

# Lipid profile and plasma atherogenic index in postmenopausal osteoporosis

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## ABSTRACT

**OBJECTIVE:** The goal of this study was to investigate the relationship between the lipid profile, plasma atherogenic index (PAI), and osteoporosis in postmenopausal women.

**METHODS:** The data of age, duration of menopause, height, weight, lipid profile, bone mineral density (BMD) value, and history of oral contraceptive use of 407 postmenopausal women who had not been menstruating for at least 12 months, were between the ages 45 and 80, and presented at the obstetrics and gynecology polyclinic of Kartal Dr. Lutfi Kirdar Training and Research Hospital were reviewed. The patients were divided into 2 groups according to the presence of osteoporosis, and the data compared. The level of significance was accepted as  $p < 0.05$ .

**RESULTS:** A total of 142 postmenopausal patients with osteoporosis were included in the study. The mean age was  $61.7 \pm 6.9$  years. In the control group, there were 263 postmenopausal women without osteoporosis, with a mean age of  $58.3 \pm 4.5$  years. There was no statistically significant difference with respect to triglyceride level; however, in the osteoporosis group, the level of total cholesterol and low-density lipoprotein (LDL) were lower, and the level of high-density lipoprotein (HDL) was higher ( $p = 0.762$ ,  $p = 0.002$ ,  $p = 0.01$ ,  $p < 0.001$ , respectively).

**CONCLUSION:** A high level of HDL, and low LDL and PAI values, which are important for the prevention of cardiovascular disease, were found to be negative factors for BMD.

*Keywords: Lipid profile; plasma atherogenic index; postmenopausal osteoporosis.*

Osteoporosis is preventable and treatable, but it is often clinically occult until the development of fracture [1]. Postmenopausal osteoporosis is directly related to a drop in the serum estrogen level, and it is an important cause of morbidity and mortality [2].

Reproductive factors, such as the number of parities, age at menarche and menopause, duration of menopause, duration of breast-feeding, and intervals between pregnancies, affect bone mineral density (BMD) [3, 4]. In addition, epidemiologically, osteoporosis has been associated with athero-



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sclerosis and hyperlipidemia [5]. Parhami et al. [6] revealed the effects of cholesterol and its metabolites on osteoblastic activity in in vivo and in vitro settings. In addition, they detected a dose-dependent increase in alkaline phosphatase activity, which is an indicator of osteoblastic differentiation [6, 7]. Buizert et al. [8] evaluated the correlation between cardiovascular disease and osteoporosis, and reported that lipid profile parameters known to have a protective role against cardiovascular disease, such as high-density lipoprotein (HDL) and a low total cholesterol (TC)/HDL ratio, did not inhibit osteoporosis. The plasma atherogenic index (PAI), related to the size of HDL cholesterol particles and low-density lipoprotein (LDL) and the esterification of cholesterol, also reflects the risk of coronary artery atherosclerosis and cardiovascular risk, and improves the overall evaluation of cardiovascular risk factors [9]. Atherogenic lipid levels change with menopause.

In this study, the aim was to investigate the correlation between lipid profile, PAI, and osteoporosis in women.

## MATERIALS AND METHODS

This retrospective investigation was performed with a total 407 postmenopausal women aged between 45 and 80 years of age who had not been menstruating for  $\geq 12$  months and who presented at the outpatient clinic of obstetrics and gynecology. The study protocol was approved by the ethics committee of Kartal Dr. Lutfi Kırdar Training and Research Hospital. Patients who were receiving hormone replacement therapy and/or drugs that could affect bone metabolism or lipid profile; and those with hepatic, renal, or cardiac disease were excluded from the study. Age, duration of menopause, height, body weight, lipid profile, BMD value, and oral contraceptive (OCS) use were recorded. Body mass index (BMI) was calculated as the ratio between body weight and height expressed as  $\text{kg}/\text{m}^2$  [10]. PAI was calculated as the logarithm of triglyceride (TG)/HDL cholesterol ratio. BMD of the lumbar region (L2-4) and femoral neck was measured and recorded. BMD values were divided into 2 categories: normal (T-score  $\geq 1$  SD), and osteoporotic (T-score  $\leq 2.5$  SD) [11]. Patients with a normal

T score constituted the control group. In our laboratory, the respective normal reference ranges were TC: 100-200 mg/dL, TG: 50-200 mg/dL, HDL: 45 mg/dL, and LDL cholesterol  $\leq 129$  mg/dL.

## Statistical analysis

SPSS Statistics for Windows, Version 17.0. (SPSS Inc., Chicago, IL, USA) was used to analyze the data. The distribution characteristics of the data were determined using the Kolmogorov-Smirnov test. An independent samples t-test was used for the data with a normal distribution, and the Mann-Whitney U test was applied to the data with non-normal distribution. Numerical variables were presented as mean $\pm$ SD. The results were evaluated within a 95% confidence interval. A p value of  $<0.05$  was considered to be statistically significant.

## RESULTS

All of the study participants were postmenopausal women aged 45 to 80 years. Among them, 144 women with a mean age of  $61.7 \pm 6.9$  years were osteoporotic. The control group consisted of 263 cases without osteoporosis, and the mean age was  $58.3 \pm 4.5$  years. The mean duration of menopause was  $13.58 \pm 7.61$  years in the osteoporotic group, and  $8.53 \pm 4.48$  years in the control group.

BMI values were significantly higher in the control group relative to the osteoporotic group ( $27.8 \pm 4.1$  vs.  $25.2 \pm 3.3$   $\text{kg}/\text{m}^2$ ;  $p < 0.001$ ). No significant difference was detected between the osteoporotic and control group in OCS use ( $p = 0.728$ ).

TC values in the control group were significantly higher ( $p = 0.002$ ). LDL ( $p = 0.01$ ) values were also comparatively higher in the control group, while HDL values were significantly lower ( $p < 0.001$ ). PAI values were found to be significantly lower in the patients with osteoporosis ( $p = 0.032$ ) (Table 1).

## DISCUSSION

The primary objective of this study was to evaluate the relationship between osteoporosis and PAI. In addition, the BMI, TC, LDL, HDL, and use of

**TABLE 1.** The demographic characteristics, lipid profile and plasma atherogenic index values of the patients

	Control (n=263)	Osteoporosis (n=144)	p
Age (years)	58.3±4.5	61.7±6.9	<0.001
BMI (kg/m <sup>2</sup> )	27.8±4.1	25.2±3.3	<0.001
Duration of menopause (years)	9.1±4.4	13.5±7.6	<0.001
Duration of OCS use (months)	9.6±23.4	10.7±41.2	0.728
LDL (mg/dL)	137.7±34.8	128.5±36.3	0.010
Triglyceride (mg/dL)	131.1±50.7	128±46.3	0.762
HDL (mg/dL)	50.1±10.6	54.8±11.3	<0.001
Total cholesterol (mg/dL)	222±43.7	208.2±38.5	0.002
PAI	0.39±0.2	0.34±0.1	0.032

Data are presented as mean±SD.

BMI: Body mass index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; OCS: Oral contraceptive, PAI: Plasma atherogenic index.

OCS were evaluated. In the osteoporotic group, the PAI, BMI, LDL, and TC levels were lower, but HDL was higher than in the control group. TG and OCS levels did not demonstrate a significant intergroup difference. Obesity may help maintain BMD with a reactive increase in bone formation and mineral density. Therefore, higher atherogenic lipid levels and PAI values are anticipated in obese patients, which is consistent with our results.

The rate of dyslipidemia increases after menopause [12]. Increases in TC, LDL, and TG levels have been demonstrated; however, HDL data have been controversial. Some authors indicated a lack of any change in HDL values [13–16], while others have reported decreased [17–19] or increased HDL levels [20]. The PAI measurement is a logarithmic transformation of the TG/HDL-cholesterol ratio, and was introduced by Dobiasova et al. [9]. PAI also demonstrates a negative correlation with the particle size of LDL cholesterol. In a study conducted by Söğüt et al. [21], PAI was demonstrated to be the most robust biochemical parameter in the prediction of coronary heart disease.

In our study, TG values did not differ significantly between groups; however, HDL levels were statistically significantly different. This finding suggests that an increased HDL level in the osteoporotic group in-

duced a drop in PAI, which may be correlated with bone metabolism. The impact of HDL on BMD is not precisely known [8]. Studies that have evaluated the relationship between HDL and BMD have yielded different results [22, 23]. In a few studies, a negative correlation was detected, as in the present study [24–29]. However, in epidemiological studies performed, type 2 diabetic patients with lower HDL levels have been associated with increased BMD values [30–33]. Furthermore, in the large, population-based Tromso study in which 27,159 patients were followed up for 6 years, a protective effect of lower HDL values against non-vertebral fractures was demonstrated [31]. PAI is a strong risk factor for cardiovascular disease. Anti-inflammatory, antioxidant, antithrombotic, and cholesterol transporter functions of the HDL component of PAI have been also reported [34–36]. In recent years, because of its HDL-cholesterol promoting effects, the importance of developing PAI-lowering treatments has been emphasized. These drugs, in combination with cholesterol-lowering drugs, may be an effective treatment alternative for cardiovascular disease. However, this approach revives the dilemma concerning whether or not HDL-increasing drugs will eliminate the protective effect of HDL on non-vertebral fractures. [34, 35]. Since osteoporosis and the related

bone fractures are among the most important health problems of our aging population, the association between HDL and BMD should be further explored.

Previously, TC was thought to be associated with cardiovascular diseases and osteoporosis, and consequently, studies investigating the correlation between TC and BMD were performed. However, these studies yielded various outcomes. Some found no relationship between the two [37, 38], while others reported a positive [24, 39] or negative correlation [40]. In our study, TC levels were higher in the control group compared with the osteoporotic group.

In conclusion, the present study demonstrated that high HDL and low LDL and PAI levels, which are important in the prevention of cardiovascular diseases, are negative factors for BMD. However, to demonstrate the pathophysiological relationship between lipid profile and BMD, and to substantiate our results, larger-scale studies are needed.

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**Authorship contributions:** Concept – G.Ş.E., E.E.Ş., D.V., H.Ö.K., B.K., Ö.S.; Design – G.Ş.E., E.E.Ş., D.V., H.Ö.K., B.K., Ö.S.; Supervision – G.Ş.E., E.E.Ş., D.V.; Materials – G.Ş.E., E.E.Ş.; Data collection &/or processing – G.Ş.E., E.E.Ş., D.V.; Analysis and/or interpretation – G.Ş.E., E.E.Ş.; Literature search – E.E.Ş., D.V.; Writing – G.Ş.E., E.E.Ş.; Critical review – G.Ş.E., E.E.Ş., D.V., H.Ö.K., B.K.

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