Lipid Profiles as a Possible Contributor to Osteoporosis

Osteoporoz için Olası Katkısı Bulunan Lipid Profilleri

Mohammad Hosein Yazdanpanah [1], Sogol Sedighi[1], Mohammad Reza Rajabi[1], Saeed Osati [2], Azizallah Dehghan[3]
Elham Ehrampoush [4,5], Reza Alipoor[6], Reza Homayounfar [4,5]

[1] Student Research Committee, Fasa University of Medical Sciences, Fasa, Iran
[2] National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3] Kerman University of Medical Sciences, Kerman, Iran
[4] Noncommunicable diseases research center, Fasa University of Medical Sciences, Fasa, Iran
[5] Nutrition department, Fasa University of Medical Sciences, Fasa, Iran
[6] Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

ABSTRACT

Objectives: Reducing bone density is a major health problem in society. There is no general agreement on the relationship between serum lipids and bone mineral density. This study was conducted to investigate the association between lipid profile and osteoporosis.
Material and Methods: In this cross-sectional study, 1500 subjects were randomly selected from Tehran. BMD was measured in pelvic, spine and total body by DEXA using the lunar device. Collected data imported to SPSS v19.0 and linear regression was performed as an analytic test. Statistical significant was defined as P-values less than 0.05.
Results: Totally 1500 subjects participate in this study (age 40.88±11.58yr), 62% of subjects were female (n=930) and 38% were male (n=570). Age, sex and menopausal status were related to pelvic BMD (p-value<0.001). Among lipid profiles, TG (p-value =0.004), HDL (p-value =0.034) and LDL (p-value =0.005) was correlated with pelvic BMD. Total cholesterol (TC) was found to have no relationship with pelvic BMD (p-value =0.780). Also, body mass index (BMI) was related to BMD (p-value =0.001).
Conclusion: The results of our study showed that both LDL and TG have an inverse relationship with BMD. Also, HDL had a positive effect on BMD. TC had no significant role in bone mineral density.

Key Words: Lipids, osteoporosis, bone density, bone mineral content

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ÖZET

Amaç: Kemik yoğunluğunun azalması toplumda büyük bir sağlık sorunudur. Serum lipidleri ile kemik mineral yoğunluğu arasındaki ilişki hakkında genel bir uzlaşı yoktur. Bu çalışma, lipid profili ve osteoporoz arasındaki ilişkiyi araştırmak amacıyla yapıldı.
Yöntem: Bu kesitsel çalışmada, 1500 denek Tahran'da rastgele seçildi. KMY, lunar cihazı kullanılarak DEXA ile pelvik, omurga ve toplam vücutta ölçülmüştür. SPSS v19.0'a aktarılan toplanan veriler ve lineer regresyon analitik bir test olarak gerçekleştirildi. İstatistiksel anlamlılık, 0.05'ten küçük p değerleri olarak tanımlandı.
Bulgular: Bu çalışmaya toplam 1500 denek (40.88 ± 11.58 yıl) katılırken, olguların% 62'si kadın (n = 930) ve % 38'i erkektir (n = 570). Yaş, cinsiyet ve menopoz durumu pelvik KMY ile ilişkiliydi (p değeri <0.001). Lipid profilleri arasında TG (p değeri = 0.004), HDL (p değeri = 0.034) ve LDL (p değeri = 0.005) pelvik KMY ile korele idi. Total kolesterolün pelvik KMY ile ilişkili olmadığı bulundu (p değeri = 0.780). Ayrıca, vücut kitle indeksi (BMI) BMD ile ilişkili olaeak bulundu (p değeri = 0.001).
Sonuç: Çalışmamızın sonuçları hem LDL hem de TG'nin BMD ile arasında ters bir ilişki olduğunu göstermiştir. Ayrıca, HDL'nin BMD üzerinde pozitif bir etkisi vardır. Total kolesterolün kemik mineral yoğunluğunda önemli bir rolü yoktur.

Anahtar Sözcükler: Lipidler, osteoporoz, kemik yoğunluğu, kemik mineral içeriği

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Address for Correspondence / Yazışma Adresi: Reza Homayounfar Noncommunicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran E-mail: r_homayounfar@yahoo.com

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INTRODUCTION

The World Health Organization (WHO) announced osteoporosis as one of the four main enemies of human health in 1991 (1). It is the most common bone disease, characterized by bone mass reduction causing a greater risk of bone fragility (2). Globally, osteoporosis results in five million fractures per year (3). Due to hormonal changes, the risk of osteoporosis in women, more than men. According to statistical investigations, there are 25 million women and 12 million men with osteoporosis (4). The lifetime risk of this disease is almost 50% in women. In addition, the lifetime risk of death related to osteoporosis for a woman is equivalent to her risk of death from breast cancer and almost four times higher than that from uterine cancer (5).

Several factors are involved with increased and decreased bone mineral density, including race, specifically among Asians. Unfortunately, bone mineral density in Iranian women is lower than global standards, which can be attributed to the race and low level of physical activity, among others (6). Many other factors, such as genetic(7), excessive alcohol consumption(8), nutrition (9-11), age (12, 13), hormonal changes, gender (14, 15), physical activity, and long-term use of some medications have negative impacts on the bone mineral density(16-18). Nutritional factors including phosphorus and calcium, vitamin D, and high intake of coffee affect osteoporosis (19-21). Hyperlipidemia is an effective factor in osteoporosis. Duration of exposure to hyperlipidemia and its severity are also important in osteoporosis (22).

Several studies have been done on the relationship of lipid content and bone mineral density, out of which some studies have found a general relationship between them (23, 24). In contrast, some studies reject the relationship between some serum lipid content and bone mineral density (25, 26).

In this study, we intended to identify an effective factor in osteoporosis by discovering [probable] relationship between serum lipid content and bone mineral density. This understanding helps us to identify osteoporosis prone people, and prevent associated complications, such as a fracture.

MATERIAL and METHODS

This cross-sectional study was conducted on 1,500 individuals in Tehran between 21 March 2015 and 20 February 2016. Subjects were selected using cluster random sampling in Tehran. The exclusion criteria were having diseases that affect bone tissue and taking medications that affect bone tissue. The research objective was explained to the subjects and their written informed consent was gathered prior to their inclusion in the study.

Demographic information, including sex, age, and menopausal status of the subjects was collected by asking from them.

The height and weight of the subjects were also measured. Venous blood specimens of them were collected and then their bone mineral densities were measured.

The height and weight of them were measured and recorded by a trained individual, using a stadiometer with an accuracy of 0.1 cm and a digital scale with an accuracy of 0.1 kg (Seca 767, Japan), respectively. The body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters.

To measure serum lipid content, 10cc of 12-hour fasting venous blood specimen was drawn and transferred to the laboratory under ideal conditions to perform the biochemical test. The measurement of HDL, TG, and TC levels was done enzymatically, using Pars Azmoon Commercial Kits. In addition, LDL was measured by using the Fried-Wald Formula (27). Finally, serum lipid values were reported in milligrams per deciliter.

The bone mineral density was measured through dual-energy x-ray absorptiometry (DEXA) method, using lunar densitometer (GE Healthcare Lunar, Madison, WI, USA). The bone mineral densities of pelvic and spine areas, as well as the overall body, were obtained in grams per square centimeter. The device was calibrated every day by a specialist.

Data analysis was done with SPSS19 (SPSS Inc., Chicago, IL, USA). Descriptive data of the main variable was reported in form of mean and standard deviation. The independent t-test was used to compare the variables between the two groups. The linear regression analysis was carried out to determine the linear relationship between four variables, namely serum lipids, sex, age, and menopausal status, with the bone mineral density. Moreover, $p<0.05$ was considered significant.

RESULTS

Among 1,500 research samples, there were 570 men (38%) and 930 women (62%), out of which 366 women (39.4%) were in the postmenopausal stage. The mean and standard deviation values of age were 40.01±11.54 in men and 41.41±11.58 in women, indicating no significant between-groups difference ($p=0.757$).

The mean and standard deviation values of BMI were 27.34±4.60 in men and 28.24±4.83 in women, indicating no significant between-groups difference ($p=0.586$). The overall mean±standard deviation values of TG were 101.39±18.94, HDL was 44.88±9.04, LDL were 198.31±28.57 and 184.89±18.12 for TC, indicating no significant difference between men and women ($p<0.05$). Table 1 presents the results from a comparison of different variables between the men and women, and between individuals with and without osteoporosis. According to this table, there was a significant difference between individuals with and without osteoporosis in all variables. With respect to the gender, there was no difference between men and women in terms of age factor and LDL level.

Table 1. The frequency of the demographic and lipid profile in the men and women, and between individuals with and without osteoporosis.

	Male n(%)	Female n(%)	P-value	No Osteoporosis n(%)	Osteoporosis* n(%)	P-value
Age(yr)						
<30	132(43.1)	174(56.9)	0.086	299(97.7)	7(2.3)	<0.001
30-50	266(37.7)	440(62.3)		592(83.9)	114(16.1)	
>50	141(35.1)	261(64.9)		218(54.2)	184(45.8)	
Menopause						
Yes	---------	366(24.4)	----------	162(44.3)	204(55.7)	<0.001
NO	---------	1134(75.6)	----------	1009(89)	125(11)	
BMI						
<24	161(43.2)	212(56.8)	0.50	358(96)	15(4)	<0.001
24-30	204(35.4)	372(64.6)		487(84.5)	89(15.5)	
<30	205(37.3)	345(62.7)		325(59.1)	225(40.9)	
TC (mg/dL)						
<199	409(35.4)	748(64.6)	<0.001	961(83.1)	196(16.9)	<0.001
>200	151(48.1)	163(51.9)		193(61.5)	121(38.5)	
TG(mg/dL)						
<149	25(64.1)	14(35.9)	<0.001	37(94.9)	2(5.1)	<0.001
150-199	333(45.7)	395(54.3)		653(89.7)	75(10.3)	
>200	193(27.6)	507(72.4)		451(64.4)	249(35.6)	
HDL(mg/dL)						
<60	558(38.6)	887(61.4)	0.005	1117(77.3)	328(22.7)	0.002
>60	7(17.1)	34(82.9)		40(97.6)	1(2.4)	
LDL(mg/dL)						
<129	523(38)	855(62)	0.981	1101(79.9)	277(20.7)	<0.001
>130	42(37.8)	69(62.2)		64(57.7)	47(42.3)	

* Osteoporosis: subjects with T-score ≤ −2.5
No osteoporosis: subjects with T-score > −2.5

The mean±standard deviation values of bone mineral density for both genders are presented in Table 2, showing some differences in three assessment areas (p<0.05). Moreover, there was a significant difference between postmenopausal and premenopausal women in three assessment areas in terms of bone mineral density (p<0.001).

Table 2. Mean ± std. values of bone mineral density for both genders and menopausal stats

	Variable		Mean(g/cm2)	Std . deviation	P-value
Pelvic BMD	**Sex**	Male	1.10	0.12	0.002
		Female	1.12	0.15	
	Menopause Status	Menopause	1.00	0.13	<0.001
		Non-Menopause	1.19	0.11	
Spine BMD	**Sex**	Male	1.17	0.11	<0.001
		Female	1.12	0.15	
	Menopause Status	Menopause	1.01	0.14	<0.001
		Non-Menopause	1.19	0.12	
Total BMD	**Sex**	Male	1.17	0.11	<0.001
		Female	1.12	0.16	
	Menopause Status	Menopause	1.01	0.14	<0.001
		Non-Menopause	1.19	0.12	

Results from Pearson's correlation test (Table 3) showed that all serum lipids have a single-variable relationship with bone mineral density. With respect to the whole body, after the inclusion of age, gender, menopausal status, and BMI in this test, a significant correlation was observed between all serum lipids, except LDL, and bone mineral density. In the pelvic and spine areas, a significant relationship was obtained between HLD, LDL, and TG serum lipids with bone mineral density; whereas, the relationship between serum cholesterol and bone mineral density in pelvic and spine areas was not significant.

Table 3. Pearson's correlation test results between lipid profiles and bone mineral density

Serum lipids	Total body BMD*	Total body BMD**	Pelvic BMD*	Pelvic BMD**	Spine BMD*	Spine BMD**
TG	-0.443[b]	-0.085[a]	-0.411[b]	-0.098[b]	-0.426[b]	-0.051
TC	-0.385[b]	-0.058[a]	-0.406[b]	-0.033	-0.361[b]	-0.18
HDL	0.433[b]	0.79[a]	0.502[b]	0.091[a]	0.426[b]	0.067[a]
LDL	-0.416[b]	-0.53	-0.461[b]	-0.095[a]	-0.422[b]	-0.064[a]
LDL/HDL	-0.456[b]	-0.071[a]	-.529[b]	-0.140[b]	-0.461[b]	-0.088[a]

* unadjusted
** adjusted for Sex, Age, Menopause and BMI
a significant with P-value level in 0.05
b significant with P-value level in 0.001

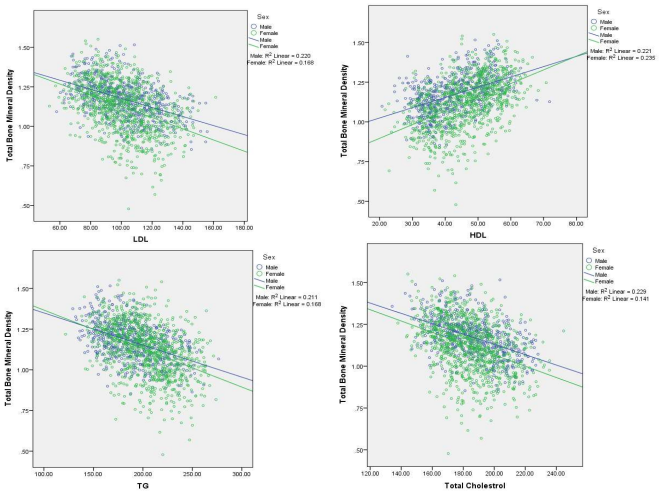

Figure 1. Diagrams of bone mineral density for different serum lipid contents: serum lipid and bone mineral density units were considered in milligrams per deciliter and grams per square centimeter.

DISCUSSION

Our results showed that serum LDL and triglyceride were inversely related to the bone mineral density. Moreover, HDL or good fat had a significant direct relationship with bone mineral density, whereas, the serum cholesterol level was not related to the bone mineral density.

According to the findings of this study, no significant relationship was found between cholesterol levels and bone density. Several relevant studies have been done, producing different results. Among the consistent studies with ours is Framingham's cohort study (28), which assessed the long-term impact of cholesterol on bone mineral density over 34 years and found no relationship between these two variables. There was no significant correlation between cholesterol and bone density in Perez and Tanko studies. These results are in line with the results of our study.(29, 30). Sahmani et al.'s study on postmenopausal women showed an inverse correlation between cholesterol level and bone mineral density (31). A study in Japan revealed a higher cholesterol level among postmenopausal women with fracture (32). Another study showed that individuals with cholesterol level higher than 240 milligrams per deciliter had lower bone mineral density (33), whereas, our study did not find any relationship between cholesterol level and bone mineral density.

In this study, we found an inverse correlation between triglyceride and pelvic bone density. Cui et al. investigated 867 Korean women and observed a direct correlation between triglyceride and pelvic bone densities (34). Adami et al. in a study in Italy reported the same results (35). The results of the Adami and Cui studies are identical with our results. In contrast, some studies reject the relationship between these two variables (26, 29, 30). However, we found an inverse correlation between triglyceride and pelvic bone density. Although further studies are required on this subject, it can be said that hyperlipidemia, with triglyceride as its main indicator, is an effective factor in the progress of osteoporosis.

According to the results of this study, the LDL inversely and significantly correlated with bone mineral density. Saghafi et al. reported an inverse correlation between LDL and bone mass (23), which was consistent with our study. In contrast, Adami et al. showed a direct relationship between LDL and bone mass (35). Other studies attributed the relationship between low bone mineral density and osteoporosis in postmenopausal women to some risk factors, such as oxidized lipids, leptin, osteoprotegerin and osteocalcin (36, 37). Increased level of oxidized lipids can result in an inflammatory reaction in vascular wall cells, leading to the progress of atherosclerosis. It can also inhibit bone mineralization (38). This mechanism can explain the results of our study, maintaining that LDL as an effective inflammatory risk factor in atherosclerosis may have an inverse correlation with bone mineral density and result in osteoporosis and atherosclerosis in postmenopausal women.

The results of this study showed that HDL has a direct and significant relationship with bone mineral density. There are several other contradictory studies about HDL. D'Amelio et al. in a case-control study concluded that HDL has an inverse relationship with bone mineral density (39) that is not consistent with our study results, whereas, Brownbill et al. did not observe any relationship between these two variables (25). In contrast, we found a direct relationship between HDL and bone mineral density.

Increased blood lipids and their metabolism can increase blood acidity, and affect bone mineral and mineral densities. Serum lipids can also affect bone cells (osteoblast and osteoclast) (40). In addition, the production of lipoproteins and oxidation of them prevent bone cell proliferation, and thus reduce bone mineral density. Lipid and lipoprotein oxidation and metabolism in bone tissues can result in the differentiation of osteoclasts, leading to bone tissue loss (41). Lipid accumulation in the bone affects osteoblast cells and inhibits bone formation (38). Studies showed that oxidized lipids may play a role in bone cell function by inhibiting osteoblast. Minimally oxidized LDL (MM-LDL), isoprostane 8-iso prostaglandin E2 (isoPGE2), and oxidized 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphorylcholine (Ox-PAPC) are such agents that cause this inhibition. These oxidized lipids can increase inflammatory response and also stop differentiation by inhibition of alkaline phosphatase activity, extracellular matrix maturation, and mineralization (42-45). Recent studies showed that oxidized lipids also might have some effects on bone by targeting osteoclast cells as well as osteoblasts. Oxidized lipids can stimulate osteoclast via a cAMP-mediated pathway that induces the RANKL-dependent osteoclastic differentiation of these cells by increasing TRAP activity, the formation of multinucleated cells, and mineral resorption(46, 47). The effects of oxidized lipids can be caused by direct interactions with the cells via receptor-mediated responses and induce the expression of cytokines such as MCP-1, M-CSF, and IL-6 both in vitro and in vivo(48, 49). Our results may be justified based on the probable mechanisms mentioned above. However, the main mechanism of serum lipid-bone mineral density relationship is still uncertain.

Accordingly, there are very different results regarding the relationship between serum lipids and bone mineral density, which can be attributed to the differences in research population, race, menopausal status, age, and bone mineral density of different body parts. Although, the conduction of more precise studies are necessary in this area also our study is a cross-sectional research that we cannot approve definitive relationship between serum lipids and bone mineral density. Our results, along with high rate of pelvic fracture suggest that serum lipids can be taken as a probable risk factor for osteoporosis. In this way, irreparable damages and high costs of pelvic fracture can be reduced, and effective steps can be taken to prevent osteoporosis. Therefore, the conduction of lipid profiles tests for those prone to osteoporosis, specifically women at the age of menopause, is recommended. The control of this probable risk factor of osteoporosis helps them to prevent multiple complications associated with this disease.

Conflict of interest

No conflict of interest was declared by the authors.

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