The European Research Journal 2019;5(2):355-360 ORIGINAL ARTICLE

The association between lipid profile and bone mineral density in subjects with ankylosing spondylitis

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DOI: 10.18621/eurj.359518

ABSTRACT

Objective: This study aims to investigate the relationship between serum lipids and bone mineral density in ankylosing spondylitis patients.

Methods: A total of 94 ankylosing spondylitis patients fulfilling the 1984 Modified New York Criteria who had serum lipid levels and bone mineral density scores in medical records were included in this study. These patients treated with nonsteroid antiinflammatory drugs. Their files were examined in detail. Later demographic and laboratory features were recorded to the research form. Dual-energy X-ray absorptiometry was used to assess bone mineral density in two bone sites of femur (neck, intertrochanteric zone and trochanter) and spinal lumbar vertebras (Lumbar 1-Lumbar 4).

Results: Significant and positive correlation was found between high density lipoprotein and femoral neck bone mineral density (r = 0.356, p = 0.021) in osteopenic group and in osteoporotic group (r = 0.005, p = 0.040).

Conclusion: According to our study significant and positive correlations are found between high density lipoprotein and femoral neck bone mineral density in osteopenic and osteoporotic group. However, we believe that more studies are needed about this research.

Keywords: Ankylosing spondylitis, lipid profile, bone mineral density

Received: November 29, 2017; Accepted: January 21, 2018; Published Online: May 16, 2018

Ankylosing spondylitis (AS) is an inflammatory rheumatic disorder and a prototype of spondyloarthritis, characterized by axial skeleton and sacroiliac joint involvement. In 90% of patients, the first symptoms develop before 40-45 years and the mean average age is 28.3 years [1].

The incidence of osteopenia or osteoporosis in these patients is reported to be 19-62% [2]. Bone loss in AS appears to be multifactorial and involves different mechanisms at different stages of disease [3]. Also there is association between inflammation and lipid changes [4]. The association between serum lipids and bone mineral density (BMD) has been investigated in previous studies [5-7] but these relationships have not yet been described in AS.

In our study, we investigated the relationship between serum lipids and BMD in AS patients. To the authors' knowledge, this is the first study in AS patients which evaluated the relationships between serum lipids and BMD.

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e-ISSN: 2149-3189

METHODS

Our study was carried out at Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Aydın, Turkey from January 2017 to June 2017. The ethics committee of the Institution approved the study and all patients signed the Informed consent form. 94 male patients who were diagnosed with AS according to the 1984 Modified New York criteria and who had serum lipid levels and BMD scores in medical records were included in this study. The all medical records of these patients in our hospital were analysed and later ages, gender, body weight and height, body mass index (BMI), serum lipid levels [high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), total cholesterol (TC) and total triglyceride (TG) and BMD scores of the patients were recorded to the research form. AS patients (94 male) were treated with nonsteroid antiinflammatory drugs (NSAIDs).

Dual-energy X-ray absorptiometry (DXA) was used to assess BMD in two bone sites of femur (neck, intertrochanteric zone and trochanter) and spinal lumbar vertebras (Lumbar 1- Lumbar 4). Calibration of bone densitometer (Hologic, Inc., Waltham, MA, USA) was performed weekly by using appropriate phantoms. The precision rror (PE) is usually expressed as the coefficient of variation (CV), which is the ratio of the standard deviation to the mean of the measurements [8]. The PE for BMD measurements was 2 to 3% in the femoral and 1 to 1.5% in the lumbar regions. All scans were performed according to the manufacturer's guidelines. In patients with spinal implant the involved lumbar vertebras were excluded and the mean BMD of noninvolved vertebras was entered into the analysis.

Baseline characteristics and differences of basic features among male subjects with AS were presented in Table 1.

HDL cholesterol (HDLc), LDL cholesterol (LDLc), TC and TG were measured by spectrophotometric enzymatic colorimetric tests using Abbott Diagnostics and VLDL cholesterol (VLDLc) by using the formula VLDLc = Triglycerides /5. Normal ranges were considered to be: 35-55 mg/dL for HDLc, 30-130 mg/dL for LDLc, 0-200 mg/dL for TC and 0-149 mg/dL for TG. Body mass index (BMI) was calculated by the formula BMI = weight/height2, where height is expressed in meters and weight in kilograms. We considered patients with a T-score etween -1.0 and -2.49 to be osteopenic and those with a T-score < -2.5 to have osteoporosis.

Inclusion criteria were male AS subjects. Because of some conditions which could potentially affect serum lipid levels, the patients who had some disorders of neurologic, endocrinologic and cardiovascular systems, and a history of using some drugs (e.g., oral contraceptives, corticosteroids, lipid lowering drugs, hormones, thyroid hormones, anticonvulsive drugs, heparin, aluminum containing antacids, lithium, omega-3 fatty acids, or other nutrients supplements) and smoking or alcohol consumption were excluded from the study.

Statistical Analysis

Normally distributed variables were tested by T-test in AS patients. To compare the correlations between serum lipids and BMD. Spearman correlation test was used. Partial correlation with adjustment for weight, height, BMI and age was used to determine the association between BMD in different bone sites and serum lipids. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), ver 19.0 (IBM Corp.; Armonk, NY, USA) and $p < 0.05$ was considered to be statistically significant.

RESULTS

Ninety four patients (age 42.44 ± 10.75 years, 94 male) diagnosed with AS were enrolled in the study. Mean weight was 84.04 ± 13.22 kg, mean height was 167.74 ± 25.79 cm, mean BMI index was 28.76 ± 4.94 kg /m2, mean disease duration was 16.3 ± 9.8 years. Mean TG was 146.70 ± 91.01 and mean of TC was 195.64 ± 41.22. Means of HDLc, LDLc and VLDLc were 41.65 ± 9.84, 123.67 ± 36.28 and 29.03 ± 18.30, respectively (Table 1).

Significant correlations were not found between HDLc, LDLc, VLDLc, TC, TG and BMD scores of the patients in normal group (Table 2).

Significant and positive correlation was found between HDLc and femoral neck BMD (r = 0.356, p = 0.021) in osteopenic group and in osteoporotic group (r = 0.005, p = 0.040) (Table 2).

Table 1. Baseline characteristics and differences of basic features among male subjects with ankylosing spondylitis

	Male subjects with ankylosing spondylitis (n = 94)
Age (year)	42.44 ± 10.75
Gender	
Male, n (%)	94 (100)
Female, n (%)	0 (0)
Weight (kg)	84.04 ± 13.22
Height (cm)	167.74 ± 25.79
BMI (kg /m^2)	28.76 ± 4.94
Disease duration (year)	16.3 ± 9.8
TG (mg/dL)	146.70 ± 91.01
TC (mg/dL)	195.64 ± 41.22
HDLc (mg/dL)	41.65 ± 9.84
LDLc (mg/dL)	123.67 ± 36.28
VLDLc (mg/dL)	29.03 ± 18.30
BMD of femoral neck T-score	-0.89 ± 0.95
BMD of spinal lumbar vertebras T-score	-1.10 ± 1.62

Data are shown as mean±standard deviation or number (%). BMD = bone mineral density, HDLc = high density lipoprotein, LDLc = low density lipoprotein, TC = total cholesterol, TG = total triglyceride, VLDLc = very low density lipoprotein

DISCUSSION

The association between serum lipids and BMD has been investigated in previous studies [5-7]. Hadis *et al*. [5] investigated the relationships between serum lipids and BMD in 85 male patients with spinal cord injury (SCI). As a result of this study a positive correlation between HDL and femoral neck BMD (r = 0.33, p = 0.004) was found although any a relation between others and BMD scores had no. Their study does not support a strong association between serum lipids and BMD in patients with SCI. Garg *et al.* [6] studied the relationships of lipid parameters with BMD in 2,347 participants. In this investigation, a total of 924 male,788 premenopausal and 635 postmenopausal female participants were included. As a result of this study, BMD of male participants at femoral neck, femur total and lumbar spine were negatively correlated with TC and LDLc and positively with TG. In premenopausal women, there was no correlation of any lipid parameters with BMD. In postmenopausal women, a significant negative correlation was found between femur total BMD with TC and LDLc. Furthermore, there was a negative correlation between TG and femur BMD, while a positive correlation was found between HDLc and the same region in these women. They reported a weak correlation between lipid parameters and BMD at various sites in men, pre- and post-menopausal women. Catalina *et al*. [7] investigated lipid profile in 610 postmenopausal women with osteoporosis. Authors were grouped according to the age (< 50 years, 51-60 years, 61-70 years and >0 years) and presence or absence of a history of fragility fracture of patients. In this research, they determined significant correlations between BMD with BMI and lipid profile. The results presented in this report provide support for an association between osteoporosis and the circulating lipid profiles. Makovey *et al*. [9] investigated the association between TC and BMD in 497 female patients (224 premenopausal and 273 postmenopausal women). They showed that BMD is significantly negatively correlated with TC and LDLc in postmenopausal

Table 2. The relationship between serum lipids and bone mineral density in male subjects with ankylosing spondylitis

Category	**Male subjects with ankylosing spondylitis (n = 94)**				
Normal Group	**TG**	**TC**	**HDLc**	**LDLc**	**VLDLc**
Femoral neck BMD T-score					
r	0.036	0.129	0.176	0.136	0.030
p	0.857	0.523	0.381	0.499	0.881
Spinal lumbar vertebras' BMD T-score					
r	0.132	0.042	0.186	0.041	0.139
p	0.510	0.834	0.353	0.838	0.489
Osteopenic Group	**TG**	**TC**	**HDLc**	**LDLc**	**VLDLc**
Femoral neck BMD T-score					
r	0.195	0.214	0.356	0.017	0.174
p	0.216	0.174	**0.021**	0.915	0.270
Spinal lumbar vertebras' BMD T-score					
r	0.264	0.072	0.280	0.123	0.317
p	0.091	0.648	0.072	0.437	0.479
Osteoporotic Group	**TG**	**TC**	**HDLc**	**LDLc**	**VLDLc**
Femoral neck BMD T-score					
r	0.233	0.110	0.005	0.109	0.237
p	0.262	0.142	**0.040**	0.604	0.254
Spinal lumbar vertebras' BMD T-score					
r	0.164	0.301	0.006	0.068	0.163
p	0.433	0.144	0.978	0.746	0.437

BMD = bone mineral density, HDLc = high density lipoprotein, LDLc = low density lipoprotein, TC = total cholesterol, TG = total triglyceride, VLDLc = very low density lipoprotein

women not receiving hormone replacing therapy (HRT) and with HDLc in postmenopausal women receiving HRT [9]. Orozco *et al*.'s [10] study included 52 overweight early postmenopausal women, with no history of HRT, or any current or past pathology or treatment that could alter bone or lipid metabolism. As a result of their study early postmenopausal women with atherogenic lipid profile, defined as TC ≥ 240 mg/dl or LDLc ≥ 160 mg/dl or lipoprotein (a) ≥ 25 mg/dl have lower lumbar and femoral BMD and have an increased risk of osteopenia than those with normal lipid profile. They suggested that hyperlipidemia could be associated with osteoporosis and bone status should be evaluated in women with hyperlipidemia. Tankó *et al*'s [11] study included 340 postmenopausal women between 50-75 years. They showed that serum TC is significant negative correlated with BMD at the lumbar spine (r = -0.21, $p < 0.0001$) and distal forearm (r =- 0.14, $p = 0.013$), but not at the hip. They suggested that the weak associations between spine BMD and TC can be explained by the fact that both variables are simultaneously affected by estrogen deficiency rather than by a direct influence of serum cholesterol on osteoblast function. Uyama *et al.* [12] investigated the relation of carotid atherosclerosis to BMD in 30 postmenopausal women aged 67 to 85 years. They demonstrated a significant correlation of plaque score with TC level and low total BMD. In the prospective study of Samelson *et al.* [13] assesed the association between TC and BMD in 712 female and 450 male patients. No significant association between TC and BMD was found in female and male patients for any of the bone sites considered. Solomon *et al*'s [14] study included 13,592 patients. In crude analyses,

higher TC and LDLc levels were associated with lower BMD (both p values for trend <0.001), whereas higher HDLc levels were associated with higher BMD (*p* value for trend <0.001). However, in fully adjusted models, there was no significant relationship between TC, LDLc, or HDLc levels and BMD (all *p* values for trend > 0.1). Wu *et al*. [15] enrolled total 5,000 individuals (2,170 male and 2,830 female patients) to their study. These patients were divided into three groups. Group 1 was composed of male subjects; group 2, female subjects under 50 years; and group 3, females aged over 50 to exclude pre-menopausal females. The results of this study showed that BMD is negatively correlated with TC, LDLc, TG for females in Group 2. But it is only negatively related to TG for females in Group 3. In this mentioned study as a result, any a correlation was not found between BMD and lipid levels.

The responsible mechanisms about the association between osteoporosis and the lipid profile was announced in some studies [16, 17]. Franceschi *et al*. [16] explained this association as a molecular level "inflammaging" theory which can lead to osteoporosis. In another theory, osteoporosis is based on the "osteo-lipo-vascular interactions". Mesenchymal stem cells are capable of differentiating into osteoblasts, vascular smooth muscle cells and adipocytes. As a result of this study bone, adipose and vascular systems provide the epidemiological link between hyperlipidemia and osteoporosis [17].

CONCLUSION

As a result of our study we aimed to investigate the relationship between serum lipids and BMD in AS patients. We enrolled a total of 94 AS patients fulfilling the 1984 Modified New York Criteria who had serum lipid levels and BMD scores. We found significant and positive correlations between between HDL and femoral neck BMD in osteopenic and osteoporotic group. Our study supported the association between osteoporosis and the lipid profile. We can suggest that lipid reducing medications such as statins increases BMD and statins can be used in OP treatment.

Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

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