



Study of osteoporosis in postmenopausal woman and its relation to vitamin D deficiency and daily calcium intake.

**Dr. Prajakta Sawai
(Aswar)**

Assistant Professor in the Dept. of Obstetrics and Gynaecology, MGIMS, Sewagram.

ABSTRACT

Objective: We evaluated the combined effects of vitamin D and daily calcium intake on bone mineral density (BMD) and osteoporosis in the postmenopausal women.

Methods: This study is a cross-sectional record based study consisting of 1,921 postmenopausal women aged 45 to 70 years without thyroid dysfunction, from 2006 to 2012.

Results: The BMD divided according to serum 25(OH)D and daily calcium intakes were not statistically different among the groups. However, when both daily calcium intake and serum 25(OH)D were not sufficient, risk of osteopenia and osteoporosis showed significant increase in both femur neck and lumbar spine (odds ratio [OR] 2.242, $P=0.006$; OR 3.044, $P=0.001$; respectively).

Conclusion: The combined effects of insufficient daily calcium intake and vitamin D deficiency may cause low BMD and increase in prevalence of osteopenia and osteoporosis in the postmenopausal women aged 45 to 70 years.

KEYWORDS : Bone density, Calcium intake, Menopause, Osteoporosis, Vitamin D

Introduction

The life expectancy of women is increasing, but the average age of women at the time of menopause is about 50 years. According to the 2015 World Health Organization's annual report, global life expectancy at birth in 2015 was 71.4 years and for Indian women it's 69.9 years [1].

As women gets older, the prevalence of complications such as osteoporosis and bone fractures increase, and these could be considerable public health problem which cause a lot of social cost [2]. Postmenopausal osteoporosis occurs very commonly because of age related bone loss [3]. In previous studies, estrogen depletion are resulted from an imbalance in bone modeling and this can lead to an accelerated phase of bone loss and an efflux of bone-derived calcium to the extracellular fluids [4]. The increased fragility of bone due to changes in metabolism has also been investigated in experimental studies in rats and women [5,6]. These conditions are closely associated with osteoporosis and fractures that require major surgery. These complications can also cause women to be restricted to bed rest which consequently reduces their quality of life after menopause.

Therefore, the present study aimed to assess the combined effects of one's daily calcium intake and vitamin D level on the BMD and prevalence of osteopenia and osteoporosis in indian postmenopausal women aged 45 to 70 years.

Materials and methods

This study was conducted under the Dept. of Obstetrics and Gynaecology of a tertiary hospital taken place from 2006 to 2012. Using rolling survey sampling, subjects participated in a complex, stratified, probability cluster survey of a representative sample.

Results

Among 1921 participants, numbers of people included in the group 1 to 6 were 669, 421, 408, 238, 97 and 88, respectively.

Table 1 shows comparisons of BMD in femur neck and lumbar spine. Among participants taking moderate amounts of calcium ($400 \leq$ calcium < 800 mg/day), femur neck BMD showed tendency of difference according to the status of serum 25(OH)D ($P=0.088$).

Contrary to table 1, table 2 shows comparisons of femur neck and lumbar spine BMD according to amounts of daily calcium intake within vitamin D sufficient and insufficient groups. There were no significant differences among the groups in both serum 25(OH)D < 20 ng/mL and ≥ 20 ng/mL groups in femur neck BMD ($P=0.508$, $P=0.311$, respectively).

Table 3 shows OR for osteopenia and osteoporosis of femur neck and lumbar spine according to daily calcium intake and serum vitamin D levels. The logistic regression model was adjusted by age, BMI, physical activity, smoking history, history of estrogen therapy and history of fracture.

Discussion

From the results obtained we concluded that a lower daily calcium intake and insufficient serum vitamin D level may result in a low BMD in both femur neck and lumbar spine, with higher prevalence of osteopenia and osteoporosis in postmenopausal women. Lumbar spine BMD seems to be more affected by both insufficient daily calcium intake and serum vitamin D level than femur neck BMD. Moreover, although daily calcium is sufficiently taken, the lumbar spine BMD could be affected negatively when serum vitamin D is insufficient.

The effects of vitamin D and calcium are known to be considerable factors for maintaining BMD levels [13,14]. Although there is no consensus on optimal serum levels of 25(OH)D, most experts consider 25(OH)D less than 20 ng/mL to be vitamin D deficiency [15,16,17,18,19]. When serum 25(OH)D is deficient, it is known to affect bone metabolism through osteoclastic bone resorption and bone loss induced by increase in parathyroid hormone secretion as well as decrease in muscle mass and function [17,20]. Calcium is a mineral component which influences the skeletal and smooth muscles, which 99% is stored in the bones in the form of hydroxyapatite. Deficient dietary consumption of calcium leads to lower bone mineral content and BMD, which in long-term leads to osteopenia and osteoporosis [21].

Previously, in one study reported that treatment of vitamin D deficiency in asymptomatic people might reduce mortality risk in elderly people and risk for falls but not fractures [22]. It emphasizes the importance of adequate level of serum vitamin D, but it is concluding that sufficient intakes of vitamin D would not decrease the fracture risk. Contrarily, our study showed the importance of maintaining adequate level of serum vitamin D by showing the increase risk of osteopenia and osteoporosis in lumbar spine, in a subgroup having insufficient amounts of serum 25(OH)D level with adequate daily calcium intake, when compared to the reference group.

One of the drawbacks of this study is that this investigation was retrospective cross-sectional design that direct relationship between the variables could not be obtained through this study. Further studies will be needed to obtain more precise values for serum vitamin D levels and amounts of dietary calcium intakes.

The vitamin D and daily calcium intake are significant variables that affect the BMD in both femur neck and lumbar spine in postmenopausal women. Also, although daily calcium intake is sufficient, the lumbar spine BMD could be affected negatively when serum vitamin D is not sufficient, increasing the risks of osteoporosis. Therefore, supplementing vitamin D and calcium for postmenopausal women would be crucial for preventing osteoporosis and fracture.

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TABLE 1: Differences in BMD of the femur neck and lumbar spine (subgroup analysis according to daily calcium intake)

	Ca ^{a)} <400 mg			400 mg ≤ Ca ^{a)} <800 mg			Ca ^{a)} ≥800 mg		
	25(OH)D <20 ng/mL	25(OH)D ≥20 ng/mL	P-value	25(OH)D <20 ng/mL	25(OH)D ≥20 ng/mL	P-value	25(OH)D <20 ng/mL	25(OH)D ≥20 ng/mL	P-value
Femur neck BMD	0.610 (0.100)	0.654 (0.099)	0.351 ^{b)}	0.626 (0.107)	0.655 (0.095)	0.088 ^{b)}	0.624 (0.967)	0.658 (0.102)	0.892 ^{b)}
Normal	129 (19.3)	117 (27.8)	<0.001 ^{c)}	93 (22.8)	75 (31.5)	0.048	21 (21.6)	28 (31.8)	0.057 ^{b)}
Osteopenia	380 (56.8)	256 (60.8)		241 (59.1)	141 (59.2)		59 (60.8)	52 (59.1)	
Osteoporosis	160 (23.9)	48 (11.4)		74 (18.1)	22 (9.3)		17 (17.6)	8 (9.1)	
Lumbar BMD	0.765 (0.115)	0.822 (0.117)	0.388 ^{b)}	0.790 (0.132)	0.824 (0.132)	0.458 ^{b)}	0.798 (0.126)	0.830 (0.132)	0.487 ^{b)}
Normal	91 (13.6)	125 (29.7)	0.003 ^{c)}	98 (24.0)	44 (18.5)	<0.001	21 (21.6)	27 (30.7)	0.017 ^{b)}
Osteopenia	341 (51.0)	198 (47.0)		163 (40.0)	124 (52.1)		50 (51.6)	44 (50.0)	
Osteoporosis	237 (35.4)	98 (23.3)		147 (36.0)	70 (29.4)		26 (26.8)	17 (19.3)	

Age and body weight were adjusted.

BMD, bone mineral density; Ca, calcium; 25(OH)D, 25-hydroxyvitamin D.

^{a)}Daily calcium intake; ^{b)}Analysis of covariance; ^{c)}Chi-square test.

TABLE 2: Differences in BMD of the femur neck and lumbar spine (subgroup analysis according to serum vitamin D levels)

	25(OH)D <20 ng/mL				25(OH)D ≥20 ng/mL			
	Ca ^{a)} <400 mg	400 mg ≤ Ca ^{a)} <800 mg	Ca ^{a)} ≥800 mg	P-value	Ca ^{a)} <400 mg	400 mg ≤ Ca ^{a)} <800 mg	Ca ^{a)} ≥800 mg	P-value
Femur neck BMD	0.610 (0.100)	0.626 (0.107)	0.624 (0.967)	0.508 ^{b)}	0.654 (0.099)	0.655 (0.095)	0.658 (0.102)	0.311 ^{b)}
Normal	129 (19.3)	93 (22.8)	21 (21.6)	0.907 ^{c)}	117 (27.8)	75 (31.5)	28 (31.8)	0.673 ^{b)}
Osteopenia	380 (56.8)	241 (59.1)	59 (60.8)		256 (60.8)	141 (59.2)	52 (59.1)	
Osteoporosis	160 (23.9)	74 (18.1)	17 (17.6)		48 (11.4)	22 (9.3)	8 (9.1)	
Lumbar BMD	0.765 (0.115)	0.790 (0.132)	0.798 (0.126)	0.624 ^{b)}	0.822 (0.117)	0.824 (0.132)	0.830 (0.132)	0.087 ^{b)}
Normal	91 (13.6)	98 (24.0)	21 (21.6)	0.907 ^{c)}	125 (29.7)	44 (18.5)	27 (30.7)	0.015 ^{b)}
Osteopenia	341 (51.0)	163 (40.0)	50 (51.6)		198 (47.0)	124 (52.1)	44 (50.0)	
Osteoporosis	237 (35.4)	147 (36.0)	26 (26.8)		98 (23.3)	70 (29.4)	17 (19.3)	

Age and body weight were adjusted.

BMD, bone mineral density; 25(OH)D, 25-hydroxyvitamin D; Ca, calcium.

^{a)}Daily calcium intake; ^{b)}Analysis of covariance; ^{c)}Chi-square test.

TABLE 3: The odds ratio of osteopenia and osteoporosis of femur neck and lumbar spine according to daily calcium intake and serum vitamin D level.

	Femur neck		Lumbar spine	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Ca ^{a)} ≥800 mg & 25(OH)D ≥20 ng/mL	Reference		Reference	
Ca ^{a)} ≥800 mg & 25(OH)D <20 ng/mL	1.820 (0.888-3.729)	0.102	2.993 (1.372-6.530)	0.006
400 mg ≤ Ca ^{a)} <800 mg & 25(OH)D ≥20 ng/mL	1.330 (0.706-2.508)	0.377	2.213 (1.090-4.492)	0.028
400 mg ≤ Ca ^{a)} <800 mg & 25(OH)D <20 ng/mL	2.167 (1.195-3.932)	0.011	2.721 (1.382-5.359)	0.004
Ca ^{a)} <400 mg & 25(OH)D ≥20 ng/mL	1.201 (0.657-2.194)	0.552	1.980 (1.001-3.915)	0.050
Ca ^{a)} <400 mg & 25(OH)D <20 ng/mL	2.242 (1.256-4.003)	0.006	3.044 (1.569-5.906)	0.001

Adjusted values; age, body mass index, physical activity, smoking history, history of estrogen therapy, history of fracture.

OR, odds ratio; CI, confidence interval; Ca, calcium; 25(OH)D, 25-hydroxyvitamin D.

^{a)}Daily calcium intake.

References

- World Health Organization. Annual report 2015 Available from: www.who.int/gho/mortality_burden_disease/life_tables/situation_trends/en/
- Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96:1911-1930.
- Khosla S, Riggs BL. Pathophysiology of age-related bone loss and osteoporosis. *Endocrinol Metab Clin North Am.* 2005;34:1015-1030.
- Khosla S, Atkinson EJ, Melton LJ, 3rd, Riggs BL. Effects of age and estrogen status on serum parathyroid hormone levels and biochemical markers of bone turnover in women: a population-based study. *J Clin Endocrinol Metab.* 1997;82:1522-1527.
- Agata U, Park JH, Hattori S, Aikawa Y, Kakutani Y, Ezawa I, et al. The impact of different amounts of calcium intake on bone mass and arterial calcification in ovariectomized rats. *J Nutr Sci Vitaminol.* 2015;61:391-399.
- Riggs BL, Khosla S, Melton LJ, 3rd. A unitary model for involutional osteoporosis: estrogen deficiency causes both type I and type II osteoporosis in postmenopausal women and contributes to bone loss in aging men. *J Bone Miner Res.* 1998;13:763-773.
- Caroli A, Poli A, Ricotta D, Banfi G, Cocchi D. Invited review: dairy intake and bone health. A viewpoint from the state of the art. *J Dairy Sci.* 2011;94:5249-5262.
- Tella SH, Gallagher JC. Prevention and treatment of postmenopausal osteoporosis. *J Steroid Biochem Mol Biol.* 2014;142:155-170.
- Chung YS, Chung DJ, Kang MI, Kim IJ, Koh JM, Min YK, et al. Vitamin D repletion in Korean postmenopausal women with osteoporosis. *Yonsei Med J.* 2016;57:923-927.
- Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 Dietary Reference Intakes for Calcium and Vitamin D: what dietetics practitioners need to know. *J Am Diet Assoc.* 2011;111:524-527.
- World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva: World Health Organization; 1994.
- Kanis JA, Melton LJ, 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. *J Bone Miner Res.* 1994;9:1137-1141.
- Hwang S, Choi HS, Kim KM, Rhee Y, Lim SK. Associations between serum 25-hydroxyvitamin D and bone mineral density and proximal femur geometry in Koreans: the Korean National Health and Nutrition Examination Survey (KNHANES) 2008-2009. *Osteoporos Int.* 2015;26:163-171.
- Krall EA, Dawson-Hughes B. Heritable and life-style determinants of bone mineral density. *J Bone Miner Res.* 1993;8:1-9.
- Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest.* 2006;116:2062-2072.
- Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc.* 2006;81:353-373.
- Holick MF, Siris ES, Binkley N, Beard MK, Khan A, Katzer JT, et al. Prevalence of Vitamin D inadequacy among postmenopausal North American women receiving osteoporosis therapy. *J Clin Endocrinol Metab.* 2005;90:3215-3224.
- Romagnoli E, Carnevale V, Biondi P, Minisola S. Vitamin D supplementation: when and how? *J Endocrinol Invest.* 2014;37:603-607.
- Reid IR. Effects of vitamin D supplements on bone density. *J Endocrinol Invest.* 2015;38:91-94.
- Cipriani C, Romagnoli E, Carnevale V, Clerico R, Pepe J, Cilli M, et al. Effect of a single oral dose of 600,000 IU of cholecalciferol on muscle strength: a study in young women. *J Endocrinol Invest.* 2013;36:1051-1054.
- Dermience M, Lognay G, Mathieu F, Goyens P. Effects of thirty elements on bone metabolism. *J Trace Elem Med Biol.* 2015;32:86-106.
- Hansen KE, Johnson RE, Chambers KR, Johnson MG, Lemon CC, Vo TN, et al. Treatment of vitamin d insufficiency in postmenopausal women: a randomized clinical trial. *JAMA Intern Med.* 2015;175:1612-1621.
- Grimnes G, Joakimsen R, Figenschau Y, Torjesen PA, Almas B, Jorde R. The effect of high-dose vitamin D on bone mineral density and bone turnover markers in postmenopausal women with low bone mass: a randomized controlled 1-year trial. *Osteoporos Int.* 2012;23:201-211.
- Bauer DC. Calcium supplements and fracture prevention. *N Engl J Med.* 2014;370:387-388.
- Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, et al. Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med.* 2006;354:669-683.
- Murad MH, Drake MT, Mullan RJ, Mauck KF, Stuart LM, Lane MA, et al. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *J Clin Endocrinol Metab.* 2012;97:1871-1880.
- LeBlanc ES, Zakher B, Daeges M, Pappas M, Chou R. Screening for vitamin D deficiency: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2015;162:109-122.