Original article

Influence of serum vitamin D levels on peak bone mass in the Iranian population

Nahid Eshagh Hosseini[1],Hamidreza Aghaei Meybodi[1],Abbasali Keshtkar[2],Mohsen Rezaei Homami[3],Patricia Khashayar[4],Bagher Larijani[5]

1- Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran,

2- Department of Health Sciences Education Development, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran,

3- Institute of Health & Wellbeing, Health Economics & Health Technology Assessment, University of Glasgow, Glasgow, UK,

4- Center for Microsystems Technology, Imec and Ghent University, Gent-Zwijnaarde, Belgium,

5- Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Aghaei Meybodi HR   Email: hraghai@tums.ac.ir

Abstract

Objective: Recent studies have reported the high prevalence of different degrees of vitamin D deficiency in Iran. The present study was conducted to determine the correlation between serum levels of vitamin D and Peak Bone Mass (PBM) in a group of Iranian population at the age of PBM..

Methods: The present cross-sectional study was conducted on 20-35 year-old adults participating in the first phase of the Iranian Multicentric Osteoporosis Study (IMOS). The correlation between serum levels of 25(OH)D and BMD values were assessed by Spearman correlation coefficient.

Results: 1941 individuals were studied. There was no significant difference between BMD values at the studied areas with vitamin D levels nor status groups in either gender.

 Conclusion: Our study revealed no association between serum vitamin D levels and BMD in individuals at the age of PBM
.

Keywords: Vitamin D; Osteoporosis; Peak Bone Mass; Bone Mineral Density

Introduction

Considering the rapid growth of the elderly population worldwide, osteoporosis and its complications, mainly fracture, have become of great concern (1). This comes while the World Health Organization (WHO) has defined osteoporosis as a disease with great economic burden on the society (2). Many studies have pointed out the importance of prevention in reducing the burden of this disease (3).

The fracture risk mainly depends on bone density, which is the end result of peak bone mass (PBM) achieved during skeletal maturity, and bone loss, which occurs later on in life (4). This points out the importance of peak bone mass attainment and its determinants. According to the available data, PBM is mostly attained in the 3rd and 4th decades of life in most individuals. Environmental and lifestyle factors, particularly physical activity and diet, are among the most important factors affecting PBM (5,6). Not many studies have reported the link between serum vitamin D levels and PBM. As for the Iranian population, based on our knowledge, no such a study is available. This is while recent studies have reported the high prevalence of different degrees of vitamin D deficiency in Iran. According to the Iranian Multicenteric Osteoporosis Study (IMOS), 57.5% of the Iranians suffer from moderate to severe degrees of vitamin D deficiency (7). The present study was therefore conducted to determine the correlation between serum levels of vitamin D and PBM.

Material and Methods

The present cross-sectional study was conducted on 20-35 year-old adults participating in the first phase of the Iranian Multicentric Osteoporosis Study (IMOS) in winter 2001. The population-based study was performed on the adults from four Iranian provinces (Tehran, Shiraz, Mashhad, Tabriz), as a representative group of the Iranian population, to access bone health (8). Individuals taking medication affecting bone metabolism as well as those with metabolic bone disease, renal and liver failure, hypercortisolism, cancers, malabsorption, infertility, oligomenorrhea and type I diabetes were excluded. Pregnant and lactating mothers along with individuals being immobile for more than a week were not recruited. The study was approved by the Ethical Board Committee of the Endocrinology and Metabolism Research Institute (EMRI) of Tehran University of Medical sciences and all the subjects signed an informed consent before being recruited.

Biochemical tests

A fasting blood sample (10 cc of venous blood) was taken from all the participants at their residence place. Sample centrifuge and serum extraction were done in the field. The samples were then frozen and sent to the EMRI laboratory. Serum Calcium (Ca) and Phosphorous (P) levels were analyzed by calorimetric methods using Chem. Enzyme Lab Kit; Iran. The normal laboratory range for serum Ca was 8.6 to 10.8 mg/dL and for serum P was 2.3 to 5 mg/dL. Serum levels of vitamin D (25 (OH) D) was measured with RIA (Radio-Immuno-Assay) method using IDS Ltd Kit; UK. The inter- and intra-assay variations for the markers was 8%/6.8%, respectively. Based on 25(OH)D values, subjects were classified in three groups: those suffering from vitamin D deficiency ($<= 10$ ng/mL), – insufficiency (mild deficiency) (10 to 30 ng/mL) and – sufficiency (higher than 30 ng/mL) (9).

Bone Mineral Density

Patients underwent bone mineral density (BMD) measurement at L1–L4 anteroposterior lumbar spine, hip and its sub-regions using a Lunar DPXMD densitometer (Lunar 7164, GE, Madison, WI) by a trained operator. Results were expressed as T- and Z-scores. Quality control procedures were carried out in accordance with the manufacturer's recommendations. Instrument variation was determined regularly through a weekly calibration procedure using a phantom supplied by the manufacturer. Precision error for BMD measurements was 1– 1.5% in the lumbar and 2–3% in the femoral regions. The device normative data of Caucasian women BMD (including the NHANES III dataset) of Hologic QDR 4500A bone densitometer were used as reference values (10). The subjects were classified into four groups based on their BMD quartile.

Statistical Analysis

Data was entered in SPSS ver. 16. Mean and standard deviation were used to explain quantitative variables. As for the qualitative variables, frequency and percentage were used. Chi-square was applied to compare the variables. The correlation between vitamin D concentration and BMD values were assessed using Spearman correlation coefficient. A P-value less than 0.5 was considered as statistically significant.

Results

1941 individuals were recruited; from among whom 852 (44%) were male and 1060 (56%) were female. Their mean age was 27.5 ± 4.6 years. Mean serum levels of vitamin D in the studied population was 30.2 ± 2 ng/mL, ranging from 6 to 217 (male: 31.8 ± 1.9 ng/mL; female: 29.8 ± 2,2 ng/mL). 613 (35.7%) were classified as sufficient, 1063 (61.9%) as insufficient, and 41 (2.4%) as deficient. There was a significant difference between the number of deficient cases in either genders (male: 1.9% vs. female: 2.8%, p-value= 0.001). The association between BMD quartile values at different areas and vitamin D status stratified by gender are presented in Table 1 and 2. As shown in these tables, the association was not statistically significant in either gender.

Mean BMD values in the studied population was 0.98 ± 0.15 g/cm^2 (0.93 ± 0.16 g/cm2 at femoral neck, 0.78 ± 0.14 g/cm2 at trochanter, 1.1 ± 0.17 g/cm2 at lumbar spine. There was no significant difference between mean BMD values at all areas with vitamin D status groups (p-value = 0.08) (Table 3). There was no significant correlation between vitamin D levels and BMD values at either studied site (Table 4).

Table 1- Vitamin D levels in different BMD quartiles in women

BMD		Sufficient (%)	Insufficient (%)	Deficient (%)	P-value
Femoral Neck	Q1	37 (13)	76 (14)	3 (11)	0.65
	Q2	66 (23)	138 (26)	6 (23)	
	Q3	92 (32)	180 (33)	12 (46)	
	Q4	90(32)	146 (27)	5 (19)	
Total Hip	Q1	50 (23)	92 (19)	6 (25)	0.78
	Q2	48 (22)	127 (27)	6 (25)	
	Q3	63 (28)	138 (29)	7 (29)	
	Q4	61(28)	118 (25)	5 (21)	
L1-L4	Q1	18 (8)	39 (8)	4 (15)	0.74
	Q2	53 (23)	103 (21)	5 (19)	
	Q3	86 (37)	165 (34)	9 (35)	
	Q4	73 (32)	176 (36)	8 (31)	

Table 2- Vitamin D levels in different BMD quartiles in men

BMD		Sufficient (%)	Insufficient (%)	Deficient (%)	P-value
Femoral Neck	Q1	29 (10)	34 (10)	1 (8)	0.22
	Q2	53 (18)	48 (13)	4 (31)	
	Q3	63 (22)	105 (29)	3 (23)	
	Q4	142 (50)	171 (48)	5 (38)	
Total Hip	Q1	30 (13)	43 (13)	0	0.24
	Q2	35 (16)	67 (21)	5 (42)	
	Q3	66 (29)	87 (27)	4 (33)	
	Q4	94 (42)	128 (39)	3 (25)	
L1-L4	Q1	29 (12)	31 (18)	3 (21)	0.15
	Q2	66 (28)	91 (27)	1 (7)	
	Q3	60 (26)	103 (31)	2 (14)	
	Q4	78 (34)	110 (24)	8(57)	

Table 3- Association between mean level of BMD and Vitamin D status by sex

		Vitamin D status			
	Sex	Sufficient	Insufficient	Deficient	P-value
BMD Femoral Neck	Female	0.97 (0.14)	0.96 (0.13)	0.94 (0.11)	0.39
	Male	1.03 (0.18)	1.03 (0.16)	0.98 (0.11)	0.56
	Total	1.11 (0.15)	0.99 (0.15)	0.96 (0.14)	0.42
BMD L1-L4	Female	1.15 (0.12)	1.16 (0.13)	1.14 (0.12)	0.28
	Male	1.14 (0.14)	1.15 (0.14)	1.15 (0.19)	0.77
	Total	1.13 (0.17)	1.16 (0.12)	1.15 (0.32)	0.56
BMD Total Hip	Female	0.95 (0.14)	0.97 (0.14)	0.99 (0.14)	0.41
	Male	0.99 (0.16)	1.01 (0.16)	0.99 (0.13)	0.68
	Total	0.97 (0.08)	0.99 (0.12)	0.99 (0.11)	0.43

One-way ANOVA test
Data in table are presented as Mean (SD)

Table 4- The correlation between various markers and BMD values at different sites by sex groups

		Vitamin D	PTH	Ca	Phosphor	ALK-PH	Albumin
Male	BMD Femoral Neck	0.014	0.010	0.105*	0.030	0.108*	-0.015
	BMD L1-L4	-0.056	0.074	0.053	0.028	0.036	-0.010
	BMD Total Hip	0.035	0.038	0.102*	0.071	0.046	-0.020
Female	BMD Femoral Neck	0.064	-0.056	0.071*	0.085*	-0.021	0.083*
	BMD L1-L4	0.008	-0.015	0.026	0.027	0.018	0.055
	BMD Total Hip	0.076*	-0.027	0.078*	0.008	-0.018	0.081*

Data are presented as Spearman Correlation Coefficient.
*$P<0.05$

Discussion

PBM is reported to be attained at the age of 18-20 years in women and 18-23 years in men (11). Optimization of PBM requires proper interaction of environmental, dietary, hormonal, and genetic factors (12). Many studies have reported that adequate Ca intake and following a vitamin D-rich diet during the growth may improve PBM and maximize bone mass (13, 5). Several studies have also reported that consuming vitamin D supplements could help improve BMD among adolescent girls (14,15). This comes while a meta-analysis showed that supplementation with vitamin D is not effective in children with normal serum levels of vitamin D, stressing that the use of these supplements improves BMD values only in those diagnosed with vitamin D deficiency (16,17).

While serum levels of vitamin D are considered as an important predictor of osteoporosis, not many studies have studied its role in PBM attainment (18). The present study failed to show any relation between vitamin D levels and BMD values in either gender. This comes while many studies have shown the contrary. According to a study conducted in 2008 in postmenopausal women, it was reported that while PTH had a positive correlation with BMD values at femoral neck; no association was found between vitamin D levels and BMD (19). This comes while the studies conducted on younger individuals have reported the contrary. In a study conducted on young males aged between 18 and 20 years, a significant reduction was noted in PBM in individuals with low serum levels of vitamin D (20). Another study showed that adolescent girls with low serum levels of vitamin D cannot attain high PBM at the spine (21). In a cross-sectional study in Saudi Arabia, there was a significant correlation between serum levels of vitamin D and BMD values. They reported low BMD

values at 50% of the women and 7% of the men of PBM age who had normal serum levels of vitamin D. As for those with vitamin D deficiency, the rate was as high as 84.2% and 88.9% respectively (22). They concluded that vitamin D levels significantly influence BMD reading among Saudi individuals. In another study in North Europe, vitamin D deficiency was significantly linked with low BMD in young men (23).

The differences noted between the above mentioned studies and that of the present research can be partially explained by differences in the studied populations, studied age groups, applied vitamin D cut-offs and BMD measurement sites.

This study had some limitations. The cross-sectional nature of the study confines its generalizability to the whole Iranian population. In addition, apart from vitamin D no other biomarkers particularly Parathyroid Hormone (PTH) were studied. Moreover, the influence of nutrition and physical activity on BMD values was not studied, and thus no multivariate analysis was carried out to evaluate the effects of other confounding factors on bone mass.

Conclusion

Our study revealed no association between serum levels of vitamin D and BMD values in individuals at the age of PBM. However, considering the high prevalence of vitamin D deficiency among young Iranians and the confirmed link between vitamin D deficiency and osteoporosis, implementing strategies to overcome vitamin D deficiency in this group is of great importance. Further studies however are needed to confirm these results.

Financial support: None
Conflict of Interest: None

References

1 Ström O, Borgström F, Kanis JA, Compston J, Cooper C, McCloskey EV et al. Osteoporosis: burden, health care provision and opportunities in the EU. Arch Osteoporos 2011; 6(1-2): 59-155

2 WHO Scientific group on the assessment of osteoporosis at primary health care level. May 2004 www.who.int/chp/topics/Osteoporosis.pdf

3 Shahnazari B, Keshtkar A, Soltani A, Aghamaleki A, Mansour A, Matin B et al. Estimating the avoidable burden of certain modifiable risk factors in osteoporotic hip fracture using Generalized Impact Fraction (GIF) model in Iran. J Diabetes Metab Disord 2013, 12:10

4 Pitukcheewanont P, Austin J, Chen P, Punyasavatsut N. Bone health in children and adolescents: risk factors for low bone density. Pediatr Endocrinol Rev. 2013;10(3):318-35.

5 Specker B, Minett M. Can Physical Activity Improve Peak Bone Mass? Curr Osteoporos Rep. 2013 Jul 7.

6 Uusi-Rasi K, Kärkkäinen MU, Lamberg-Allardt CJ. Calcium intake in health maintenance - a systematic review. Food Nutr Res. 2013 16;57.

7 Heshmat R, Mohammad K, Majdzadeh SR, Forouzanfar MH, Bahrami A, Ranjbar Omrani GH et al. Vitamin D Deficiency in Iran: A Multi-center Study among Different Urban Areas. Iran J Public Health 2008. 37(sup):72-78.

8 Khashayar P, Meybodi HR, Homami MR, Amini MR, Mohajeri-Tehrani MR, Heshmat R, Larijani B. The discriminative value of various biochemical parameters in detecting varying degrees of vitamin D deficiency in the Iranian population. Clin Lab. 2011;57(3-4):163-70.

9 Holick MF. Vitamin D deficiency. NEJM 2007; 357:266-281

10 Looker A, Johnston CJ, Wahner H, Dunn W, Calvo M, Harris T, et al. Prevalence of low femoral bone density in older U.S. women from NHANES III. J Bone Miner Res 1995;10(5):796-802.

11 Boot AM, de Ridder MA, vandersluis IM, slobbe, krenning EP, keizerschrama sm. Peak bone mineral density, Lean body mass and Fractures. Bone. 2010;46(2):336-41.

12 Valimaki MJ, Karkkainen M, Lamberg-Allardt G, Laitinen K, Alhara E, Heikkinen J et al. Exersise, Smoking and calcium intake during adolescence and early adulthood as determinants of Peak Bone Mass. BMJ 1994; 309(6949):230-5.

13 Uusi-Rasi K, Kärkkäinen MU, Lamberg-Allardt CJ. Calcium intake in health maintenance - a systematic review. Food Nutr Res. 2013;57.

14 Mølgaard C, Larnkjær A, Cashman KD, Lamberg-Allardt C, Jakobsen J, Michaelsen KF. Does vitamin D supplementation of healthy Danish Caucasian girls affect bone turnover and bone mineralization?. Bone 2010, 46(2):432–439.

15 Grene DA, Naughton GA. Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomised controlled trial. Osteoporos Int 2011; 22(2): 489-498.

16 Rizzoli R, Bianchi ML, Garabédian M, McKay HA, Moreno LA. Maximizing bone mineral mass gain during growth for the prevention of fractures in the adolescents and the elderly. Bone 2010; 46(2): 294–305.

17 Winzenberg T, Powell S, Shaw KA, Jones G. Effects of vitamin D supplementation on bone density in healthy children: systematic review and meta-analysis. BMJ 2011; 342: c7254. A

18 Malavolta N, Pratteli L, Frigato M, Mule R, Masica ML, Gnudi S. The relationship of vitamin D status to bone mineral density in an Italian population of postmonopausal women. Osteoporos Int 2005; 16:1691-1697

19 Hosseini Panah F, Rambod M, Hosseini nejad A, Larijani B, Azizi F. Association between Vitamin D and bone mineral density in Iranian postmenopausal women. J Bone Miner Metab 2008; 26:86-92

20 Valimaki UV, Al Fthan H, Lehmuskallio E, Loythyniemi E, sahi T, stenman U, suominen H, j.valimaki M. Vitamin D status as determination of Peak Bone Mass in young Finnish Men. J Clin Endocrinol Metab 2004; 89:76-80

21 Lehtonen-Veromaa MK, Möttönen TT, Nuotio IO, Irjala KM, Leino AE, Viikari JS. Vitamin D and attainment of Peak Bone Mass among pripubertal Finnish girls. Am J Clin Nutr 2002; 76: 1446-1453

22 Mir Sadat A, Al Elq A, Al-Turki H, Al-Mulhim F, Al-Ali A. Influence of vitamin D levels on bone mineral density and osteoporosis. Ann Saudi Med. 2011; 31(6):602–608.

23 Frost M, Abrahamsen B, Nielsen TL, Hagen C, Andersen M, Brixen K. Vitamin D status and PTH in young men: a cross-sectional study on associations with bone mineral density, body composition and glucose

Metabolism. Clin Endocrinol 2010; 73(5): 573–580.