ORIGINAL ARTICLE

Association between serum 25-hydroxyvitamin D levels and bone mineral density in normal postmenopausal women

Vasundhara Kamineni, Akkenapally Prasanna Latha, K. Ramathulasi

Department of Obstetrics and Gynaecology, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India

ABSTRACT

Aim: This study was conducted with the objective of assessing serum 25-hydroxyvitamin D (25(OH)D) in postmenopausal women (PMW), to detect osteopenia or osteoporosis in PMW and to establish a correlation between serum 25(OH)D levels and bone mineral density (BMD).

Materials and Methods: A total of 100 healthy PMW were selected, and a prospective observational study was conducted to correlate the BMD with serum 25(OH)D levels. Their laboratory investigations along with serum 25(OH)D levels were done. Their BMD was assessed with dual-energy X-ray absorptiometry at lumbar spine and neck of femur; T-scores were derived. Correlation analysis was done to investigate the relationship between serum 25(OH)D levels and BMD.

Results: The proportion of osteoporosis at the hip was 31.9% in deficient group, 16.1% in insufficient, and 18.2% in sufficient group and at lumbar spine, it was 27.7%, 16.1%, and 22.7%, respectively. Forty-seven percent of PMW had deficient (<20 ng/ml) serum 25(OH)D levels and 31% had insufficiency. T-score at hip in deficient group was −2.05 ± 0.25, and in an insufficient group, it was −1.79 ± 0.13; T-score at lumbar spine was −1.92 ± 0.12 and −1.79 ± 0.12, respectively, but both were not statistically significant. Osteoporosis was seen in 24%, osteopenia in 55% at hip level and 23% and 59% respectively at lumbar spine. There was no association between serum 25(OH)D levels and BMD neither at hip nor at lumbar spine ($P = 0.51$ and $P = 0.79$ respectively).

Conclusion: In this study, among our cohort of patients there was no correlation between serum 25(OH)D levels and BMD. However, Vitamin D deficiency coexists with low BMD. Vitamin D insufficiency is a common risk factor for osteoporosis associated with increased bone remodeling and low bone mass.

Key Words: Bone mineral density, postmenopausal women, Vitamin D

INTRODUCTION

Osteoporosis is the most prevalent bone disorder among postmenopausal women (PMW). Poor nutrition, inadequate exposure to sunlight and low Vitamin D status contribute to severe osteoporosis in India.[1,2] Current standard approach for diagnosing osteoporosis is the estimation of bone mineral density (BMD) using dual energy X-ray absorptiometry (DEXA). Studies have shown that women whose intake of calcium is high exhibit high BMD when compared to women with low calcium intake. Vitamin D and calcium supplements aid in the prevention of bone loss

Address for Correspondence: Dr. Akkenapally Prasanna Latha, House No. 16-10-227/4, Vijayalaxmi Nilayam, Old Malakpet, Hyderabad - 500 036, Telangana, India.
E-mail: drlatasri@gmail.com

Access this article online

Quick Response Code:

Website: www.jmidlifehealth.org

DOI: 10.4103/0976-7800.195694

How to cite this article: Kamineni V, Latha AP, Ramathulasi K. Association between serum 25-hydroxyvitamin D levels and bone mineral density in normal postmenopausal women. J Mid-life Health 2016;7:163-8.

by reducing bone renewal and the number of nonvertebral fractures.[3]

The serum 25-hydroxyvitamin D (25(OH)D) level is thought to reflect the Vitamin D nutritional status accurately. Severe Vitamin D deficiency can cause osteomalacia, which is characterized by inadequate mineralization of the newly formed osteoid. Vitamin D deficiency is believed to cause secondary hyperparathyroidism, leading to an increase in the bone turnover and bone loss.[4,5] It is hypothesized that low 25(OH)D levels by virtue of development of secondary hyperparathyroidism could be a contributing factor to low BMD. Although there is no consensus on the definition of optimal serum 25(OH)D levels, Vitamin D deficiency is defined by most experts as a serum 25(OH)D level of <50nmol/L (<20 ng/ml), whereas a serum 25(OH)D level of >75 nmol/L (>30 ng/ml) is considered to be normal and a level of 50–75 nmol/L (20–30 ng/ml) defines Vitamin D insufficiency.[6]

BMD is measured by standard deviation (SD) and expressed as T-score. It is calculated as the difference between the measured BMD of the patient and the expected bone density value in a normal young person (YN) divided by the population SD. T-score = (BMD − YN)/SD. Osteopenia is defined with T-score between −1 and −2.5, and osteoporosis was defined with T-score <−2.5.[7,8]

MATERIALS AND METHODS

This is a prospective observational study. The study population included 100 healthy postmenopausal patients (complete cessation of periods over a period of >1 year) seen primarily at our out-patient department and patients referred by the Department of Orthopaedics and General Medicine at Kamineni Institute of Medical Sciences and Research Centre, LB Nagar, Hyderabad, Telangana State over a period of 2 years. The study was duly approved by the Institutional Ethics Committee. Patients were included in the study after obtaining informed consent. All women belong to semi-urban/urban locality. A detailed history regarding menstrual history, duration of menopause, menopausal symptoms is obtained. A social and medical history, features of osteoporosis including fragility fracture, intake of medications and supplements, personal history and family history of fractures, loss of height, bone pain and other complaints were elicited. Other important assessments included dietary intake of calcium and exposure to sunlight per day. Body mass index (BMI) was calculated as weight in kilograms divided by square of height in meters. A comprehensive physical examination was done.

Inclusion criteria

Healthy PMW attaining menopause naturally, i.e., cessation of menstruation for 1 year due to loss of follicular activity.

Exclusion criteria

Women who have undergone surgery for bilateral oophorectomy, patients with a major medical illness such as hepatic dysfunction, significant thyroid dysfunction, renal disease, metabolic bone disorders, and malignancies. Women on steroid therapy, any medications which affect bone metabolism, use of calcium or Vitamin D supplements, hormone replacement therapy, tamoxifen, bisphosphonates.

Biochemical measurements

Laboratory tests included serum creatinine, albumin, total calcium, inorganic phosphates liver enzymes, thyroid function tests, and serum 25(OH)D levels. Serum calcium and serum phosphorus were determined by spectrophotometric analysis. Albumin-corrected calcium was calculated using the formula:

Corrected calcium = 0.8 × [normal albumin (4.0) - patients albumin] + total serum calcium

Serum 25(OH)D was measured by enhanced chemiluminescent immunoassay. Women were classified based on Vitamin D levels as deficient (<20 ng/ml); insufficient (20–30 ng/ml); and sufficient (>30 ng/ml).

Bone mineral density

The T-score, bone mineral content and BMD were determined at two anatomic sites, namely, the lumbar spine, L2–L4 anteroposterior (LSAP), and femoral neck using DEXA. The BMD of the subjects were recorded in terms of absolute mineral content (g/cm^2) at these sites. BMD values were interpreted as T-score. Osteopenia was defined as T-score <−1 and osteoporosis as T-score ≤−2.5.

Statistical analysis

Analysis was performed with the use of SPSS (version 20; SPSS Inc., Chicago, IL, USA). Descriptive results are presented as mean ± standard error of mean. Pearson's coefficient was calculated for the correlation between continuous variables. Correlation computes the value of the Pearson's correlation coefficient (r). Its value ranges from -1 to 0, to +1. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 100 patients were selected. Baseline demographic characteristics and relation to Vitamin D characterization

are mentioned in Table 1. The mean age was found to be significantly higher in those with deficient level of Vitamin D (65.4 ± 0.53) compared to insufficient (59.2 ± 0.86) and sufficient (49.9 ± 0.54) levels. Similarly, the mean duration after menopause was found to be significantly higher in those with deficient level of Vitamin D (12.68 ± 0.77) compared to insufficient (7.58 ± 0.91) and sufficient (2.81 ± 0.24) levels. The mean BMI was however found to be significantly higher in insufficient category (29.12 ± 0.81) compared to deficient (27.14 ± 0.6) and sufficient (26.09 ± 0.91) levels. The dietary intake of calcium was found to be significantly higher in sufficient level (685.7 ± 166.9) followed by insufficient (575.4 ± 104.7) and deficient (484.4 ± 19.8) levels. The mean BMD at the neck of femur and lumbar spine were similar in all categories, and the differences were also not statistically significant. Similarly, the mean T-score at hip and lumbar spine were found to be highest in those with deficient level (−2.05 ± 0.15 and −1.92 ± 0.12, respectively) compared to insufficient and sufficient levels, but however, the differences were not statistically significant ($P > 0.05$; not significant).

Categorization of Vitamin D levels and BMD at the level of hip is shown in Table 2. The proportion of osteoporosis at the level of hip was found to be highest in those with deficient Vitamin D category (31.9%) followed by sufficient (18.2%) and insufficient (16.1%) levels. However, the differences were not statistically significant ($P = 0.46$; not significant).

Table 3 shows the categorization of Vitamin D by BMD at the level of lumbar spine. The proportion of osteoporosis at the level of lumbar spine was found to be highest in deficient level (27.7%) followed by sufficient (22.7%) and insufficient (16.1%) levels. However, the differences were not statistically significant ($P = 0.62$; not significant).

There is no significant correlation between serum 25(OH) D levels and BMD at neck of femur [Figure 1, $r = 0.11$; $P = 0.29$; not significant] and at lumbar spine [Figure 2, $r = 0.09$; $P = 0.35$; not significant]. There was a positive correlation between serum 25(OH)D levels and dietary calcium [Figure 3, $r = 0.48$; $P < 0.001$; significant] and duration of sunlight exposure [Figure 4, $r = 0.72$; $P < 0.001$; significant] and negative correlation with years after menopause [Figure 5, $r = 0.61$; $P < 0.001$; significant].

DISCUSSION

The present study investigated the association of serum 25(OH)D levels and BMD in healthy PMW consuming optimal diet, exposed to sunlight and performing physical activity. Several studies have documented hypovitaminosis D in people living in countries with abundant sunshine.[2,9-11] Prevalence of Vitamin D deficiency in India is alarmingly high.[2,12] Vitamin D deficiency is an important risk factor for the development of osteoporosis. In the present study, 47% of PMW have low serum 25(OH)D, deficiency (<20 ng/ml) and 31% have insufficiency and osteoporosis at hip was 31.9% and 16.1% respectively and at LSAP it was 27.7% and 16.1% respectively. Harinarayan *et al*.[13] reported the prevalence of Vitamin D deficiency of 70% and insufficiency of 23% in PMW and osteoporosis at hip of 28% and LSAP of 22% in PMW. Maintenance of adequate serum 25(OH)D level is of paramount importance as future bone loss is to be prevented in women

Table 1 : Relationship of certain variables by vitamin D categorization

Parameter (mean±SE)	Vitamin D categorization			*P* value and significance
	Deficient (47)	Insufficient (31)	Sufficient (22)	
Age (years)	65.4±0.53	59.2±0.86	49.9±0.54	*F*=87.9; **P*<0.001; S
Duration of menupause (years)	12.68±0.77	7.58±0.91	2.81±0.24	*F*=29.6; **P*<0.001; S
BMI (Kg/m^2)	27.14±0.6	29.12±0.81	26.09±0.91	*F*=3.54; **P*=0.003; S
Dietary intake of calcium (mg/dl)	484.4±19.8	575.4±104.7	685.7±166.9	*F*=17.1; **P*<0.001; S
BMD at neck of femur (gm/cm^2)	0.62±0.03	0.66±0.03	0.64±0.04	*F*=0.24; **P*=0.78; NS
BMD at lumbar spine (gm/cm^2)	0.62±0.02	0.64±0.02	0.64±0.03	*F*=0.26; **P*=0.77; NS
T score at hip	−2.05±0.15	−1.79±0.13	−1.94±0.22	*F*=0.66; **P*=0.51; NS
T score at lumbar spine	−1.92±0.12	−1.79±0.12	−1.87±0.17	*F*=0.22; **P*=0.79; NS

*Statistically significant

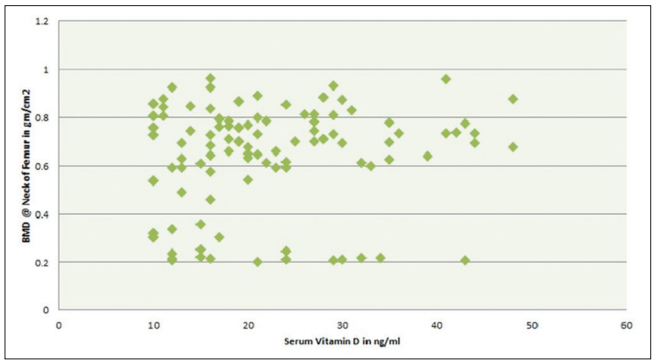

Figure 1: Correlation analysis between serum Vitamin D and bone mineral Density. Scatter plot showing correlation between serum Vitamin D and bone mineral Density at neck of femur

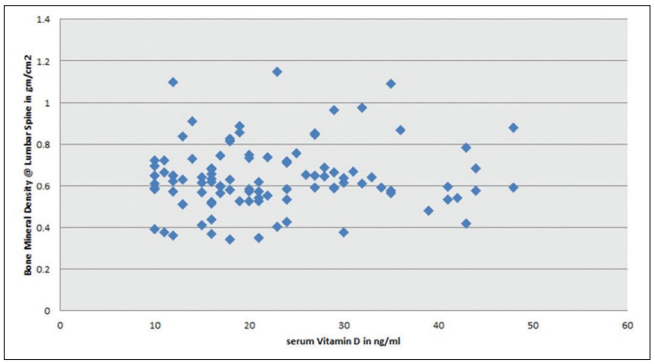

Figure 2: Correlation between serum Vitamin D and bone mineral Density at lumbar spine

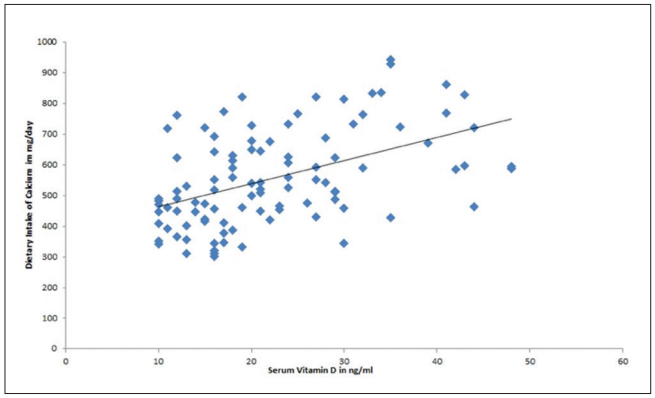

Figure 3: Correlation analysis between serum Vitamin D and dietary calcium intake in all subjects included in the study

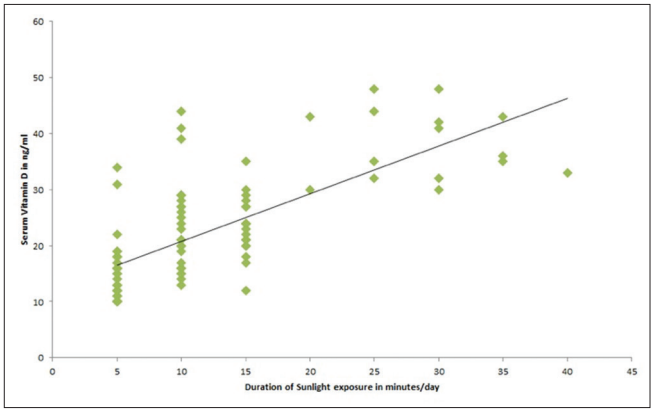

Figure 4: Correlation analysis between serum Vitamin D and duration of sunlight exposure in all subjects included in the study

Table 2 : Vitamin D categorization by bone mineral density categorization at the level of hip

Vitamin D categorization	No of subjects	Bone mineral density categorization at hip level		
		Normal	Osteopenia	Osteoporosis
Deficient	47	10 (21.3)	22 (46.8)	15 (31.9)
Insufficient	31	7 (22.6)	19 (61.3)	5 (16.1)
Sufficient	22	4 (18.2)	14 (63.6)	4 (18.2)
Total	100	21 (21.0)	55 (55.0)	24 (24.0)

χ^2=3.55 ; *P*=0.46 ; NS. Values in parenthesis indicate percentages

Table 3 : Vitamin D categorization by bone mineral density categorization at the level of lumbar spine

Vitamin D categorization	No of subjects	Bone mineral density categorization at lumbar spine		
		Normal	Osteopenia	Osteoporosis
Deficient	47	10 (21.3)	24 (51.1)	13 (27.7)
Insufficient	31	5 (16.1)	21 (67.7)	5 (16.1)
Sufficient	22	3 (13.6)	14 (63.6)	5 (22.7)
Total	100	18 (18.0)	59 (59.0)	23 (23.0)

χ^2=2.63 ; *P*=0.62 ; NS. Values in parenthesis indicate percentages

once they have crossed the watershed of menopause. The BMD T-scores had no relation to 25(OH)D status in correlation analysis in PMW. Serum 25(OH)D levels depict the current Vitamin D status of an individual while BMD denotes bone mineral accrual over a period of time depending upon a variety of other factors. They suggested that Vitamin D deficiency presents as osteopenia in BMD measurements in PMW. Study of BMD without knowing 25(OH)D status can be misleading. Due to daytime high temperature and tropical climate, any advice on sun exposure is less likely to be followed. Hence, in South Indian PMW, dietary enrichment/supplementation with calcium and Vitamin D should be considered in therapy of osteoporosis along with antiresorptive agents. Because of diversity of dietary and social habits, more multicentric studies are to be undertaken to document the problem in different parts of India. The prevalence of hypovitaminosis D in our study was 78% as shown in other studies on Indian PMW.[14,15] Lavanya *et al*.[16] showed 25% Vitamin D insufficiency and 75% deficiency in PMW. Prevalence of hypovitaminosis D in PMW was found to be 47% in Thailand, 49% in Malaysia, 90% in Japan and 92% in South Korea.[17] Many studies have found almost 80% of PMW have low BMD of osteoporotic range.[18-23]

In our study, there is no correlation between serum 25(OH)D levels and BMD neither at hip nor at LSAP. In

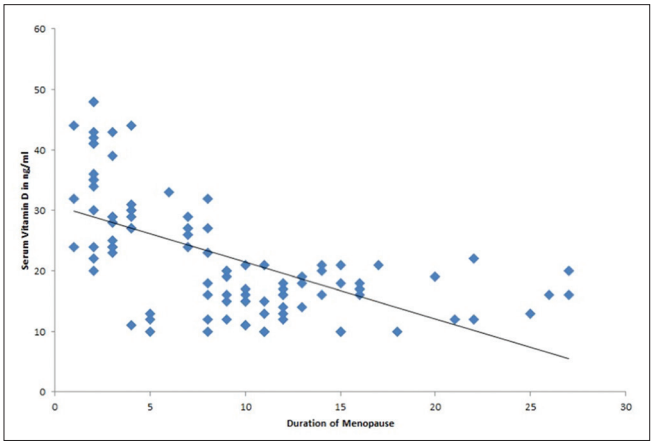

Figure 5: Correlation analysis between serum Vitamin D levels and duration of menopause

earlier studies Harinarayan *et al*.,[13] demonstrated that BMD had no relation to serum 25(OH)D status.[24-26] Few studies have shown a positive correlation of serum 25(OH)D levels and BMD.[20,22,23,27] Vitamin D is a fundamental vitamin to maintain calcium level in the bone by increasing calcium absorption in the intestines, stimulating bone resorption by increasing number of osteoclasts, and maintain level of parathyroid hormone to stabilize serum calcium levels.[23]

Beg *et al*.[21] reported, prevalence of hypovitaminosis D in PMW was 88.5% and Vitamin D deficiency of 68.24% and insufficiency of 20.27%. The BMD at lumbar spine was 1.20 ± 0.18 in PMW without osteoporosis as compared to 0.81 ± 0.13 in the osteoporosis group. Their study showed a positive correlation between Vitamin D and BMD, although the relation was not statistically significant ($r^2 = 0.201$, $P < 0.089$). Skin complexion, poor sun exposure, vegetarian food habits, low milk intake, high phytates in food, and lack of Vitamin D fortification program explain the high prevalence of Vitamin D deficiency in India despite it is sunny climate. The association between 25(OH)D levels and BMD is still debatable. The heterogeneity in the results of this relationship can be partially explained by differences in population, differences in age group and differences in the sites of the body studied. More important is the fact that different Vitamin D levels were used to define Vitamin D deficiency and insufficiency during such studies.

In this study, there was a positive correlation between 25(OH)D level and dietary calcium intake and duration of sunlight exposure.[2,12,16] In our study, there was a negative correlation between 25(OH)D levels and duration of menopause.[17,28] Lavanya *et al*.,[16] have shown time and duration after menopause also has a significant effect on Vitamin D and BMD. PMW have significantly lower BMD due to estrogen deficiency, ageing associated with decreased osteoblast function, decreased calcium absorption, and decreased ability to synthesize Vitamin D leading to osteoporosis.

CONCLUSION

Although a direct relationship could not be established between 25(OH)D and BMD, Vitamin D deficiency coexists with low BMD in our study. Vitamin D insufficiency is a common risk factor for osteoporosis associated with increased bone remodeling and low bone mass. Simple measurement of BMD without knowing the Vitamin D status is not of much use. Calcium and Vitamin D supplementation should be an integral part of therapy of osteoporosis in India.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Malhotra N, Mithal A. Osteoporosis in Indians. Indian J Med Res 2008;127:263-8.
2. Londhey V. Vitamin D deficiency: Indian scenario. J Assoc Physicians India 2011;59:695-6.
3. Nieves JW. Nutrition and osteoporosis in osteoporosis. In: Cummings S, Cosman F, Jamal S, editors. Osteoporosis: An Evidence Based Approach to the Prevention and Management. Philadelphia: American College of Physicians; 2002.
4. Ooms ME, Lips P, Roos JC, van der Vijgh WJ, Popp-Snijders C, Bezemer PD, *et al.* Vitamin D status and sex hormone binding globulin: Determinants of bone turnover and bone mineral density in elderly women. J Bone Miner Res 1995;10:1177-84.
5. Dawson-Hughes B. Calcium, Vitamin D and Vitamin D metabolites. In: Papapolous SE, Lips P, Pols HA, Jhonston CC, Delmas PD, editors. Osteoporosis 1996: Proceedings of the 1996 World Congress on Osteoporosis. Excerpt Med Int Congr Ser 118. Amsterdam, The Netherlands: Elsevier; 1996. p. 299-303.
6. Holick MF. Vitamin D status: Measurement, interpretation, and clinical application. Ann Epidemiol 2009;19:73-8.
7. World Health Organisation. Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis. Report of a WHO Study Group. (WHO Technical Report Series, No. 843). Geneva, Switzerland: WHO; 1994.
8. World Health Organisation. WHO Scientific Group on the Assessment of Osteoporosis at Primary Health Care Level. Summary Meeting Report. Brussels, Belgium: World Health Organisation; 2004.
9. Rahman SA, Chee WS, Yassin Z, Chan SP. Vitamin D status among postmenopausal Malaysian women. Asia Pac J Clin Nutr 2004;13:255-60.
10. Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. Osteoporos Int 2004;15:56-61.
11. Fuleihan GE, Deeb M. Hypovitaminosis D in a sunny country. N Engl J Med 1999;340:1840-1.
12. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, *et al.* Global Vitamin D status

and determinants of hypovitaminosis D. Osteoporos Int 2009;20:1807-20.
13. Harinarayan CV, Sachan A, Reddy PA, Satish KM, Prasad UV, Srivani P. Vitamin D status and bone mineral density in women of reproductive and postmenopausal age groups: A cross-sectional study from South India. J Assoc Physicians India 2011;59:698-704.
14. Deng WM, Wei QS, Tan X, Shao Y, Chen XH, Sun WS. Relation of serum 25 hydroxyvitamin D levels to bone mineral density in Southern Chinese postmenopausal women: A preliminary study. Indian J Med Res 2015;142:430-7.
15. Mehrotra RN, Ranjan A, Lath R, Ratnam R. Postmenopausal osteoporosis: Our experience. Indian J Endocrinol Metab 2012;16 Suppl 2:S421-2.
16. Lavanya Y, Srikanth S, Satya CM. Vitamin D, serum calcium and bone mineral density in pre and post menopausal women – A pilot study. Indian J Basic Appl Med Res 2015;5:371-8.
17. Lim SK, Kung AW, Sompongse S, Soontrapa S, Tsai KS. Vitamin D inadequacy in postmenopausal women in Eastern Asia. Curr Med Res Opin 2008;24:99-106.
18. Mishra S, Manju M, Toora BD, Mohan S, Venkatesh BP. Comparison of bone mineral density and serum minerals in pre and post-menopausal women. Int J Clin Trials 2015;2:85-90.
19. Sharma S, Khandelwal S. Effective risk assessment tools for osteoporosis in the Indian menopausal female. J Midlife Health 2010;1:79-85.
20. Singh A, Singh H, Patel S. Screening of bone mineral density by densitometer and correlation with serum calcium and Vitamin D levels to detect early osteoporotic changes in postmenopausal women in slum areas of Raipur and Kalupur of Ahmedabad. Int J Basic Clin Pharmacol 2015;4:960-5.
21. Beg M, Akhtar N, Alam MF, Rizvi I, Ahmad J, Gupta A. Vitamin D status and serum osteocalcin levels in postmenopausal osteoporosis: Effect of bisphosphonate therapy. J Indian Acad Clin Med 2014;15:172-6.
22. Vuceljic M, Ilic-Stojanovic O, Lazovic M, Grajic M. Vitamin D and parathyroid hormone in relation to bone mineral density in postmenopausal women. Vojnosanit Pregl 2012;69:243-8.
23. Li S, Ou Y, Zhang H, Zhang Z, Zhou H, Liu L, *et al.* Vitamin D status and its relationship with body composition, bone mineral density and fracture risk in urban central South Chinese postmenopausal women. Ann Nutr Metab 2014;64:13-9.
24. Kota S, Jammula S, Kota S, Meher L, Modi K. Correlation of Vitamin D, bone mineral density and parathyroid hormone levels in adults with low bone density. Indian J Orthop 2013;47:402-7.
25. Jolanta D, Alma C, Egidija R, Jolita B, Jelizaveta B, Ieva S, *et al.* Association between Vitamin D and bone mineral density in post-menopausal women with metabolic syndrome. Acta Med Lituanica 2015;22:7-14.
26. Kruavit A, Chailurkit LO, Thakkinstian A, Sriphrapradang C, Rajatanavin R. Prevalence of Vitamin D insufficiency and low bone mineral density in elderly Thai nursing home residents. BMC Geriatr 2012;12:49.
27. Bener A, Saleh NM. Low Vitamin D, and bone mineral density with depressive symptoms burden in menopausal and postmenopausal women. J Midlife Health 2015;6:108-14.
28. Malavolta N, Pratelli L, Frigato M, Mulè R, Mascia ML, Gnudi S. The relationship of Vitamin D status to bone mineral density in an Italian population of postmenopausal women. Osteoporos Int 2005;16:1691-7.