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Comparative Cross-Sectional Study

Correlation of Lipid Profile with Bone Mineral Density in Postmenopausal Women

Jyoti Jain[1], Sunita Hemani[2], Lata Rajoria[3], Jyotsna Vyas[4], Shrikant Sharma[5]

[1]Senior Registrar, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur, Rajasthan, India.

[2]Associate Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur, Rajasthan, India.

[3]Senior Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur, Rajasthan, India.

[4]Senior Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur, Rajasthan, India.

[5]Associate Professor, Department of Medicine, S.M.S. Medical College, Jaipur, Rajasthan, India.

Corresponding author: Sunita Hemani, Associate Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur, Rajasthan, India.

Email: skant_sunita@yahoo.co.in

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Abstract

Introduction: Osteoporosis is a major health problem in postmenopausal women and is most often diagnosed late. These women are also prone to developing dyslipidaemia and cerebrovascular disease. A correlation between serum level of lipids and bone mineral density has not been established. The possible relationship between lipid profile and bone mineral density (BMD) in postmenopausal women of India was investigated.

Aim: The study was aimed to examine the correlation of lipid profile with bone mineral density in postmenopausal women.

Methodology: This hospital-based comparative and cross-sectional study included 110 postmenopausal women who fulfilled the inclusion and exclusion criteria. A proper history was taken and clinical examination was done. Following this, lipid profile was done after 12 hours of fasting and was considered abnormal if serum cholesterol was >200 mg/dL; triglycerides (TG) ≥150 mg/dL and high-density lipoproteins (HDL) ≤50 mg/dL. Then, dual-energy x-ray absorptiometry (DEXA) was done at the lumbar spine (L2-L4) to assess the bone mineral density and diagnose osteoporosis. The women were then divided into two groups. Group 1 consisted of 55 women who had osteoporosis and Group 2 consisted of the same number of women, but without osteoporosis. A correlation between lipid profile and osteoporosis were done in both the groups by using various statistical tests.

Results: The two groups showed no significant difference in the mean age, parity, body mass index (BMI) and menstrual years. Mean cholesterol and low-density lipoprotein (LDL) levels were significantly higher in Group 1 (women with osteoporosis). The mean triglyceride and HDL levels were also higher in postmenopausal women with osteoporosis, though not statistically significant. When data were entered into the model of multivariate regression, it showed that an elevated level of total cholesterol was an independent risk factor for osteoporosis in postmenopausal women (p=0.01).

Keywords: Postmenopausal, osteoporosis, lipid profile, serum cholesterol, bone mineral density

Introduction

Every woman experiences a transition phase in her life, from reproductive to non-reproductive. Apart from the reproductive functions, menopause a much more range of wider implications. This is the time when women are prone to develop a series of non-communicable diseases like diabetes, hypertension, etc.[1,2]

Natural menopause occurs between 45 and 55 years of age. However in India, the range of mean age at menopause is less and is between 41.9 and 49.42 years.[3,4] Life expectancy has increased all over the world, and hence, more women face menopause-related problems, osteoporosis being one of them.

Osteoporosis is a systemic skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissues with a consequent increase in bone fragility and susceptibility to fracture and involves the wrist, spine, hip, pelvis, ribs or humerus.[5] It is important to identify the risks associated with osteoporosis to prevent fractures.

For women, a DEXA scan and clinical fracture risk assessment (FRAX) is appropriate at menopause. The Indian Menopausal Society recommends that bone mineral density should be measured by DEXA scan in all postmenopausal women more than 5 years of menopause or even less than 5 years, but with risk factors those with fragility fractures, menopause transition with secondary causes, radiological evidence of osteopenia and presence of vertebral compression fracture and to initiate or monitor pharmacotherapy for osteoporosis.[6]

According to the World Health Organization (WHO), BMD should be used as a primary diagnostic index for osteopenia and osteoporosis. However, BMD is not a reliable marker for early diagnosis as it lacks sensitivity.[7] Atherogenic lipid profile is associated with osteopenia and osteoporosis. It is postulated that in atherogenic lipid profile, LDL particles may accumulate in the subendothelial matrix of bone vessels and are oxidised.[8] They in turn reduce the viability of osteoblasts.[9]

They were also found to affect bone resorption by increasing osteoclastogenesis and cytokines production such as receptor activator of nuclear factor-κb (RANK) and interleukin 6 (IL-6) from both T lymphocytes and osteoblasts resulting in reduced bone mineralisation. It has also been reported that oxidized lipids downregulate parathyroid hormone receptor (PTHR) in osteoblasts causing resistance to PTH.[10,11]

It is important to diagnose osteoporosis and measure bone mineral density. DEXA scan constitutes the most important test for this. In this, an enhanced form of x-ray technology is used to measure the bone mineral content (calcium) or bone loss and density of specific skeletal sites or whole body. It is the most effective technique to measure bone mineral density.

This technique is rapid, taking only 3 to 7 minutes, and delivers a radiation dose that is so low as to be equivalent to approximately 5% of the radiation dose of one chest radiograph. This study is aimed at diagnosing osteoporosis in postmenopausal females and correlating it with lipid profile with the purpose that if an association is found, then an altered lipid profile might guide the clinician for a possibility of development of osteoporosis.

Material and Methods

It was a hospital-based comparative and cross-sectional study conducted in the Department of Obstetrics and Gynaecology, S.M.S Medical College, Jaipur, Rajasthan, India. Approval was obtained from the Ethics Committee, S.M.S Medical College, Jaipur, Rajasthan, India. Those women who did not have any menstrual period for the last one year were screened. Demographic characteristics of these postmenopausal women were noted which included age, occupation of self and family, educational status, the total income of family, smoking or alcohol intake was noted. These were then subjected to a detailed history taking regarding any illness and drug intake including calcium and vitamin D supplementation. A thorough clinical examination including BMI and biochemical tests were done on those with no such history or treatment records. These tests included a complete blood count, erythrocyte sedimentation rate, C-reactive protein, fasting blood sugar, renal and liver function tests, thyroid profile, vitamin D levels, parathyroid hormone levels, calcium levels. Those women who fulfilled the inclusion and exclusion criteria were included in the study. The sample size was calculated at 80% study power and an alpha error of 0.05. For a minimum detectable mean difference of 23.2 mg/dL in total cholesterol between the two groups, 51 patients in each group were required as sample size which was enhanced and rounded off to 55 patients as final sample size expecting 10% dropouts/attrition. Thus, the study included 110 postmenopausal women fulfilling the inclusion and exclusion criteria. Two groups were made. Group 1 consisting of postmenopausal females who had been diagnosed with osteoporosis while Group 2 consisted of a similar number of postmenopausal females who did not show osteoporosis.

Inclusion Criteria

Postmenopausal women (atleast 1 year without menses) with body mass index (BMI) in the range 18.5 to 25 kg/m^2, willing to participate in the study and give written informed consent were included in the study.

Exclusion Criteria

- Malignant disease

- Women who were suffering from diseases like diabetes, thyroid, parathyroid and adrenal gland disorders, chronic renal failure, inflammatory arthritis and diseases of the gastrointestinal tract
- Women using drugs like statins, corticosteroids, hormones and diuretics for more than three months
- Secondary osteoporosis due to endocrine diseases
- History of peptic ulcer surgery
- Osteoporosis induced by medications

These women were subjected to detailed menstrual and obstetric history. Detailed clinical examination was done. For assessing lipid profile, samples were taken from a peripheral vein after 12 hours of fasting and were immediately centrifuged at 4°C. Plasma was used to analyse the lipid profile-total cholesterol, LDL, TG and HDL.

Lipid profile was estimated by using the enzyme calorimetric technique. It was considered abnormal if cholesterol >200 mg/dL; triglycerides ≥150 mg/dL and HDL ≤50 mg/dL.

Along with that, a DEXA scan was done at the lumbar spine (L2-L4) and at the neck of the femur to assess the bone mineral density to diagnose osteoporosis. T-score measured in standard deviation showed the difference between a patient's BMD and that of healthy young adults of the same sex. A positive score indicated bone to be stronger than normal.[12] Z-score showed the amount of bone, compared with other people in same age group and of the same size and gender.[12]

Results were interpreted graphically and osteoporosis was diagnosed when the T score was less than or equal to 2.5.

A correlation between lipid profile and osteoporosis was done in both the groups.

The data obtained was tabulated, compared and analysed by $\chi 2$ test to identify differences in baseline characteristics between both the groups. Data were presented as mean±standard error values for continuous variables and as percentage±standard error for categorical variables. Statistical analysis was performed. A p-value <0.05 was considered to be statistically significant.

Results

A total of 110 postmenopausal women were included in the study, with 55 each in the two groups. The mean age of women in Group 1 (with osteoporosis) was 53.7±5.07 years while it was 54.47±4.64 years in Group 2 (p=0.354). There was no statistically significant difference in the mean age of the two groups. Most of the women in both the groups belonged to the middle class (78.18% in Group 1 and 72.72% in Group 2). No statistically significant difference was found when the two groups were compared for socio-economic status. None of the women included had a history of calcium or vitamin D intake in the past six months. 76.36% of osteoporotic postmenopausal women (Group 1) were multiparous while 81.82% of women in Group 2 were multiparous. When this factor was compared between the two groups, the difference was not found statistically significant.

Postmenopausal women in the BMI range of 18.5 to 25 kg/m^2 only were included in the study. Others were excluded from the study to avoid confounding factors. The mean BMI in women with osteoporosis was 22.16±1.88 kg/m^2 and in Group 2 was 21.98±2.18 kg/m^2. This difference was insignificant (**Table 1**). It was observed in many studies that a fewer number of menstrual years was associated with an increased incidence of osteoporosis, hence the two groups were compared for age at menarche. No statistically significant difference was observed in the two groups when age at menarche was compared (**Table 1**). 24 women in Group 1 and 27 women in Group 2 attained menopause during 51-55 years of age. When women in the two groups were compared for age at which menopause was achieved, no statistically significant difference was observed (**Table 1**). Similarly, there was no difference between the two groups when the time since the last delivery was compared (**Table 1**).

Table 1 shows that in group 1, 42 women (76.36%) were parity ≥3 or more while in Group 2, their number was 45 (81.8%). When this factor was compared, this difference was not found statistically significant. None of the women in both groups was smokers or consumed alcohol and none had a history of spontaneous fracture in the past. Hypertension was seen in 8 (14.5%) women in Group 1 and 7 (12.7%) in Group 2. The difference in the number of hypertensives in the two groups was not statistically significant. These women were on anti-hypertensives other than those mentioned in the exclusion criteria (**Table 1**).

Table 1. Demographic characteristics of women included in study

Demographic characteristics	Group 1 (n=55)	Group 2 (n= 55)	p-value
Age at menarche mean (SD)	13.25 years (0.67)	13.24 years (0.65)	0.912
Age at menopause mean (SD)	50.32 years (1.41)	49.67 years (1.36)	0.865
Time since last delivery mean (SD)	16.81 years (3.99)	18.43 years (3.98)	0.038
Body mass index (kg/m^2) mean (SD)	22.16 (1.88)	21.98 (2.18)	0.616
Parity 0-2 n (%)	13 (26.63%)	10 (18.2%)	Overall p=0.62
Parity ≥3 n (%)	42 (76.36%)	45 (81.8%)	Overall p=0.62
Smokers n (%)	0 (0%)	0 (0%)	--
Women taking alcohol n (%)	0 (0%)	0 (0%)	--
H/o spontaneous fracture n (%)	0 (0%)	0 (0%)	---
Hypertensives n (%)	8 (14.5%)	7 (12.7%)	0.47

Table 2 shows the mean value of total cholesterol, TG, HDL and LDL. A ratio of TG/HDL was also calculated. Difference between the two groups was seen and it was found that the mean cholesterol levels and LDL levels were significantly higher in Group 1 (women with osteoporosis). The mean triglyceride level was also higher in postmenopausal women with osteoporosis, though not statistically significant. The mean levels of HDL were also higher in Group 1, but the difference between the two groups was statistically insignificant. The ratio of TG/HDL was greater in Group 1 (not statistically significant).

Table 2. Comparison of lipid profile in the two groups. Abbreviations: HDL- High-density lipoprotein; LDL- Low-density lipoprotein; TG- Triglycerides.

	Group 1		Group 2		
Lipid profile	**Mean**	**SD**	**Mean**	**SD**	**p-value**
Total cholesterol (mg/dL)	199.06	38.71	177.94	71.76	0.001
Triglyceride (mg/dL)	176.43	68.63	150.40	81.18	0.004
HDL (mg/dL)	45.76	6.31	45.10	7.27	0.607
LDL (mg/dL)	133.00	24.31	121.29	28.87	0.01
TG/HDL ratio	4.04	1.98	3.52	2.22	0.15

The examined factors that were statistically significant in the model of univariate logistic regression were entered into the model of multivariate regression, the results of which showed that elevated levels of total cholesterol was an independent risk factor for osteoporosis in postmenopausal women (p=0.01), while the other parameters of lipid profile were not relevant for osteoporosis development (**Table 3**).

Table 3. Risk factors for osteoporosis identified by multivariate logistic regression. Abbreviations: HDL- High-density lipoprotein; LDL- Low-density lipoprotein; TG- Triglycerides.

Risk factor	p-value
Cholesterol	0.01
LDL	0.45
TG	0.92
HDL	0.952

Discussion

Our study aimed at finding an association between atherogenic lipid profile and the development of osteoporosis. Many studies have suggested that hyperlipidemia has a role in the development of both atherosclerosis and osteoporosis. Our results were similar to many studies. BMI is one of the factors which affects the development of osteoporosis, so only those patients were included in the study whose BMI was normal. Sadat Ali *et al.* found a statistically significant difference in BMD with a difference of 10 in mean BMI among postmenopausal women.[13] Skrzek A *et al.* suggested that 26.9 kg/m^2 is the optimal value of BMI which would indicate the most favourable preservation of the bone mineral density in postmenopausal women.[14] We also found that early menarche and late menopause was protective against osteoporosis. Mendoza-Romo MA *et al.* found that women who attained menarche at an age more than 13 years were more prone for osteoporosis in postmenopausal age (OR 4.46; p=0.035).[15] Parker SE *et al*. observed that women who attained menarche at 11 years of age or less were associated with a reduced incidence of osteoporosis.[16] They also found an incidence rate ratio for the association between age at menopause (≥50 years) and osteoporosis risk and it was 0.61 (CI 0.40, 0.92). Women who menstruated for ≤25 years were more strongly associated with osteoporosis than women who had menses for ≥35 years (IRR 1.80; CI 1.14, 2.86). Sioka C *et al.* studied that the women who attained their menopause at ≤45 years of age had decreased bone mineral density (p=0.034).[17] We JS *et al.* found that the age at last childbirth significantly influenced the prevalence of osteoporosis irrespective of BMI ≥25 kg/m^2 (p <0.001) in postmenopausal women.[18]

When levels of serum cholesterol in the two groups were compared, there was a statistically significant difference with increased values in women with osteoporosis. Similar findings were observed by Shukla J *et al.* who found that postmenopausal women with osteoporosis had significantly increased values of total cholesterol (mean=137.11 mg/dL, SD=7.28) and triglycerides (mean=137.11 mg/dL, SD=7.28).[19]

YY Chen *et al*. found that postmenopausal women with osteoporosis had a significantly higher total cholesterol level compared to those with the normal bone mineral density.[20] Garg MK *et al.* observed that BMD at femur (0.887±0.152) decreased significantly with increasing quartiles of total cholesterol (<200 mg/dL, p=0.024).[21]

Few studies have dismissed any association between these two. Adami and colleagues found no significant association of elevated serum cholesterol with a decrease in bone mineral density at the hip level in women aged 68-75 years.[22] Li *et al*. observed the same.[23]

Sivas *et al*. found that the mean serum cholesterol of women with vertebral fractures was significantly lower than the patients without fractures (mean=214.4±4.3 mg/dL with p<0.05).The results of this study are in contrast to our study.[24] However, they suggested a significant correlation between serum triglycerides and women prone to fractures (mean=139.4±7.8 mg/dL with p <0.05) which is by our study results.

Adami and colleagues found a strong positive correlation of lumbar spine bone mineral density Z (BMD-Z) score values and triglycerides level in postmenopausal women (mean=1.50 mmol/L, SD=0.71).[22] Bijelic R *et al*. found that elevated serum triglyceride levels (p=0.033) were significantly associated with osteoporosis.[25]

We did not find any significant difference in HDL values between the two groups as did Adami and colleagues and Sivas *et al.* who also found no significant association of decreased serum HDL cholesterol with a decrease in bone mineral density.[22,24] However, YY Chen *et al.* showed that osteoporosis group had a significantly higher HDL level compared to the normal density group.[20] Yamaguchi *et al.* evaluated the relationships between plasma levels of HDL-cholesterol and observed that it was significantly and positively correlated (p<0.05) with BMD values and hence associated with the presence of vertebral fractures in postmenopausal women.[26]

In the study conducted by Bijeclic R *et al.,* the results of univariate logistic regression analysis show that the total cholesterol (p=0.000, OR=1.006, 95% CI=1.003 to 1.0009), LDL (p=0.005, OR=1.005, 95% CI=1.001 to 1.008) and triglycerides (p=0.033, OR=1.004, 95% CI=1.000 to 1.008) are significant risk factors for osteoporosis, although in the multivariate logistic regression, LDL cholesterol and TG were not identified as independent risk factors.[25] Results of multivariate regression analysis showed that the increased value of total cholesterol is a significant independent risk factor for osteoporosis in postmenopausal women (p=0.018, OR=1.006, 95% CI=1.001 to 1.010).[24] This is similar to the results of our study which also suggests increased total cholesterol values in postmenopausal women with osteoporosis.

Limitation of the Study

The sample size is small for the results to apply to the general population. Further studies on a larger population may be required to consolidate the findings of the study.

Conclusion

Altered lipid parameters (serum cholesterol and LDL cholesterol) are found to be associated with decreased bone mineral density in postmenopausal women. If the results of this study are considered, testing of lipid profile in preventing cardiovascular diseases may have unexpected ramifications beyond that in the area of osteoporosis as well. Preventive measures can be instituted in these women in the form of lifestyle modifications, diet and drugs so as to improve their quality.

Declaration of conflicting interests

The authors have no conflicts of interest to declare.

Ethical approval

Ethical approval was obtained from the Ethics Committee, S.M.S Medical College, Jaipur, Rajasthan, India (ethical approval no. 2437/M/EC/2016). Written informed consent was obtained from patients.

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