

Dyslipidemia – A Risk Factor for Osteoporosis in Women: A Cross-Sectional Study

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ABSTRACT

Background: Osteoporosis has been extensively studied in postmenopausal women but there is a paucity of studies for detection of osteoporosis in premenopausal women. Recent studies point out that dyslipidemia could be a risk factor for osteoporosis in postmenopausal women. It is unclear whether dyslipidemia in premenopausal women is a risk factor for osteoporosis after menopause. This study is an attempt to find whether dyslipidemia in premenopausal and postmenopausal women is associated with decreased bone mineral density (BMD). **Methods:** The study was conducted from November 2013 to March 2014 at Lady Hardinge Medical College, New Delhi. Sixty patients (30 premenopausal and 30 postmenopausal) who were not having any comorbidity and not on any drug affecting lipid or bone metabolism were evaluated for lipid profile and BMD. **Result:** In premenopausal women, there was a negative correlation between very low-density lipoprotein cholesterol (VLDL-C), triglycerides (TGs), and BMD (lumbar vertebra) while a positive correlation was observed between high-density lipoprotein cholesterol (HDL-C) and BMD, which was statistically significant (VLDL-BMD $r = -0.363$, $p = 0.049$; TRI-BMD $r = -0.363$, $p = 0.049$; HDL-BMD $r = 0.359$, $p = 0.05$). Similarly, in postmenopausal women, the negative correlation between VLDL, TG, and BMD was statistically significant (TG-BMD $r = -0.377$, $p = 0.04$; LDL-BMD $r = 0.415$, $p = 0.02$), as was the positive correlation between HDL and T-score (HDL-BMD $r = 0.366$, $p = 0.04$). **Conclusion:** There is statistically significant correlation between BMD and serum lipid levels in both premenopausal and postmenopausal women. Lipid profile variables show a significant association with BMD and can be used as risk factors for osteoporosis.

Keywords: Osteoporosis, lipid profile, premenopausal, postmenopausal, bone mineral density, T-score

Skeleton is a dynamic tissue, getting remodeled constantly throughout life. Compact and cancellous bones are arranged in a fashion to provide tensile strength and density for mobility and protection of the body. Remodeling is achieved by two different cell types: osteoblasts, which synthesize bone matrix, and osteoclasts, which reabsorb it¹. Osteoporosis in postmenopausal women has been extensively studied and an epidemiological study by Saghaei et al has suggested a correlation between cardiovascular disease and osteoporosis². There is paucity of studies done for

detection of osteoporosis in premenopausal women, especially in metropolitan cities. Dyslipidemia is an established risk factor for cardiovascular diseases, but recent studies by Adami et al³ and Wu et al⁴ suggest that it might also be a risk factor for osteoporosis. While much emphasis is given to the morbidity associated with osteoporosis in postmenopausal women after the speculated protective effect of estrogen wanes off, epidemiological data suggest that estrogen deficiency is a risk factor for cardiovascular diseases and osteoporosis. Estrogen receptors have been demonstrated to have effects on osteoblasts and osteoclasts⁵. No study has found a reliable way of detecting these in the premenopausal period itself. While it is true that bone mineral density (BMD) decreases in postmenopausal women⁶, it is unclear whether dyslipidemia in premenopausal women is a risk factor for osteoporosis in their postmenopausal period^{7,8}. Various studies in mice with controlled age, genetics, and environment have proved to be helpful in identifying the relation between high-density lipoprotein cholesterol (HDL-C) and BMD^{9,10}. There is a possible relationship between bone loss and dyslipidemia. Immunological and inflammatory

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factors play an important role in the pathophysiology of both diseases. One of these factors is osteoprotegerin (OPG), a soluble glycoprotein that belongs to the tumor necrosis factor (TNF) receptor super family. It acts as a decoy receptor of the receptor activator of nuclear factor κ B ligand (RANKL), which is an important regulator of osteoclastogenesis. OPG is known to inhibit osteoclastogenesis by binding to RANKL, preventing it from binding to the receptor activator of NF- κ B on osteoclasts. It has been reported that OPG is highly expressed in the bones, heart, and major arteries. Recently, OPG has been shown not only as an inhibitor of osteoclastogenesis, but also as a preventive mediator of cardiovascular diseases, such as arterial calcification and atherogenesis^{11,12}. Both osteoporosis and atherosclerosis are chronic degenerative diseases with high incidence in developed countries. The prevalence of both pathologies increases with advancing age^{13,14}. This study aimed to find if dyslipidemia in premenopausal and postmenopausal women was associated with decreased BMD.

MATERIALS AND METHODS

This cross-sectional observational study was conducted from November 2013 to March 2014 in the Institute of Internal Medicine and Department of Radiology, Lady Hardinge Medical College, New Delhi. A total of 60 patients were included. Patients were divided into two groups: premenopausal (30-45 years who had not attained menopause) and postmenopausal (women aged 45 years and older who had attained menopause), with 30 patients in each group. We excluded patients with diabetes mellitus, cancer, hypertension, smoking, bone disease, chronic kidney disease, hypothyroidism, hyperthyroidism, and those receiving antiepileptics, levothyroxine, statins, antithyroid drugs, steroids, estrogen derivatives, bisphosphonates, selective estrogen receptor modulators, or any other drug affecting lipid or bone metabolism.

Each patient was subjected to appropriate history and clinical examinations as per the Proforma and subjected to the following investigations: measurement of height, weight and waist circumference, blood glucose, fasting lipid profile, and dual-energy X-ray absorptiometry (DEXA) scan (lumbar spine). Blood glucose samples were transported in fluoride containers, and samples for lipid profile were transported in plain containers. Both were measured by fully automated analyzer AU480 (BECKMANN) using Randox kits.

DEXA scan was done by Hologic Version 13.0:5, model Discovery Wi (S/N 84571). Statistical analysis

was performed by the SPSS program for Windows, version 20.0. Continuous variables were presented as mean $\pm$ SD using unpaired *t*-test and Mann-Whitney *U* test. Data was checked for normality before statistical analysis using Shapiro-Wilk test. Pearson correlation was also used to measure the direct correlation between various lipid parameters and DEXA scan reports. For all statistical tests, a *p* value <0.05 was considered to be statistically significant.

RESULTS

This study included 30 premenopausal women with mean age of 36.10 ± 4.06 years and 30 postmenopausal women with mean age of 59.60 ± 7.29 years. The demographic and anthropometric profile of the patients has been shown in Table 1. The lipid profile and BMD of the patients are shown in Table 2. Pearson's correlation between lipid profile and BMD at lumbar spine is shown in Table 3. The correlation between total cholesterol and BMD in lumbar spine was assessed with the help of the Pearson Product Moment

Table 1. Characteristics of the Anthropometric Parameters of Study Population

Parameters	Premenopausal		Postmenopausal		P value
	Mean	$\pm$ SD	Mean	$\pm$ SD	
Height (m)	1.55	0.05	1.51	0.06	0.008
Weight (kg)	54.10	7.05	53.10	7.79	0.302
BMI	22.62	2.78	23.35	3.12	0.173
Waist circumference	68.63	3.96	66.68	3.62	0.040

Table 2. Characteristics of Lipid Profile and DEXA Scan of Study Population

	Premenopausal		Postmenopausal		P value
	Mean	$\pm$ SD	Mean	$\pm$ SD	
Total cholesterol	123.83	24.87	163.63	54.65	≤ 0.001
LDL-C	59.55	24.84	99.87	55.18	≤ 0.001
VLDL-C	22.65	3.21	24.33	4.62	0.054
HDL-C	41.67	6.27	39.43	7.47	0.107
TG	113.27	16.06	121.67	23.09	0.054
DEXA BMD (L)	0.90	0.10	0.74	0.19	<0.001

Table 3. Correlation Between Lipid Profile and DEXA Scan at Lumbar Vertebra

Lipid profile variables	DEXA BMD (L) Premenopausal		DEXA BMD (L) Postmenopausal	
	Pearson correlation “r”	P value	“r”	P value
LDL-C	-0.318	0.087	-0.358	0.052
VLDL-C	-0.363	0.049	-0.064	0.738
HDL-C	0.359	0.051	0.357	0.053
TG	-0.363	0.049	-0.064	0.738

Correlation (PPMC) denoted as “r”. The correlation (*r*) between low-density lipoprotein (LDL) and BMD in lumbar spine was -0.318 in premenopausal group and -0.358 in postmenopausal female. This indicates that both groups had moderate negative correlation; however, the correlation was statistically not significant in both groups (*p* = 0.087 and 0.052, respectively). The correlation coefficient (*r*) between very low-density lipoprotein (VLDL) and BMD in lumbar spine was -0.363 in premenopausal group. This indicates a moderate negative correlation, which was statistically significant (*p* = 0.049). In postmenopausal group, *r* was -0.064 indicating negligible relationship and the correlation was not statistically significant (*p* = 0.738). PPMC coefficient (*r*) between HDL and BMD in lumbar spine was +0.359 in premenopausal group and 0.357 in postmenopausal females. It indicates a moderate positive correlation; in both the groups the correlation was statistically nonsignificant (*p* = 0.051 and 0.053). The PPMC coefficient between triglycerides (TGs) and BMD in lumbar spine was -0.363 in premenopausal group. It indicates a moderate negative correlation and the correlation was statistically significant (*p* = 0.049). In postmenopausal group, “*r*” was -0.064 indicating a negligible relationship and the correlation was not statistically significant (*p* = 0.738).

DISCUSSION

Our results show that the levels of LDL-C and BMD (lumbar spine) show moderate negative correlation in premenopausal as well as postmenopausal women. An inverse association has been described by Yamaguchi et al¹⁵ between BMDs at two (radius and lumbar spine) of the four sites measured (total body, radius, lumbar spine, and femoral neck) and serum LDL-C levels. However, in the study by Poli et al¹⁶, BMD of only the lumbar spine (2-4) site showed a negative association with serum LDL-C levels in postmenopausal women.

The result of these two studies indicating inverse relationship between LDL-C and BMD are similar to our findings but they differ from our results with respect to site of BMD measurement. These differences can be explained by different age distribution, different study population (premenopausal females not included in both studies) and differences in the methodology (skeletal sites of BMD measurement - radius, femoral neck, and spine). Previous studies have also shown differences in age-related BMDs at various skeletal sites in different races¹⁶. Therefore, it is possible that BMD values at different sites produce different outcomes. Our results indicate that the levels of VLDL-C and BMD show moderate negative correlation in lumbar spine for premenopausal as well as postmenopausal women^{17,18}.

Literature indicating the effect of serum TGs on BMD is very scarce. Our study shows that the levels of TGs and BMD are also moderately negatively correlated in lumbar spine for premenopausal as well as postmenopausal women. However, Cui et al¹⁹ and Adami et al³ found a positive correlation between TGs and BMD.

In our study, the levels of HDL-C and BMD show a moderate positive correlation in premenopausal as well as postmenopausal females. Notably, studies conducted by Yamaguchi et al¹⁵ and D’Amelio et al²⁰ have reported an association between BMD and HDL-C, although these results were not in accordance. Positive relationship was pointed out by Yamaguchi et al¹⁵, while a negative correlation between two parameters was described by D’Amelio et al²⁰. However, Poli et al¹⁶ did not find any association between BMD and serum HDL-C levels in postmenopausal women.

CONCLUSION

Our data indicate a relationship between BMD values and serum lipid levels. It suggests that for the lumbar spine, the levels of VLDL-C and serum TGs had negative, while HDL-C had positive association with BMD in premenopausal as well as postmenopausal women. Hence, lipid profile variables show a significant association with BMD and can be used as risk factors for osteoporosis in both premenopausal and postmenopausal women.

However, our study had few limitations. Since this study was conducted in a hospital in a metropolitan city, it might not be representative of the entire female population. Serum vitamin D levels were not considered in the study. The sample size of the study is small and so the power of the study is reduced. Further studies with large sample size are needed to validate the findings of our study.

BENEFITS AND RECOMMENDATIONS OF STUDY

We hypothesized that dyslipidemia is related to BMD and may independently predict the risk for osteoporosis. By controlling dyslipidemia with lifestyle modifications and pharmacotherapy, osteoporosis can potentially be prevented.

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