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Original Article

Vitamin D Deficiency in Healthy Male Population: Results of the Iranian Multi- Center Osteoporosis Study

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Abstract

Background: The prevalence of vitamin D deficiency and its causative factors has been estimated more frequently in elder population, women, and patients with osteoporosis in different countries, but this issue is less defined in male population within different age groups especially in Asian countries. Therefore, we studied the role of effective factors in vitamin D deficiency and its prevalence in Iranian healthy men.

Methods: This study was a multi center and carried out in five metropolitans in Iran. Serum 25 Hydroxy vitamin D and other biochemical variables were determined in 2396 healthy men in late winter of 2001.

Results: 68.8% of participants suffered from vitamin D deficiency. Vitamin D levels were the highest in Bushehr (n= 111, 40.3%) ($P< 0.05$) and between Shiraz and Tabriz, Shiraz had the better values ($P< 0.05$). Tehran had the highest prevalence of vitamin D deficiency (n= 380, n= 85.7%). Geographical zone independently predicted vitamin D status ($P< 0.05$). There was not any association among age (r= 0.035, $P> 0.05$), physical activity (r= 0.023, $P> 0.05$), and exposure of face & hands to sunlight (r= 0.022, $P> 0.05$) with vitamin D levels.

Conclusion: Prevalence of vitamin D deficiency in Iranian male population is high, considering Iranian cultural and geographical zones, food fortification and life style modification is recommended.

Keywords: *Vitamin D, Deficiency, Healthy male, Osteoporosis, Iran*

Introduction

Normal levels of serum 25 Hydroxy Vitamin D (OHD) is necessary to maintain regular bone metabolism which facilitates bone growth (1, 2). It is well documented that chronic and severe vitamin D deficiency leads to depletion of bone reservoirs of calcium and phosphate and insufficient bone matrix mineralization, which is considered as rickets in children and osteomalacia in adults (3, 4). Subclinical vitamin D deficiency has been reported to be related to calcium-phosphorus imbalance, serum PTH elevation, and bone mineral density depletion (5-8). Prostate, colon and breast cancers, hypertension, lack of immune modulation and diabetes are among other conditions which are related to vitamin D deficiency (2, 9, 10).

The prevalence of vitamin D deficiency is different in European, Asian, and Middle East countries (11-19). Most of the researches have focused on the prevalence and -in some cases- the causative factors of vitamin D deficiency in elder population, women especially during postmenopausal period and women with different kinds of Hijab in Middle East countries (12, 17, 20-24). In Iran, there are several studies that indicate the prevalence of vitamin D deficiency in different urban areas (25), in healthy boys and girls in Isfahan (26), some causative factors of vitamin D deficiency in Tehran population (19), and the relation of severe vitamin D deficiency with musculoskeletal pain in men and women in Tehran (27). To the best of our knowledge, there is not enough evidence to allude to the status of vitamin D and

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effective factors in vitamin D deficiency in a healthy male population in Iran.
Thus, the purpose of this study was to: 1) determine the prevalence of vitamin D deficiency (25 OHD level≤ 35 ng/ml) in healthy male population; 2) Identify effective factors in vitamin D deficiency in men.

Materials and Methods

Study design

This study was a multi center and carried out to determine the prevalence of vitamin D deficiency and its causative factors in healthy male population of five urban areas in late winter of 2001 (February-March). Participants were selected through a random- cluster approach. In order to pick out clusters in each city, we recorded data of the first labor in private and general hospitals in urban areas and considered that the distribution of labors to be random. Fifty women, who had hospitalized, were recruited randomly and their addresses were obtained; then we selected the neighbors of these fifty women and picked out one person per house around the selected women, in a clockwise manner. Finally 2396 healthy men took part in this study in Tehran, Tabriz, Mashhad, Shiraz and Bushehr. Subjects would excluded from the study if they reported a history of rheumatoid arthritis, thyroid or parathyroid dysfunction, renal, adrenal or heart failure, type-I diabetes mellitus, sterility, malignancies, alcoholism, bone metabolic disorders, immobility for more than one week and using drug or any substance which affects bone metabolism.

Measurements

A fasting venous blood sample (10 ml) was taken from each participant; samples were centrifuged and serums were extracted in each city but biochemical analyses of samples were done in the laboratory of EMRC. ELISA/EIA Kits (IDF Company, USA) technique was applied in order to determine 25- Hydroxy vitamin D levels. We considered serum 25-Hydroxy vitamin D levels which were 12.5 ng/ml or less as severe deficiency, 12.5-25 ng/ml as moderate deficiency, 25-35 ng/ml as mild deficiency and higher than 35 ng/ml as normal serum concentration of vitamin D (28).
To determine participants' life style characteristics, a questionnaire was prepared which covered several items such as; duration of sun exposure, parts of the body exposed to sun light through routine clothing style and physical activity. Life style questionnaire was prepared by research team, regarding its content validity, ten experts evaluated it and finalized one was applied in the study. Cronbach's alpha for the questionnaire was 0.83.

Ethical considerations

Informed consent was obtained from participants. Research protocol was approved by research ethics committee of endocrinology and metabolism research center (EMRC) of Tehran University of Medical Science (TUMS) (29).

Statistical analysis

Data were collected from five metropolitans. To analyze the data, STATA version 8/SE and SPSS version 11.5 were used. Descriptive statistics were applied in order to estimate prevalence of vitamin D deficiency. To assess associations between vitamin D status and predictor variables, simple bivariate association, ANOVA and linear regression were applied. Multiple regression models were used in order to determine the independent effects of variables on vitamin D status.

Results

Serum 25 (OHD) levels were measured in 2396 men. Characteristics of participants are presented in Table 1, 2. 496 (20.6%) men in Tehran, 600 (25%) in Tabriz, 386 (16.1%) in Mashhad, 496 (20.7%) in Bushehr and 420 (17.5%) in Shiraz took part in the study. Participants' age was 19 to 83 years old, with a mean of 43.08 (14.683). All participants were Iranian and claimed that they were in good to excellent heath condition.
Generally, vitamin D levels of 1423 (68.8%) men were in the insufficient range (25 OHD level ≤

35 ng/ml) which was the highest in Tehran (n= 380, 85.7%) and the lowest in Bushehr (n= 111, 40.3%). The prevalence of vitamin D deficiency within subgroups is listed in Table 3. Severe vitamin D deficiency was shown in 81 participants (3.9%), moderate deficiency was reported in 807 (39.2%) and 532 of participants (25.8%) suffered from mild deficiency (Table3). One way analyses of variance pointed out that vitamin D levels varied significantly with age groups; in fact mean values of 25 OHD levels were significantly lower in men younger than 50 yr old rather than those were between 50- 60 yr old ($P< 0.05$) and older than 60 yr old ($P< 0.05$). No significant difference was in serum 25 OHD between men aged 50- 60 compared to those older than 60 yr old ($P> 0.05$) (Table 4). Considering different urban areas, vitamin D levels were significantly high in Bushehr rather than other metropolitans ($P< 0.05$), and compared to Tabriz and Tehran, Shiraz had the highest levels of vitamin D ($P< 0.05$) (Fig. 1). Participants who did not exposed their skin to sunlight, had significantly lower vitamin D status rather than those who exposed their face and hands ($P< 0.05$) or even more parts of their bodies to the sunlight ($P< 0.05$); moreover, participants who exposed only their face & hands to the sunlight had significantly lower levels of vitamin D compared to men who exposed most parts of their bodies to the sunlight ($P< 0.05$) (Table 4). According to our results, geographical location significantly predicted vitamin D status ($P< 0.05$). In our multiple regression, no significant association was shown in age ($r= 0.035$, $P> 0.05$), physical activity (r= 0.023, $P> 0.05$), and exposing face & hand to sunlight ($r= 0.022$, $P> 0.05$) with vitamin D status.

Table 1: Descriptive and biochemical characteristics of the study population

	Mean (SD)					Total
	Tabriz	**Tehran**	**Mashhad**	**Shiraz**	**Bushehr**	
Age (yr)	43.45 (7.32)	43.08 (14.68)	47(12.12)	46.9 (9.31)	47.09 (15.08)	2386
Height (cm)	175.01 (9.01)	172.93 (7.32)	173.76 (8.77)	174.32 (5.66)	172.80 (8.99)	2202
Weight (kg)	82.23 (9.88)	73.35 (12.91)	77.09 (12.32)	71(10.02)	73 (13.03)	2200
BP sys (mmHg)	121.1 (12.30)	123.15 (18.30)	132.11 (15.81)	127.14 (17.20)	128.20 (15.20)	1389
BP dia (mmHg)	70.66 (11.34)	80.51 (10.12)	80.62 (12.25)	77.01 (18.62)	92.04 (15.44)	1388
Alb (g/dl)	4.09 (0.68)	4.3 (0.7)	3.9 (0.4)	4.7 (0.62)	4.59 (0.71)	2253
P (mg/dl)	3.30 (0.77)	3.89 (0.61)	3.31 (0.65)	2.90 (0.8)	4.51 (0.67)	1763
Ca (mg/dl)	9.03 (1.11)	9.38 (1.26)	8.98 (1.34)	9.08 (0.7)	9.99 (1.41)	2116
PTH (pg/ml)	54.09 (28.75)	25.99 (19.06)	43.37 (21.12)	29.41 (18.77)	31.84 (19.04)	2113

Table 2: Lifestyle characteristics of the study population

	Tabriz	Tehran	Mashhad	Bushehr	Shiraz	Total
Physical activity (times/wk)						
0	155 (71.42)	183 (61.20)	161 (75.58)	161(70.30)	143 (72.58)	803 (69.53)
2 - 3	40 (18.43)	81 (27.1)	34 (15.96)	45 (19.66)	29 (14.73)	229 (19.83)
> 3	22 (10.15)	35 (11.70)	18 (8.46)	23 (10.04)	25 (12.69)	123 (10.64)
Total subjects	217 (100)	299 (100)	213 (100)	229 (100)	197 (100)	1155 (100)
Sun exposure (minute/day)						
0	49 (28.33)	65 (33)	37 (21.03)	50 (29.25)	49 (29.35)	250 (28.28)
0 - 15	15 (8.67)	13 (6.60)	15 (8.52)	7 (4.09)	14 (8.38)	64 (7.25)
>15	109 (63)	119 (60.40)	124 (70.45)	114 (66.66)	104 (62.27)	570 (64.47)
Total subjects	173 (100)	197 (100)	176 (100)	171 (100)	167 (100)	884 (100)
Type of exposing to sunlight						
None exposure	49 (17.07)	43 (16.28)	52 (18.57)	47 (17.93)	56 (18.30)	247 (17.66)
Just face & hands	188 (65.51)	180 (68.18)	190 (67.86)	179 (68.33)	201 (65.68)	938 (67.05)
More than face & hands	50 (17.42)	41 (15.54)	38 (13.57)	36 (13.74)	49 (16.02)	214 (15.29)
Total subjects	287 (100)	264 (100)	280 (100)	262 (100)	306 (100)	1399 (100)

Table 3: Prevalence of vitamin D deficiency in different subgroups

Total (n)	**Total n (%)**	**Severe [a] n (%)**	**Moderate [b] n (%)**	**mild [c] n (%)**	**Normal [d] n (%)**
	2061	81 (3.9)	807 (39.2)	532 (25.8)	641 (31.1)
age					
≤ 19	4	0 (0)	3 (75.0)	1 (25.0)	0 (0)
20 – 29	468	13 (2.8)	178 (38.0)	143 (30.6)	134 (28.6)
30 – 39	413	21 (5)	175 (42.4)	104 (25.2)	113 (27.4)
40 – 49	415	18 (4.3)	171 (41.2)	105 (25.3)	121 (29.20)
50 – 59	393	13 (3.3)	139 (35.4)	100 (25.4)	141 (35.9)
60 – 69	334	16 (4.8)	134 (40.1)	73 (21.9)	111 (33.2)
70 – 79	33	0 (0)	7 (21.2)	6 (18.2)	20 (60.6)
≥ 80	1	0 (0)	0 (0)	0 (0)	1 (100)
Area of residence					
Tabriz	582	22 (3.78)	220 (37.8)	172 (29.56)	168 (28.86)
Tehran	443	15 (3.38)	266 (60.06)	99 (22.34)	63 (14.22)
Mashhad	375	29 (7.73)	152 (40.53)	95 (25.33)	99 (26.41)
Shiraz	385	12 (3.1)	130 (33.8)	97 (25.2)	146 (37.9)
Bushehr	276	3 (1.1)	39 (14.1)	69 (25.1)	165 (59.7)
Physical activity, times/wk					
0	659	24 (3.64)	315 (47.8)	165 (25.04)	155 (23.52)
2 - 3	217	8 (3.6)	74 (34.2)	76 (35.02)	59 (27.18)
> 3	117	4 (3.41)	48 (41.02)	38 (32.47)	27 (23.07)
Total subjects	993				
Sun exposure (minute/day)					
0	238	11 (4.62)	99 (41.6)	74 (31.1)	54 (22.68)
<15 min	653	14 (2.14)	185 (28.34)	172 (26.34)	282 (43.18)
≥15 min	223	8 (3.6)	124 (55.6)	55 (24.66)	36 (16.14)
Total subjects	1114				
BMI (mean, SD)		24.71 (3.7)	25.2 (4.13)	25.17 (4.33)	25.4 (3.99)

[a]25 OHD level ≤ 12.5, [b]12.5 < 25 OHD level ≤ 25, [c]25 < 25 OHD level ≤ 35, [d]35.1 < 25 OHD level≤ 150
- cut – off value units are ng/ml

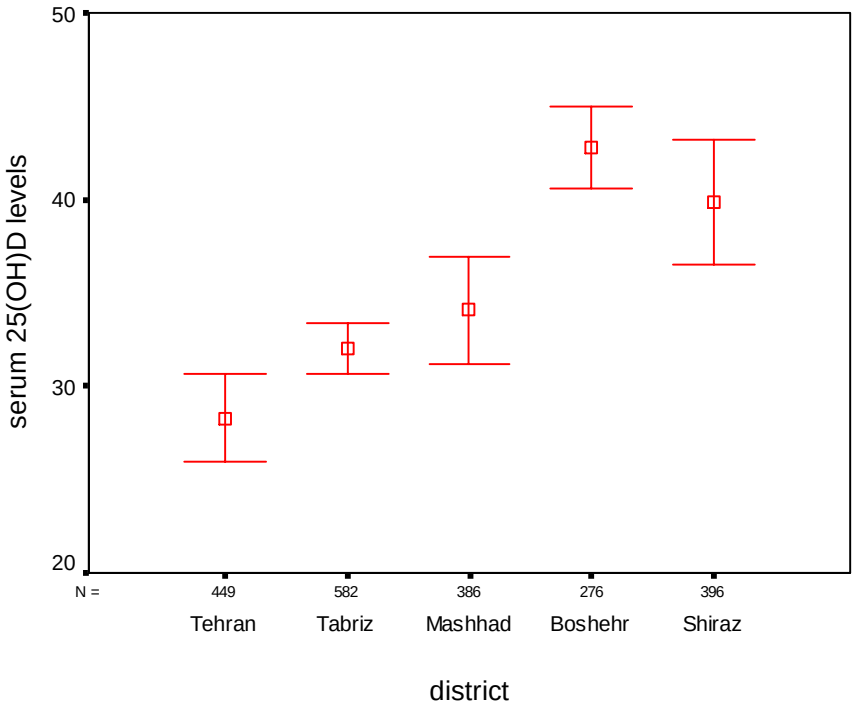

Fig. 1: geographical variation in serum 25 OHD level

Discussion

According to the present knowledge, vitamin D has a crucial role in skeletal system like bone formation, hypertension, osteoporosis and cancer prevention (30, 31). It also regulates immune function and differentiates immune cells directly and indirectly (32, 33). Therefore, obtaining a clear picture of the vitamin D status and exploring effective factors in vitamin D deficiency is important especially in developing countries.

We measured serum 25 O (HD) levels in 2396 healthy men in five urban areas including Tehran, Tabriz, Mashhad, Shiraz, and Bushehr. Most participants suffered from vitamin D deficiency (vitamin D levels less than 35 ng/ml), the highest prevalence was in Tehran and the lowest one belonged to Bushehr. Among five cities; Serum vitamin D in Bushehr was significantly different from other cities; in addition, Shiraz had better serum vitamin D values than Tabriz and Tehran.

Our result indicated that the majority of participants had low levels of vitamin D. In five urban areas; hypovitaminosis D was most prevalent in Tehran and least common in Bushehr. Some authors have reported an association among air pollution, industrial lifestyle, and low intake of seafood with low levels of serum vitamin D. Air pollution in Tehran may play a role in the highest rate of hypovitaminosis D; further investigations are required in this field to confirm this issue. On the other hand, lower rate of vitamin D deficiency in Bushehr may be due to its latitude (29.0' N) (34). Consumption of marine products is reported to associate with serum vitamin D status (35). As Bushehr is a coastal city and seafood is available there, assessing the effect of seafood consumption on vitamin D status in Boshehr may be helpful in understanding if it is a predictor of vitamin D status in that population compared to other cities.

Packard et al in USA, found a significant correlation between fortified milk (with vitamin D) intake and serum 25 OHD (36). Food fortification strategies in US and some European countries led to a very low prevalence of vitamin D deficiency (1.6-14.8%) (37, 38), so food fortification with vitamin D seems essential in Iran.

High prevalence of vitamin D deficiency in elderly is reported in many studies (17, 20, 21). In our study elder men had significantly higher levels of vitamin D compared to younger adults. The onset of most musculo-skeletal complications in adults is relatively high in 4^{th} to 5^{th} decade of life which frequently causes referral to specialist; so it's probable that most participants, older than fifty receive a prescription of taking supplements (including vitamin D and calcium). Although, we excluded participants who have taken vitamin D supplements, participants who took vitamin D supplements in previous mounts, were not excluded. Continuous use of vitamin D supplements, long half life of vitamin D and also the significant inverse correlation between elders' vitamin D status and BMD which is pointed out in our study can justify our findings.

Vitamin D levels were significantly high in metropolitans with lower latitude including Bushehr rather than other cities, and compared to Tehran and Tabriz, Shiraz had the highest vitamin D levels. This finding confirms that 25 OHD levels is related to geographical zone in addition to other factors such as duration of sun exposure, melanin pigmentation, age and physical activity (34, 37).

Although participants who exposed their face & hands to the sunlight had higher levels of vitamin D compared to non exposure, after adjustment for geographical area, age and physical activity; exposing only face & hands to the sunlight (which is common clothing style of Iranian men) did not predict vitamin D levels. In a similar study, Alagol et al. in Turkey reported that women with hijab had significantly lower levels of vitamin D compared to women with western clothing style in same latitude (23). Considering this issue, exposing more areas to sunlight or lengthening the duration of sun exposure is needed for Iranian men in order to optimize the synthesis of pre-vitamin D.

In our study we included those men who did not report to use vitamin D supplements; however, we included those who previously used such supplements. Therefore younger adults showed lower rates of vitamin D status comparing to older adults. Further investigation on the prevalence and causative factors of vitamin D deficiency is recommended in this area in a sample with no history of vitamin D/calcium supplement intake. Moreover, we did not assess some variables (such as seafood consumption, air pollution, etc.) in our study. Further investigations are needed in these areas in order to investigate their effect on vitamin D deficiency. We did not include rural areas, therefore, assessing the prevalence of vitamin D deficiency and factors affecting hypovitaminosis D in rural areas is recommended.

Our results showed a high prevalence of vitamin D deficiency in Iranian male population, which calls the need for food fortification in Iran and providing changes in life style of Iranian men.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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