme hydrolyzing one micromole of phenylacetate in a minute and was expressed as U/L.

High sensitive-CRP (hs-CRP) levels were measured by BN Prospec (Siemens Healthcare Diagnostics, Deerfield, IL, ABD) nephelometer by using a commercial kit and employing a nephelometric method.

Glucose, triglyceride, HDL-C, total cholesterol, apo A-I, apo B, creatinine, direct-LDL-C (D-LDL-C) and serum insulin levels were measured with chemiluminescence microparticle enzyme immunological method by using Abbott commercial kits (Chicago, IL, ABD) and Abbott Arcitect c8200i analyzer. Of the calculated biochemical parameters, Homeostasis model insulin resistance (HOMA-IR) index was calculated with the following formula: fasting plasma glucose (mg/dL) x fasting plasma insulin (µIU/dL)/ 405 (10). MDRD (Modification of Diet in Renal Disease) renal function was assessed with the help of the estimated glomerular filtration rate (eGFR) calculated with MDRD equation (11).

Ethics

An approval was obtained from Abant Izzet Baysal University Clinical Research Ethics Committee stating that the study was in abidance with ethical principles (10.09.2008; Decision Number 105).

Statistical Analysis

Whether the numerical changes showed a normal distribution or not was assessed with Kolmogorov Smirnov test and its homogenicity was analyzed with a Levene test. All the data were presented as mean± standard deviation. For parameters with normal distribution, the groups were evaluated with a one-way ANOVA. For parameters that were significant, a post-hoc Tukey test was used to see the differences between the groups. For parameters that did not have a normal distribution following a Kruskal Wallis variance analysis, the difference between the groups was analyzed with a Mann Whitney U test. Arithmetical mean and standard deviations were used for parametric data, median and standard error were used for nonparametric data. Pearson correlation and BMI were calculated with multiple linear regression analysis. Results were evaluated within a 95% confidence interval and a p-value of <0.05 was accepted as the statistical significance level.

RESULTS

The study group consisted of healthy non-obese control group (group 1, n=30), abdominal obesity group (group 2, n=30) and gynoid obesity group (group 3, n=30) making up 90 female subjects.

Mean age, SD and range of the groups were as follows: group 1 31.5 ± 7.5 (21-48) years, group 2 35.6 ± 8.6 (18-47) years and group 3 34.0 ± 8.2 (18-47) years. There was no no statistically meaningful age difference among the groups (p=0.163).

The duration of obesity was 5.0 (2.0 – 10.0) years for group 2 and 4.0 (1.0 – 12.0) years for group 3. There was a statistically significant difference between the groups (p<0.0001). A statistically significant difference was seen between group 1 and 2 (p<0.0001) and group 1 and 3 (p<0.0001), but not with group 2 and 3 (p=0.525).

The measured and calculated values for the study groups were classified as parametric and nonparametric with Kolmogorov Smirnov test based on their distributions. Nonparametric tests were identified as the duration of obesity, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), insulin, HOMA-IR and ARE activity and the results were presented as median and standard error. Parametric tests were identified as age, WTH ratio, glucose, creatinine, MDRD, Total cholesterol, triglyceride, HDL-C, apo A-I, apo B, PON1 activity, D-LDL-C and hsCRP and the results were presented as arithmetical mean and standard deviations. The results are presented on Tables 1 and 2.

Pearson correlation was used to detect relationships between the measured test results. Significant positive correlations were observed between total cholesterol and triglyceride (r=0.614, p<0.0001), apo A-I (r=0.358, p=0.001), apo B (r=0.840, p<0.0001) and D-LDL-C (r=0.781, p<0.0001). Triglyceride had a negative correlation with HDL-C (r=-0.281, p=0.007) and a positive correlation with apo B (r=0.677, p<0,0001), HOMA-IR (r=0.353, p=0.001), D-LDL-C (r=0.512, p<0.0001) and BMI (r=0.357, p=0.001) (Table 3).

HDL-C had a positive correlation with apo A-I (r=0.817, p<0.0001) and a negative correlation with hsCRP (r=-0.237, p=0.025) and BMI (r=-0.384, p<0.0001). Apo B had a positive correlation with D-LDL-C (r=0.811, p<0.0001) and BMI (r=0.284, p=0.007). A positive correlation was detected between HOMA-IR and BMI (r=0.381, p<0.0001). There were positive correlations between D-LDL-C and hsCRP (r=0.262, p=0.013), as well as between D-LDL-C and BMI (r=0.399, p<0.0001). A positive correlation was identified between BMI and hsCRP (r=0.570, p<0.0001) (Table 3).

When multiple linear regression analysis was performed for BMI and all other measured parameters, statistically significant differences were detected (r^2=0.524, p<0.0001, BMI = 23.24 - 0.003 × total cholesterol + 0.010 × triglyceride - 0.218 × HDL-C + 0.046 × apo A - 0.061 × apo B- 0,014 × PON - 0.000 × ARE + 0.932 × HOMA-IR + 0,066 × D-LDL–C + 1.015 × hsCRP).

When the other parameters were analyzed separately, the most statistically significant ones were BMI and hsCRP (p<0.0001) and BMI and HOMA-IR index (p=0.006). The results are shown on Table 4.

Table 1. Results of the nonparametric tests of the study groups presented as median and standard error.

	Group 1 n=30	Group 2 n=30	Group 3 n=30	1-2 p	1-3 p	2-3 p
BMI, kg/m^2	21.0 ± 0.42	33.5± 0.63	32.0± 0.87	<0.0001	<0.0001	0.534
SBP, mm/Hg	100 ± 1.71	120 ± 2.57	120 ± 1.83	<0.0001	<0.0001	0.671
DBP, mm/Hg	65 ± 1.41	80 ± 1.30	80 ± 1.67	<0.0001	<0.0001	0.185
Insulin, µU/mL	8.6 ± 0.60	11.3± 1.23	10.4± 1.50	<0.0001	0.003	0.336
HOMA-IR, mg/L	1.90 ± 1.87	2.75± 0.35	2.53± 0.35	<0.0001	0.001	0.496
ARE, U/L	953 ± 89.7	1110± 9.6	1042±85.8	*	*	*
ALT, U/L	12.0 ± 0.81	16.0± 1.06	12.5± 0.75	*	*	*

*Kruskal Wallis did not identify any statistical significance.
BMI, body mass index; SBP, sistolic blood pressure; DBP, diastolic blood pressure; HOMA-IR, homeostasis model of assessment-insulin resistance; ARE, arylesterase; ALT, alanine aminotrasferase.

Table 2. The results of the parametric tests of the study groups presented as mean and SD.

	Group 1 n=30	Group 2 n=30	Group 3 n=30	1-2 p	1-3 p	2-3 p
Glucose, mg/dL	92.0 ± 12.2	96.3 ± 9.7	98.7 ± 16.8	*	*	*
Creatinine, mg/dL	0.72 ± 0.07	0.71 ± 0.07	0.71 ± 0.08	*	*	*
MDRD	104.3 ± 11.4	101.5 ± 12.8	101.7 ± 13.7	*	*	*
Total cholesterol, mg/dL	162.7 ± 29.3	174.4 ± 35.5	175.2 ± 29.0	*	*	*
Tryglicerids, mg/dL	94.2 ± 42.2	151.1 ± 70.1	128.9 ± 55.1	0.001	0.055	0.294
HDL-C, mg/dL	52.9 ± 9.6	43.9 ± 6.8	47.2 ± 7.8	<0.0001	0.023	0.250
apo A-I, mg/dL	133.7 ± 20.1	126.5 ± 14.9	125.5 ± 16.8	*	*	*
apo B, mg/dL	68.7 ± 21.4	83.3 ± 21.6	75.9 ± 16.6	0.016	0.355	0.322
PON, U/L	31.5 ± 19.3	29.2 ± 16.4	30.6 ± 18.7	*	*	*
D-LDL-C, mg/dL	97.9 ± 23.9	122.6 ± 30.1	116.2 ± 28.1	0.001	0.023	0.627
hsCRP	0.77 ± 0.70	5.05 ± 3.35	3.76 ± 2.06	<0.0001	<0.0001	0.080

*ANOVA did not identify any statistical difference.
MDRD, modification of diet in renal disease; HDL-C, high-density lipoprotein cholesterol; apo, apolipoprotein; PON, Paraoxonase; D-LDL-C, direct low-density lipoprotein cholesterol; hsCRP, high sensitive C-reactive protein.

DISCUSSION

At the heart of the disease causing mechanisms related to obesity, lays the low degree inflammatory process triggered by the metabolic events (12). Although, the changes in lipid and lipoprotein metabolisms have been demonstrated in obese cases, the level of PON1 activity and its relationship to lipid metabolism is not clear (13-14). In this study, the changes in PON1 activity in premenopausal abdominal and gynoid obesity groups were similar. Changes have been shown in the D-LDL-C, HDL-C, triglyceride and apo B components of the lipid panel together with changes in the levels of hsCRP, which is an indicator for endothelial inflammation.

In a study analyzing the effects of different genetic and environmental factors on PON1 metabolism, in addition to different substrates, Rainwater et al. compared serum PON1 activity of 922 subjects by three different substrates as paraoxone, phenylacetate and lactone dihydrocoumarine (15). Depending on the substrate, the activity differed by up to 88-97%. Based on the allele they were located for PON1 activity, the order was as follows; QQ< QR< RR and MM< LM< LL (16). Browne et al. conducted a study in which they analyzed PON1 method and its biological variations. Human serum PON1 activity was measured in 70 individuals with Q192R polymorphisms grouped as 41 (QQ), 31 (QR) and 7 (RR) alleles; five different kinetic measurements were performed as paraoxonase activity, salt-stimulated paraoxonase activity, ARE activity with phenyl acetate, ARE activity with p-nitrophenyl acetate and finally ARE activity with phenyl acetate and p-nitrophenyl acetate in an attempt to identify the activity differences between the methods. Based on the alleles, PON1 acitvity was as follows; QQ< QR<RR. In the biological variation study conducted on 17 individuals, they demonstrated the differences between the alleles (17).

Veiga and colleagues performed a study on 81 obese and 75 healthy Portuguese women. They measured the PON1 activity by using paraoxone substrate, and similar to the findings of our study, they could not show any difference between the groups. When all the samples were classified on the basis of Q192R and L55M polymorphisms, PON1 activity changed depending on the alleles as has been shown in other studies.

Similar to our findings, in this study, obese group had increased levels of SBP, DBP, triglyceride and hsCRP (a p<0.001, p<0.001, p<0.001 and p<0.001 respectively) and HDL-L level was decreased (p<0.001) (18). A study by Tabur and colleagues including 30 obese and 40 non-diabetic metabolic syndrome patients together with 30 control subjects could not find a difference in PON1 activity between the groups, confirming our findings(4).

In a study by Seres et al. conducted on patients with adult and childhood obesity, adiponectin, resistin and PON1 activity were shown to have decreased. In this research study, the PON1 form with decreased activity was in Q192R polymorphism group; of the A and B isoenzymes, the activity was related to the B isoenzyme (13). In a study by Ferretti et al., 30 obese and 62 control children were found to have decreased PON1 activity (p<0.05), increased ARE activity (p<0.01), increased leptin levels (p<0.0001) and decreased adiponectin levels (p<0.001) (19). The findings of this study are not in line with with ours. As a specific polymorphism or allele was not chosen, the samples used in our study represented a heterogeneous group. In order not to be affected by other hormonal or metabolic problems, the obese group consisted of women at the reproductive age; furthermore, these individuals did not have any diabetic, renal, hepatic or endocrine problems. Adding to all these limitations, the duration of obesity was considerably short and the number of patients was inadequate in our study.

Table 3. Pearson correlation results of total cholesterol, triglycerides, high-density lipoprotein cholesterol, apolipoprotein A-I and B, high sensitive C-reactive protein, paraoxonase, arylesterase, direct low-density lipoprotein cholesterol and body mass index in all groups.

		Tryglycerids	HDL-C	Apo A-I	Apo B	PON	ARE	HOMA-IR	D-LDL-C	BMI	hsCRP
Total cholesterol	R	0.614	*	0.358	0.840	*	*	*	0.781	*	*
	P	<0.0001	*	0,001	<0,0001	*	*	*	<0,0001	*	*
Tryglycerids	R		-0.281	*	0.677	*	*	0.353	0.512	0.357	*
	P		0.007	*	<0.0001	*	*	0.001	<0.0001	0.001	*
HDL-C	R			0.817	*	*	*	*	*	-0.384	-0.237
	P			<0.0001	*	*	*	*	*	<0.0001	0.025
Apo A-I	R				*	*	*	*	*	*	*
	P				*	*	*	*	*	*	*
Apo B	R					*	*	*	0.811	0.234	*
	P					*	*	*	<0.0001	0.007	*
PON	R						*	*	*	*	*
	P						*	*	*	*	*
ARE	R							*	*	*	*
	P							*	*	*	*
HOMA-IR	R								*	0.381	*
	P								*	<0.0001	*
D-LDL-C	R									0.399	*
	P									<0.0001	*
BMI	R										0.570
	P										<0.0001

*Pearson correlation did not identify any statistical difference.
HDL-C, high-density lipoprotein cholesterol; apo, apolipoprotein; PON, Paraoxonase; ARE, arylesterase; HOMA-IR, homeostasis model of assessment-insulin resistance; D-LDL-C, direct low-density lipoprotein cholesterol; BMI, body mass index; hsCRP, high sensitive C-reactive protein.

In a study by Ayer et al., 19 obese and 19 non-obese young individuals were recruited; the study included arterial dilatation with exogenous nitrate stimulation in a subgroup and these individuals had significantly high levels of hsCRP and insulin together with low levels of HDL-C (20). In studies performed with the aim of identifying the correlation between calculated and direct LDL-C, for providing guidance in antilipemic therapy, direct measurements proved to be more valuable (21-22). In our study, we also preferred direct LDL-C.

In a study by Revenga-Faruca et al. on obese children (126) and adolescents (60 boys and 66 girls), when belly fat and metabolic risks were analyzed, as in our study, differences were shown in the levels of insulin, hsCRP, triglyceride and HDL-C levels (23).

The studies conducted in the field show that abdominal obesity has higher cardiometabolic risks than gynoid obesity (24-25). In our study, when we compared the abdominal obesity group with controls, we found that they had developed insulin resistance and that they had increased levels of triglyceride, apo B, D-LDL-C and hsCRP together with low levels of HDL-C. When gynoid obesity group was compared to controls, there was no insulin resistance; their D-LDL-C and hsCRP levels were high and HDL-C levels were low. The insulin resistance seen in abdominal obesity is responsible for diabetes mellitus, hypertension and CVD (26). When we compared the two obese groups with each other in our study, there was a statistically significant difference for HOMA-IR. Only abdominal obesity group was shown to have developed insulin resistance (> 2.7). In our study, the frequency of those with HOMA-IR of > 2.7, was 53% (n=16) in the abdominal obesity group and 46% (n=14) in gynoid obese group.

Table 4. Multiple linear regression analyses of BMI and other tests

	β coefficient	p
Total cholesterol	0.012	0.957
Trylycerids	0.087	0.536
HDL-C	-0.286	0.153
apo A-I	0.119	0.498
apo B	-0.187	0.329
ARE	0.010	0.900
PON	0.036	0.665
D-LDL-C	0.275	0.103
HOMA-IR	0.238	0.006
hsCRP	0.436	<0.0001

HDL-C, high-density lipoprotein cholesterol; apo, apolipoprotein; PON, Paraoxonase; ARE, arylesterase;; D-LDL-C, direct low-density lipoprotein cholesterol; HOMA-IR, homeostasis model of assessment-insulin resistance; hsCRP, high sensitive C-reactive protein.

CONCLUSION

When we analyzed the relationship of PON1 to lipid metabolism in obese women, we arrived at the following conclusions:

PON1 activity was similar between the groups. PON1 activity might be measured by different methods and can be influenced by polymorphisms, even alleles. Moreover, in the biological variation studies of these tests, as individual index was <0.6, instead of choosing a reference range, the suggestion was to monitor individual differences. When PON1 activity was being identified, for it to be affected minimally by demographical variables, women of similar age who did not smoke or use oral contraceptives were included in the study. PON1 activity tests can only be monitored for an individual for certain genotypes and by employing certain substrates.

Abdominal obesity group was shown to have developed insulin resistance. When compared with the controls, abdominal obesity group had higher levels of triglyceride, apo B, D-LDL-C and hsCRP and low levels of HDL-C; gynoid obesity group had high levels of D-LDL-C and hsCRP and low levels of HDL-C. These results point out to the fact that metabolic dysfunction has started both in gynoid and abdominal obesity groups. This process has obviously affected the abdominal obesity group more significantly. D-LDL-C is a marker that is currently used in clinical biochemistry labs. Its levels were found to be high for both groups of obesity and was more significantly so in the abdominal obesity group; this is a new information that contributes to the literature and can be regarded as important for that very reason.

Funding
This research has been supported by the Scientific Research Unit of Abant Izzat Baysal University (Project Number: 2008.08.01.296).

Conflict of Interest
No conflict of interest was declared by the authors.

REFERENCES

1. Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. The epidemiology of obesity. Gastroenterology 2007; 132: 2087-102.
2. Kota SK, Meher LK, Kota SK, Jammula S, Krishna SVS. Implications of serum paraoxonase activity in obesity, diabetes mellitus, and dyslipidemia. Indian J Endocrinol and Metab 2013; 17: 402-12.
3. Faraj M, Lavoie ME, Messier L, Bastard JP, Prud'homme D. Reduction in serum apoB is associated with reduced inflammation and insulin resistance in post-menopausal women: A MONET study. Atherosclerosis 2010; 211: 682-8.

4. Tabur S, Torun AN, Sabuncu T, Turan MN, Celik H, Ocak AR et al. Non-diabetic metabolic syndrome and obesity do not affect serum paraoxonase and arylesterase activities but do affect oxidative stress and inflammation. Eur Journal Endocrinol2010; 162: 535-41.
5. Furlong CE, Suzuki SM, Stevens RC. Human PON1, a biomarker of risk of disease and exposure. Chem Biol Interact 2010; 187: 355-61.
6. Dragonov DI, La Du NB. Pharmacogenetics of paraoxonases: a brief review. Naunyn-Schmiedeberg's. Arch Pharmocol 2004; 369: 78-88.
7. Camps J, Marsillach J, Joven J. The paraoxonases: role in human diseases and methodological diffuculties in measurement. Crit Rev Clin Lab Sci 2009; 46:83-106.
8. Chudek J, Wiecek A. Adipose tissue, inflammation and endothelial dysfunction. Pharmacol Rep 2006; 58: 81-8.
9. National Institutes of Health, National Heart, Lung, and Blood Institute: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults-in evidence report. Obes Res 1998; 6: 51-209.
10. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher BF, Turner RC. Homeostasis model assesment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabeteologia 1985; 28: 412-9.
11. Salgado JV, Neves FA, Bastos MG, Franca AK, Brito DJ, Santas EM. Monitoring renal function: measured and estimated glomerular filtration rates - a review. Braz J Med Biol Res 2010; 43: 528-36.
12. Monteiro R and Azevedo I. Chronic inflammation in obesity and the metabolic syndrome. Mediators of Inflammation 2010; doi: 10.1155/2010 289645.
13. Seres I, Bajnok L, Harangi M, Sztanek F, Koncsos P, Paragh G. Alteration of PON1 activity in adult and childhood obesity and its relation to adipokine levels. Adv Exp Med Biol 2010; 660: 129-42.
14. Tabak O, Gelişgen R, Çicekci H, Şenateş E, Erdenen F, Müderrisoğlu C et al. Circulating levels of adiponectin, orexin-A, ghrelin and the antioxidant paraoxonase-1 in metabolic sydrome. Minerva Med 2012; 103: 323-9.
15. Rainwater DL, VandeBerg JL, Mahaney MC. Effects of diet on genetic regulation of lipoprotein metabolism in baboons. Atherosclerosis 2010; 213: 499-504.
16. Hong-Liang L, De-Pei L, Chihj-Chuan L. Paraoxonase gene polymorphisms, oxidative stress and diseases. J Mol Med 2003; 81: 766-79.
17. Browne RW, Koury ST, Marion S, Wilding G, Muti P, Trevisan M. Accuracy and Biological Variation of Human Serum Praoxonase I Activity and Polymorphism (Q192R) by Kinetic Enzyme Assay. Clin Chem 2007; 53: 310-7.
18. Veiga L, Silva-Nunes JA, Melão A, Olivera A, Duarte L, Brito M. Q192R polymorphism of the paraoxonase-1 gene as a risk factor for obesity in Portuguese women. Eur J Endocrinol 2011; 164: 213-8.
19. Ferretti G, Bacchetti T, Masciangelo S, Biocchiega V. HDL-paraoxonase and membrane lipid peroxidaiton: a comparison between healthy and obese subjects. Obesity 2010; 18: 1079-84.
20. Ayer JG, Harmer JA, David C, S Steinbeck K, Seale JP, Celermajer DS. Severe obesity is associated with impaired with arterial smooth muscle function in young adults. Obesity 2011; 19: 54-60.
21. Agrawal M, Spencer HJ, Faas FH. Method of LDL cholesterol measurement influences classification of LDL cholesterol treatment goals: clinical research study. J Investig Med 2010; 58: 945-9.
22. Otokozawa S, Ai M, Asztalos BF. Direct assessment of plazma low density lipoprotein and high density lipoprotein cholesterol levels and coronary heart disease: results from the Framingham Offspring Study. Atherosclerosis 2010; 213: 251-65.
23. Revenga-Frauca J, Gonzales-Gil EM, Bueno-Lozano G, De Miguel-Etayo P, Velasco-Martinez P, Rey Lopez JP. Abdominal fat and metabolic risk in obese children and adolescents. J Physiol Biochem 2009; 65: 415-20.
24. Souza FAC, Dias R, Fernandes CE, Pimentel F, Dias D. Menstrual irregularity: a possible clinical marker of metabolic dysfunction in women with class III obesity. Gynecol Endocrinol 2010; 26: 768-72.
25. Ghandehari H, Le V, Kamal-Bahl S, Bassin SL, Wong ND. Abdominal obesity and the spectrum of global cardiometabolic risks in US adults. Int J Obes 2009; 33: 239-48.
26. Carey DG, Jenkins AB, Campbell LV, Freund J, Chisholm DJ. Abdominal fat and insulin resistance in normal and overweight women: Direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM. Diabetes 1996; 45: 633-8.