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Vitamin D Deficiency in Iran: A Multi-center Study among Different Urban Areas

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Abstract

Background: Recent studies have reported different prevalence of vitamin D deficiency in different sex and age groups in developing countries. In the present survey, we elucidated the prevalence of vitamin D deficiency in a multi-center study among Iranian population.

Methods: In a random cluster sample of healthy men and women (ranged 20 to 69 years old), a number of 5232 subjects from five urban metropolitans' cities (Tehran, Tabriz, Mashhad, Shiraz and Booshehr) were recruited in 2001. Fasting blood sample was taken from participants and sent to the laboratory for measurement of 25-hydroxy vitamin D level. Meta-analysis was performed using fixed effect method for estimation of vitamin D deficiency prevalence in a national level.

Results: Moderate to severe vitamin D deficiency was estimated in urban areas (except for Booshehr because of its heterogeneity) equal to 47.2, 45.7 and 44.2% in age groups of <50, 50-60 and 60≤ years, respectively among men and 54.2, 41.2 and 37.5 percent among women in the same age groups. The highest prevalence of moderate to severe vitamin D deficiency in men was observed in Tehran. Mashhad and Booshehr had also the lowest prevalence of moderate to severe vitamin D deficiency among men and women.

Conclusion: Iran is a country with high prevalence of moderate to severe vitamin D deficiency and the prevalence of this deficiency is more evident in Tehran, capital of Iran. Therefore, consideration of main predictors for vitamin D deficiency in all age groups especially in Tehran is recommended.

Keywords: *Vitamin D, Deficiency, Prevalence, Severity, Urban*

Introduction

Vitamin D has an important role in bone development and muscle function. It also facilitates absorption of calcium and phosphate from the gut and kidney, suppresses parathyroid hormone (PTH), and acts on osteoblasts to stimulate bone formation. Thus, its deficiency is not only a strong predictor of bone metabolism disturbances, but is also an independent predictor of risk for cancer and other chronic diseases (1). Vitamin D deficiency is defined as serum 25-Hydroxy vitamin D lower than 25 nmol/l (2).

Several studies carried out within the two previous decades have shown a high prevalence of vitamin D deficiency in tropical countries such as China, Turkey, India, Iran and Saudi Arabia and estimated its prevalence between 30% and 93% (3-11). Although the role of some factors such as different exposure to sunshine, low dietary intake of vitamin D and low consumption of supplements has been confirmed as the main causes of this deficiency in these countries (12), the majority of the recent studies have reported different prevalence of vitamin D deficiency in dif-

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ferent sex and age groups especially in developing countries. Furthermore, for the estimation of the prevalence of vitamin D deficiency, most of the studies were limited to a small sample size or assessed a specific age group (especially elderly) (13).

In the present study, we planned to elucidate the prevalence of vitamin D deficiency in a multi-center study among Iranian population with a large sample size.

Material and Methods

Study design and population

Using a random cluster sample of apparently healthy men and women (ranged 20 to 69 yr old), this multi-centric cross-sectional study was carried out for the estimation of vitamin D deficiency and prevalence of osteoporosis among Iranian population (IMOS-Iranian Multi-centric Osteoporosis Study) in late winter of 2001 (February-March). A number of 6032 subjects were invited among urban areas of five great cities with different climates (Tehran, Tabriz, Mashhad, Shiraz and Booshehr) (Table 1& Fig. 1) that among them, 5369 subjects participated in this study (response rate was 89%). These subjects were categorized to three age groups (<50, 50-60 and 60≤ yr old). For selection of clusters in each city, the data of the first labor in the entire private and general hospitals were recorded, assuming that referral pattern and distribution of labors were randomly dispensed. Among these, 50 women who were admitted to these hospitals were selected. The women's addresses were found and the neighborhood's were met with a specific method, which was choosing one person in each house around the first selected address, in a clockwise manner. According to self reporting, cases with the history of rheumatoid arthritis, thyroid or parathyroid disorders, adrenal insufficiency, renal failure, heart failure, bone metabolic disorders, diabetes mellitus type I, sterility, oligohomennuria, malignancies, malabsorption, immobility for more than one week, pregnancy or alcoholism were all excluded. In addition, subjects with the history of using drugs and other substances that could affect bone metabolism were excluded from the study. Finally, 137 cases were excluded and other 5232 cases were eligible to participate in the study.

The study protocol was approved by the research ethics committee of Endocrinology and Metabolism Research Center (EMRC) of Tehran University of Medical Sciences (TUMS) and informed consents were obtained from all participants.

Measurements

One fasting venous blood sample (10 mL) was taken from each participant in his/her place of residence. Sample centrifuge and serum extraction were done in the field. Then samples were sent to the laboratory of Endocrinology and Metabolism Research Center of TUMS and were frozen immediately. 25-hydroxy vitamin D level was measured with RIA (Radio-Immuno-Assay) method (Biosource Europes.A,Ò). Inter-assay and Intra-assay for 25-hydroxy vitamin D were 8.2% and 5.3%, respectively. 25-hydroxy vitamin D level ≤12.5 nmol/l was considered as severe vitamin D deficiency and between 12.5 nmol/l and 25 nmol/l was considered as moderate deficiency (2).

Statistical analysis

Measured data have been entered to Microsoft Access Databank, checked, and cleaned before analysis. Data analysis has been performed using STATA version 9/SE statistical software. Survey analysis was used for estimation of vitamin D deficiency prevalence in each city and in different sex and age groups considering the sampling method. Indirect standardized prevalence of different levels in vitamin D deficiency was calculated for each city according to sex and age distribution of 2006 national census data (Iranian Statistical Center). Meta-analysis was performed using fixed effect method for estimation of vitamin D deficiency prevalence in a national level. Heterogeneity analysis showed that vitamin D deficiency rates for Booshehr were heterogenic with other four metropolitans' rates (*P* for heterogeneity= 0.000). Therefore, meta-analy-

sis was performed for summarizing the rates of other urban areas except Booshehr.

Results

Vitamin D deficiency and its severity in different age and sex groups in five studied metropolitans are shown in Table 2 and 3. In both sex groups, almost half of subjects suffered from moderate to severe vitamin D deficiency.

Among five great cities, the highest prevalence of moderate to severe vitamin D deficiency in men was observed in Tehran and Mashhad in different age groups. So that, its prevalence in Tehran among subjects less than 50 yr old and more than 60 yr old in this great metropolitan was 66.0% and 60.2%, respectively. Moreover, its prevalence among male subjects aged between 50 and 60 yr old was 58.5%. Booshehr had the lowest prevalence of moderate to severe vitamin D deficiency among men that its prevalence in above three age groups was 16.7%, 8.5% and 21%, respectively. These rates for Booshehr were statistically different with other studied urban areas (P= 0.000) (Table 2).

Vitamin D deficiency and its severity in women in five great cities are summarized in Table 3. Among selected cities, the lowest prevalence of moderate to severe vitamin D deficiency among women in three age groups was reported in Booshehr (33.1%, 24.4% and 20.5%, respectively). In women less than 50 yr old and between 50 and 60 yr old, the highest prevalence of moderate to severe vitamin D deficiency was reported in Tehran, 73.7% and 51.4%, respectively, whereas, in women > 60 yr old, its prevalence was the highest in Mashhad city (61.3%). Among female subjects, the moderate to severe deficiency rates for Booshehr were statistically different with other studied urban areas too (P= 0.000).

Point estimations and their 95% confidence intervals (CI95%) on vitamin D deficiency frequency and its severity in different sex and age groups in studied metropolitans except Booshehr (Tabriz, Tehran, Mashhad and Shiraz) are summarized in Table 4. There was no statistically significant difference between vitamin D deficiency estimations of two genders among age groups (P <50, 50-60 and >60 yr old age groups were 0.396, 0.568 and 0.388, respectively).

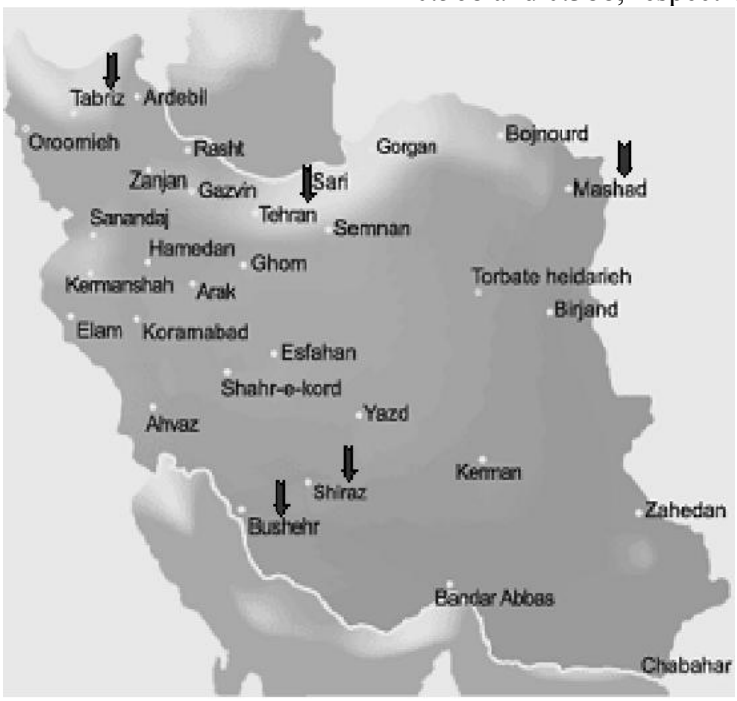

Fig. 1: Coverage map of five metropolitans selected for the study

Table 1: Geographical and meteorological characteristics of five metropolitans selected for the study

	Latitude	Longitude	Elevate(m)	Mean Temperature (C^{o})	Sunny Hours/Year
Tabriz	38.0’ N	46.0’ E	1361	13.5	2918
Tehran	36.0’ N	51.0’ E	1190	18.5	3022
Mashhad	36.0’ N	60.0’ E	999	15.5	2958
Shiraz	29.5’ N	52.5’ E	1481	18.9	3432
Booshehr	29.0’ N	51.0’ E	19	25.3	3117

- N=North; E=East

Table 2: Vitamin D deficiency and its severity in men in five great cities

City	Severe deficiency (vit D ≤ 12.5)	Moderate deficiency (12.5<vit D ≤ 25)	Mild deficiency (25<vitamin D ≤ 35)	Normal (35.1<vit D ≤ 150)
< 50 years old				
Tabriz	3.1	36.8	31.0	29.1
Tehran	3.2	62.8	21.0	13.0
Mashhad	8.3	37.6	27.8	26.3
Shiraz	3.3	38.4	28.9	29.4
Booshehr	0.6	16.1	24.7	58.6
50 – 60 years old				
Tabriz	5.5	41.8	26.3	26.4
Tehran	4.7	52.9	28.2	14.2
Mashhad	9.4	49.1	13.2	28.3
Shiraz	2.6	26.3	22.4	48.7
Booshehr	0.0	8.5	28.2	63.3
> 60 years old				
Tabriz	5.1	38.5	25.6	30.8
Tehran	2.7	57.5	20.5	19.3
Mashhad	3.6	46.4	25.0	25.0
Shiraz	3.0	25.4	14.9	56.7
Booshehr	4.7	16.3	20.9	58.1

- Data are presented as frequency percent (%) in each age group
- Cut-off values units are nmol/L

Table 3: Vitamin D deficiency and its severity in women in five great cities

City	Severe deficiency (vit D ≤ 12.5)	Moderate deficiency (12.5<vit D ≤ 25)	Mild deficiency (25<vitamin D ≤ 35)	Normal (35.1<vit D ≤ 150)
< 50 years old				
Tabriz	10.6	49.8	16.6	23.0
Tehran	15.4	58.3	8.6	17.7
Mashhad	6.9	37.5	22.1	33.5
Shiraz	3.0	43.0	27.4	26.6
Booshehr	0.3	32.8	29.9	37.0
50 – 60 years old				
Tabriz	4.9	32.9	20.7	41.5
Tehran	5.6	45.8	8.4	40.2
Mashhad	4.0	37.4	21.2	37.4
Shiraz	4.4	29.7	25.3	40.6
Booshehr	1.4	23.0	31.1	44.5
> 60 years old				
Tabriz	1.6	35.9	6.3	56.2
Tehran	5.1	39.0	10.2	45.7
Mashhad	3.2	58.1	12.9	25.8
Shiraz	1.4	25.7	6.8	66.1
Booshehr	0.0	20.5	28.2	51.3

- Data are presented as frequency percent (%) in each age group
- Cut-off values units are nmol/L

Table 4: Estimations of Vitamin D deficiency and its severity in different sex and age groups in four urban areas except Booshehr

Age groups	Severe deficiency (vit D ≤ 12.5) (CI95%)	Moderate deficiency (12.5<vit D ≤ 25) (CI95%)	Mild deficiency (25<vitamin D ≤ 35) (CI95%)	Normal (35.1<vit D ≤ 150) (CI95%)
< 50 years old				
Men	3.7 (2.6-4.8)	43.5 (40.7-46.2)	29.3 (26.3-32.2)	22.8 (20.5-25.2)
Women	7.1 (5.9-8.3)	47.1 (44.8-49.4)	15.5 (13.9-17.2)	24.3 (22.3-26.3)
50 – 60 years old				
Men	4.5 (2.1-6.8)	41.2 (35.8-46.7)	22.4 (17.8-27.1)	25.6 (20.9-30.4)
Women	4.7 (2.5-6.8)	36.5 (31.7-41.4)	15.8 (12.2-19.4)	39.8 (34.9-44.8)
> 60 years old				
Men	3.4 (1.3-5.6)	40.8 (35.1-46.5)	20.8 (16.0-25.6)	30.7 (25.4-36.0)
Women	2.0 (0.2-3.8)	35.5 (29.4-41.6)	7.8 (4.3-11.3)	52.2 (45.9-58.5)

- Data are presented as percentages and 95% Confidence Intervals (CI95%)
- Cut-off values units are nmol/L

Discussion

In recent investigations, it has been clearly found that the vitamin D is an essential factor not only for bone formation and osteoporosis prevention, but also for extra skeletal functions such as immune system regulation, cancer and hypertension prevention (14, 15). Therefore, assessment of the distribution of vitamin D deficiency in all populations especially developing countries is necessary.

Our recent study for the assessment of the prevalence of vitamin D deficiency in different age and sex groups and in different urban areas, obtained two important findings. Firstly, it was found that both genders considerably suffered from vitamin D deficiency in all urban areas. In another analysis of IMOS data based on normative values of vitamin D according to PTH level alternations, prevalence of mild and moderate to severe vitamin D deficiency was notably high in both genders in Iran so that the 75.1% of women and 72.1% of men suffered from this disorder (16). In our study, the majority of individuals in all studied regions had moderate to severe vitamin D deficiency and this finding was more evident in the elderly. In another study in Iran, prevalence of severe, moderate and mild vitamin D deficiency was 9.5%, 57.6% and 14.2%, respectively (13). It has been even shown that vitamin D deficiency is prevalent in both men and women in Iranian populations residing in other countries. The prevalence of vitamin D deficiency in those countries is higher in women than in men (17). It seems that the skin complexion, poor sun exposure, vegetarian food habits and lack of vitamin D food fortification program can explain the high prevalence of vitamin D deficiency in Iran and other similar Middle East countries despite their sunny climate (18). It was also indicated that vitamin D deficiency is highest among people who are elderly, institutionalized, or hospitalized. It is reported that 60% of the elderly in nursing homes were vitamin D deficient in the United States (19). In addition, nearly one third of healthy adults were vitamin D deficient at the end of winter (20).

Finally, we found that the vitamin D deficiency was less prevalent in Booshehr as a southern port and more prevalent in Tehran as capital of Iran and in Mashhad (in Northeast of Iran) in some age groups. It seems that the high prevalence of this disorder in Tehran and Mashhad can be related to unsuitable dietary habits and air pollution. It also seems that the low prevalence of vitamin D deficiency in Booshehr can be related to high consumption of fish and its oil supplements in that city. It has been clear that the use of fatty fish and cod liver oil or other fish oil supplements is associated with reduced vitamin D deficiency in all groups. Vitamin D sup-

plement is well known to influence 25-hydroxy vitamin D levels in blood, particularly when sun exposure is limited (21, 22). It has been also believed that the clothing habits, especially among women, may be an important factor affect the prevalence of vitamin D deficiency in Middle East and Islamic countries so that a greater prevalence of vitamin D deficiency has been shown in people who cover all of their exposed skin with clothing in countries such as Saudi Arabia, Jordan, Turkey and Lebanon (12, 23). Nevertheless, the role of this factor in high prevalence of vitamin D deficiency in different age groups of females in our study is doubtful, because we observed the same rates of deficiency among men. Meanwhile, clothing habits are almost the same around the country and even, covering rate of skin with clothing in Booshehr, an urban area with the lowest rates of vitamin D deficiency, is higher than other metropolitans.

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References

1. Holick MF (2004). Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am J Clin Nutr*, 79: 362-71.
2. Lips P (2001). Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications, *Endocr Rev*, 22: 477-501.
3. Du X, Greenfield H, Fraser DR, et al. (2001). Vitamin D deficiency and associated factors in adolescent girl in Beijing. *Am J Clin Nutr*, 74: 494-500.
4. Alagol F, Shihadeh Y, Boztepe H, et al. (2000). Sunlight exposure and vitamin D in Turkish women. *J Endocrinol Invest*, 23: 173-77.
5. Dawodu A, Agarwal M, Hossain M, et al. (2003). Hypervitaminosis D and vitamin D deficiency in exclusively breast feeding infants and their mother in summer: a justification for vitamin D supplementation of breast-feeding infants. *J Pediatr*, 142: 169-73.
6. Sedrani SH (1984). Low 25-Hydroxy vitamin D and normal serum calcium concentrations in Saudi Arabia: Riyadh region. *Ann Nutr Metab*, 28:181-85.
7. Sedrani SH, Elidrissy AW, Arabi KM (1983). Sunlight and vitamin D status in normal Saudi subjects. *Am J Clin Nutr*, 38:129-32.
8. Azizi F, Rais-Zadeh F, Mir Said Ghazi A (2000). Vitamin D deficiency in a group of Tehran Population. *Research In Medicine*, 4: 291-303.
9. Taha S, Dost S, Sedrani S (1984). 25-hydroxy vitamin D and total calcium extra ordinarily low plasma concentrations in Saudi mothers and their neonates. *Pediatr Res,* 18: 739-41.
10. Fonseca V, Tongia R, el-Hasmi M, et al. (1984). Exposure to sunlight and vitamin D deficiency in Saudi Arabian women. *Postgrad Med J*, 60: 589-91.
11. Gowami R, Gupta N, Gosuwami D, et al. (2000). Prevalence and significance of low 25-Hydroxy vitamin D concentrations in healthy subjects in Dehli. *Am J Clin Nut*r, 72: 422-75.
12. Lips P (2007). Vitamin D status and nutrition in Europe and Asia. *J Steroid Biochem Mol Biol*, 103: 620-25.
13. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, Soltani A, Shafaei AR, Hamidi Z, Fard AR, Hossein-Nezhad A, Booya F (2004). Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public Health*, 25; (4):38.
14. Khazai N, Judd SE, Tangpricha V (2008). Calcium and vitamin D: skeletal and ex-

traskeletal health. *Curr Rheumatol Rep*, 10(2):110-17.
15. Kimball S, Fuleihan Gel-H, Vieth R (2008). Vitamin D: a growing perspective. *Crit Rev Clin Lab Sci*,, 45(4): 339-414.
16. Moradzadeh K. Larijani B, Keshtkar AA, Hossein-Nezhad A, Rajabian R, Nabipour I, Omrani GH, Bahrami A, Gooya MM, Delavari A (2008). Normative Values of Vitamin D among Iranian Population: A Population Based Study. *Int J Osteoporosis Metabolic Dis,* 1(1): 8-15.
17. Holvik K, Meyer HE, Haug E, Brunvand L (2005). Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway: the Oslo Immigrant Health Study. *Eur J Clin Nutr*, 59(1): 57-63.
18. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N (2000). Prevalence and significance of low 25- hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr*, 72: 472-75.
19. Elliott ME, Binkley NC, Carnes M, et al. (2003). Fracture risks for women in long-term care: high prevalence of calcaneal osteoporosis and hypovitaminosis D. *Pharmacotherapy*, 23(6): 702-10.
20. Tangpricha V, Flanagan JN, Whitlatch LW, et al. (2001). 25-hydroxyvitamin D-alpha-hydroxylase in normal and malignant colon tissue. *Lancet*, 357(9269): 1673-74.
21. Brustad M, Sandanger T, Wilsgaard T, Aksnes L, Lund E (2003). Change in plasma levels of vitamin D after consumption of cod liver and fresh cod-liver oil as part of the traditional north Norwegian fish dish 'Mølje'. *Int J Circumpolar Health*, 62: 40-53.
22. Davies PS, Bates CJ, Cole TJ, Prentice A Clarke PC (1999). Vitamin D: seasonal and regional differences in preschool children in Great Britain. *Eur J Clin Nutr*, 53: 195-98.
23. Gartner LM, Greer FR (2003). Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics*, 111(4 Pt 1): 908-10.