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The Association Between Lipid Profile and Bone Density in Postmenopausal Women

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Aim: The aim of this research was to examine the correlation between lipid profile and bone density in postmenopausal and premenopausal women. **Material and methods:** This research covered 53 subjects who were in post-menopause and 30 subjects who had regular menstruation, older than 45. **Results and discussion:** The postmenopausal subjects have lower bone density of the lumbar spine, if triglyceride levels were higher (p=0.030) and VLDL is higher (p=0.032). In subjects with regular menstruation, the density of the neck of the femur was greater if the cholesterol values were higher (p=0.002) and the density of the lumbar spine was greater where the levels of triglycerides (p=0.002) and of ApoB (p=0.026) were higher. In subjects in postmenopause there was a correlation between the density of the lumbar spine (p=0.04) and the density of the neck of the femur (p=0.008) with the length of menopause. The effect of lipid profile on bone density differs in women with regular menstruation and in postmenopausal women. The triglyceride levels in postmenopausal women contribute to a reduction in bone density, whilst the effect on bone density in women with regular menstruation is reversed, which indicates that the lipid profile is not an isolated factor affecting bone density, but that other factors, such as oestrogen levels and the length of post-menopause, have a significant effect on bone density. Key words: post-menopause, pre-menopause, lipid profile, bone density

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1. INTRODUCTION

The end of menstrual bleeding–menopause–marks the end of the reproductive cycle of a woman and usually occurs between 45 and 55 years of life. Changes in the production and activities of hormones produced by the ovaries and gonadotropines lead to subjective disturbances and clinical difficulties, such as a disturbed menstrual cycle, vasomotor disturbances, changes in the function of the central nervous system, metabolic changes, increases in body weight and changes in the distribution of fatty tissue, cardiovascular diseases and the occurrence of osteoporosis, as one of the most serious consequences of post-menopause.

The standpoint accepted until now has been that osteoporosis occurs due to the lack of oestrogen. Oestrogen receptors are found in the osteoclasts and osteoblasts, which means that oestrogen acts directly on the balance of their functions. Due to the lack of oestrogen, bone resorption increases, earlier and most strongly in the trabecular- spongy bones and later in the compact bones (1, 2, 3, 4, 5). These changes are not only present in women in post-menopause, but also in those with other disorders of the menstrual cycle related to reduced concentrations of oestrogen. Changes in lipid profiles are characterised by increased values of cholesterol, triglycerides, LDL (low density lipoprotein), apolypoprotein B and lower values of HDL (high density lipoprotein) and apolypoprotein A (7). Concentrations of triglycerides during the menopausal transition also rise and are related to increased quantities of abdominal fat. HDL concentrations are reversely proportional to the degree of abdominal obesity (4). On the other hand, alongside changes in hormone and lipid profiles, in menopause there are also changes in the metabolism of bone tissue and a resulting reduction in bone density, which has been confirmed by a large number of studies.

A connection between changes in the lipid profile and the density of bone

Parameter	Subjects	AM	SD	p-value
Z score of lumbar spine	Subjects in post-menopause	-1.02	1.30	**0.01**
	Subjects with regular menstruation	-0.32	1.09	
T score of lumbar spine	Subjects in post-menopause	-1.01	1.35	**0.01**
	Subjects with regular menstruation	-0.25	1.15	
Z score of neck of femur	Subjects in post-menopause	-.09	1.27	**0.20**
	Subjects with regular menstruation	25	0.92	
T score of neck of femur	Subjects in post-menopause	-0.14	1.27	**0.02**
	Subjects with regular menstruation	0.44	0.92	

Table 1. Bone density of the lumbar spine and neck of the femur in women in post-menopause and women with regular menstruation. AM- arithmetic mean, SD–standard deviation, significant p-values are marked in bold font

tissue has been discovered in women who used statin in therapy for hyperlipidaemia (8,9). Research relating to monitoring changes in the mineral density of bones of the lumbar spine when statin is used together with HNT, has shown that a reduction in LDL and an increase in HDL occurs within only three months, and there is also a more rapid and significant reduction in triglycerides. When only HNT is used, these results are not reached before six months or longer (10, 11). After several months' therapy an increase in bone mass was noticed in the same patients, which launched a large number of clinical and basic studies, to examine the connection between lipid profile, bone density and sexual steroids.

The aim of this study was to examine the connection between lipid profile and bone density in women in menopause as well as the connection between bone density with the levels of estradiol, progesterone, testosterone, FSH and LH.

2. SUBJECTS AND METHODS

This prospective study was undertaken in the period from October 2007 to July 2008 in Tuzla, comprising 83 subjects aged over 45 years, divided into two groups: the test group consisted of 53 subjects who were already in natural postmenopause, and the control group consisted of 30 subjects with regular menstruation. The average age of the subjects in postmenopause was 51.8±4.2 years, whilst the subjects with regular menstruation were 46.7 ±1.8 years old. The Body Mass Index (BMI) of women in post-menopause was 27.79 kg/m^2±4.73 and in the subjects with regular menstruation it was 25.46±2.71 kg/m^2. The average duration of post-menopause was 48±.... months. An interview was conducted with each subject by the author, who also created a form with the following data: name and surname, year of birth, menopause, length of menopause, data on use of hormone replacement therapy or other medication, and personal history of heart disease, thyroid disease, diabetes or kidney disease, which according to knowledge so far could cause changes in lipid profile or bone density.

Blood was taken from the cubital vein and divided into two samples, from one of which concentrations of lipids and lipoproteins were determined, and from the other the concentrations of hormones: (FSH), (LH), estradiol (E2), progesterone (P) and testosterone (T) were found.

After this, each subject underwent densitometry (dual energy X-ray absorptiometry) at the Radiology Clinic of University Clinical Hospital, Tuzla, on a LUNAR DPX-L machine. The bone density of the lumbar spine was determined from the L1-L4, and the neck of the femur, and the values were compared to the standards in the apparatus for age, race and gender. The results were expressed as deviations from the normal values as standard deviations Z-score or T-score, or standard deviations.

Statistical analysis was undertaken using the SPSS 15.0 program package (Chicago, IL, USA). The basic descriptive statistical tests were performed, as well as the Mann-Whitney U test, the X^2-test, the Fisher's exact test, and non-parametric Spearman rang correlation. Linear regression analysis was used to determine the strength of the effect of individual variables on the parameters of bone density. All statistical tests were performed to the level of statistical probability of 95% ($p<0.05$).

3. RESULTS

The subjects in postmenopause had statistically significantly lower bone density of both the lumbar spine and the neck of the femur (Table 1). Apo A lipoprotein levels were significantly higher in patients with regular menstruation while there were no differences in the concentrations of other lipids and lipoproteins.

In subjects in postmenopause a significant negative correlation was found between bone density of the lumbar spine (T-score) and triglycerides ($p=0.030$) and VLDL ($p=0.032$) whilst there was no connection between other fractions of lipids and lipoproteins (Table 3). A significant positive correlation existed between concentrations of cholesterol and the density of the neck of the femur (T-score) ($p=0.002$), triglyc-

Parameter	Group	AM	SD	p-value
Cholesterol	Subjects in post-menopause	5.84	1.19	**0.54**
	Subjects with regular menstruation	6.01	1.19	
Triglycerides	Subjects in post-menopause	2.00	1.06	**0.09**
	Subjects with regular menstruation	1.61	0.79	
HDL	Subjects in post-menopause	1.26	0.30	**0.19**
	Subjects with regular menstruation	1.38	0.45	
VLDL	Subjects in post-menopause	0.91	0.48	**0.08**
	Subjects with regular menstruation	0.73	0.38	
LDL	Subjects in post-menopause	3.90	0.99	**0.14**
	Subjects with regular menstruation	4.29	1.35	
ApoA	Subjects in post-menopause	1.70	0.22	**<0.001**
	Subjects with regular menstruation	2.08	0.32	
ApoB	Subjects in post-menopause	1.33	0.23	**0.27**
	Subjects with regular menstruation	1.26	0.28	
apoA/apoB ratio	Subjects in post-menopause	0.79	0.16	**0.001**
	Subjects with regular menstruation	0.63	0.20	
Lipoprotein (a)	Subjects in post-menopause	0.22	0.25	**0.65**
	Subjects with regular menstruation	0.25	0.26	

Table 2. Lipid profiles in women in postmenopause and women with regular menstruation AM- arithmetic mean, SD–standard deviation, significant p-values are marked in bold font

Parameter	Z score of lumbar spine		T score of lumbar spine		Z score of neck of femur		T score of neck of femur	
	coefficient correlation	p value	coefficient correlation	p value	coefficient correlation	p value	coefficient correlation	p value
Cholesterol	-0.105	**0.455**	0.023	**0.870**	-0.095	**0.496**	-0.068	**0.631**
Triglycerides	-0.257	**0.063**	-0.298	**0.030**	-0.080	**0.568**	-0.092	**0.512**
HDL	0.217	**0.119**	0.093	**0.507**	-0.114	**0.417**	-0.105	**0.454**
VLDL	-0.255	**0.065**	-0.295	**0.032**	-0.078	**0.578**	-0.089	**0.529**
LDL	-0.026	**0.851**	0.100	**0.476**	0.026	**0.854**	0.022	**0.877**
ApoA	0.010	**0.953**	-0.056	**0.728**	-0.306	**0.051**	-0.257	**0.104**
ApoB	-0.084	**0.600**	-0.025	**0.877**	-0.071	**0.658**	0.020	**0.903**
apoA/apoB ratio	-0.190	**0.234**	-0.141	**0.378**	0.041	**0.798**	0.024	**0.881**
Lipoprotein (a)	-0.037	**0.818**	0.011	**0.946**	-0.096	**0.550**	-0.095	**0.555**

Table 3. The connection between bone density and lipid profile in subjects in post-menopause. AM- arithmetic mean, SD–standard deviation, significant p-values are marked in bold font

erides and the bone density of the lumbar spine (Z-score) (p=0.022), and Apo B and the bone density of the lumbar spine (T-score) (p=0.026) in subjects with regular menstruation (Table 4).

The subjects in postmenopause had higher concentrations of FSH (p<0.001) and LH (p<0.001), and lower concentrations of estradiol (p<0.001) and progesterone (p<0.05), whilst there were no differences in the concentrations of testosterone.

Univariant linear regression analysis was conducted in order to establish the level of the effect of each individual parameter of lipid and hormonal status, and the duration of post-menopause and age on the values of bone density of the lumbar spine (t-score). After this analysis, only the values of estradiol (p=0.03) and the length of post-menopause in months (p=0.02) were shown to have a statistically significant effect on the density of the lumbar spine. Multivariant regression analysis was also undertaken, with the bone density of the lumber spine (T-score) as the dependent variable, whilst testing the level of the effect of all the parameters of the lipid profile on this score, adjusting it by the level of the effect of estradiol and the length of post-menopause. None of the parameters of lipid profile had any significant effect, but there was a tendency towards a significant effect by triglycerides (p=0.09) and VLDL (p=0.09).

4. DISCUSSION

The connection between changes in the lipid profile and the density of bone tissue has been discovered in women who used statin in therapy for hyperlipidemia (8, 9). After several months' therapy an increase in bone mass was noticed in the same patients, which launched a large number of clinical and basic studies, to examine the connection between lipid profile, bone density and sexual steroids (10, 11).

The subjects in postmenopause in this study had significantly lower bone density in the area of the lumbar spine and also in the area of the hip, in comparison with the subjects with regular menstruation, which is also confirmed by the results of other studies. The changes in the lipid profile of the same group of subjects indicated higher levels of triglycerides and VLDL and lower concentrations of HDL without statistical significance, whilst the concentrations of Apo A were significantly lower in the group of subjects in postmenopause. The results in the literature are not consistent. According to most, women in postmenopause have an altered lipid profile, characterized by increases in cholesterol and triglycerides, and increased LDL and apolypoprotein B and lipoproteins(a) and a fall in HDL and apolipoprotein A. Testing the connection between lipid profile and bone density, a statistically significant negative correlation was found between bone density of the lumbar spine and triglyceride and VLDL values in postmenopausal women. In most studies the level of cholesterol is mentioned as a factor which correlates negatively with bone density in women in post-menopause (12, 15), although there are also newer studies which do not confirm this association. Triglycerides themselves are more rarely mentioned as factors that would independently affect bone density. So for example, in a similar study dealing with the connection be-

Parameter		Z score of lumbar spine	T score of lumbar spine spine	Z score of neck of femur	T score of neck of femur
Cholesterol	coefficient correlation	0.159	0.183	0.116	0.532
	p value	0.402	0.334	0.541	0.002
Triglycerides	coefficient correlation	0.418	0.341	-0.155	0.029
	p value	0.022	0.065	0.414	0.878
HDL	coefficient correlation	-0.060	-0.054	0.215	-0.014
	p value	0.754	0.778	0.253	0.940
VLDL	coefficient correlation	0.329	0.247	-0.132	0.122
	p value	0.075	0.188	0.486	0.522
LDL	coefficient correlation	-0.043	0.047	-0.122	0.297
	p value	0.820	0.804	0.521	0.111
ApoA	coefficient correlation	-0.093	-0.126	0.416	0.320
	p value	0.680	0.576	0.054	0.147
ApoB	coefficient correlation	0.364	0.475	-0.365	-0.324
	p value	0.096	0.026	0.095	0.142
apoA/apoB ratio	coefficient correlation	0.212	0.286	-0.338	-0.287
	p value	0.345	0.197	0.124	0.195
Lipoprotein (a)	coefficient correlation	-0.052	0.091	0.109	0.131
	p value	0.817	0.686	0.628	0.562

Table 4. The connection between the parameters of bone density and lipid profile in women with regular menstruation. AM- arithmetic mean, SD–standard deviation, significant p-values are marked in bold font

tween lipid profile and bone density in women in pre- and postmenopause in Korea, it was shown that triglycerides have a negative effect on bone density in women in premenopause, whilst in women in postmenopause they have a positive effect (12, 14). The results of our study indicate that in women in premenopause both cholesterol levels and Apo B have a positive effect on bone density. The different effects of lipid profiles on bone density in women in premenopause and postmenopause has also been confirmed by the results of other studies (13, 14, 21).

It is pointed out that these lipid changes lead in an indirect way to changes in bone density. If the skeletal supply takes place through the end arteries, then indirectly through atherosclerosis lipid changes lead to changes in bone metabolism, or changes in bone density (16). More recent studies, which had examined the effect of triglycerides and cholesterol on the occurrence of ischemic insults in the general population, have confirmed that in women, and to a lesser extent in men, increased risk is related to triglyceride and not cholesterol levels (17). Bearing the results of this study in mind and the importance of triglyceride levels in the occurrence of atherosclerosis, we can explain the effect of the level of triglycerides on bone density in postmenopause by the results of this study.

According to the results of this study, HDL did not have any significant connection with the bone density values, whether in postmenopausal women or in women with regular menstruation. These data are identical to some other research (17) where levels of HDL did not have a significant connection to bone density values in any location in premenopausal or post-menopausal women.

The results of other authors are completely opposite (18, 19), finding that women in post-menopause who had increased levels of HDL suffered from osteoporosis and suggested that determining HDL could serve as a screening method for osteoporosis. The same research states that total cholesterol or LDL did not have any significant connection with bone density. According to the results of our study, no correlation was found between LDL and bone density values in women with regular menstruation or in women in postmenopause, whilst data in the literature indicate the significant influence of high LDL levels on reducing all bone density values in postmenopausal women (19). Postmenopausal women with raised LDL values are classified as at risk for osteoporosis, and these data suggest that increased LDL values should be a risk factor for reduced mineral bone density (20). Subjects with regular menstruation had a statistically significant positive correlation between cholesterol and bone density of the hip, triglycerides and density of the lumbar spine, and ApoB and bone density of the lumbar spine. In the group of subjects in postmenopause there was no significant correlation between age and bone density values, however, there was a positive correlation between bone density values of the lumbar spine and the density of the neck of the femur and the length of post-menopause and oestrogen levels. Since there is a difference in the connection between bone density and lipid profile in women in postmenopause and women with regular menstruation, it seems that menopause itself is an important factor and hormonal changes modulate the connection between lipid profile and bone density (22, 23).

5. CONCLUSION

The effect of lipid profile on bone density differs in premenopausal and in postmenopausal women. The triglyceride levels in postmenopausal women contributes to a reduction in bone density, whilst its effect on bone density in women with regular menstruation is reversed, which indicates that the lipid profile is not an isolated factor affecting bone density, but that other factors, such as oestrogen levels and the length of postmenopause, have a significant effect on bone density.

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