Vitamin D status among Adult Saudi Females visiting Primary Health Care Clinics

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Abstract:

Background: Vitamin D plays an important role in diverse physiological functions in addition to its role in bone health. Vitamin D deficiency is very common in elderly people, but there are few reports on its prevalence in young adults.

Method: A cross-sectional study was carried out on a total of 465 young adult Saudi females aged 19 to 40 years old who were selected from primary health care centers of King Abdulaziz medical city, Riyadh, KSA. A questionnaire was used to identify socio-demographic characteristics and risk factors such as sunlight exposure and dietary intake. 25-hydroxy vitamin D [25(OH)D], Parathyroid hormone (PTH) and bone biochemical parameter were measured. The cutoff values for Vitamin D were defined as follows: deficient (<25nmol/L), insufficient (25-75 nmol/L) and normal (≥ 75 nmol/L).

Result: Overall, hypovitaminosis D were identified in all participants, with a mean level of 18.34 ±8.2 nmol/L. Of all the participants, 79.1% exhibited severe vitamin D deficiency (serum 25(OH) D < 25 nmol/L), while 20.9% exhibited vitamin D insufficiency (serum 25(OH) D between 25-50 nmol/L). There was a significant inverse correlation between serum 25 (OH) D concentrations and PTH, where secondary hyperparathyroidism was evident in 61.4% of participants with deficient vitamin D compared to 39.2% of participants with insufficient vitamin D.

Conclusion: Despite the abundant sunlight in Saudi Arabia, the prevalence of hypovitaminosis D among young healthy Saudi females is 100%. This finding should be considered a public health problem. Case identification, health education and prevention should be encouraged.

Keywords: Vitamin D, prevalence, women, Saudi, secondary hyperparathyroidism, sunlight, dietary supplement.

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Introduction

Vitamin D is a fat-soluble vitamin and hormone precursor that is present in two forms, ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). It plays an important role in bone health and neuromuscular functions. [1] The major source of vitamin D is from cutaneous synthesis by exposure to sunlight`s ultraviolet B. [2, 3] Another source is through the diet, including foods such as seafood, shrimp, mushroom, egg yolk and fortified milk. [4] Vitamin D deficiency leads to secondary hyperparathyroidism due to low serum calcium. This condition can result in high bone turnover, increased bone resorption and the development of osteopenia, leading to rickets in children and both osteomalacia and osteoporosis in adults. [5-8] Vitamin D deficiency is considered a major public health problem in many countries. Hypovitaminosis D was reported in numerous studies in Europe (UK, France, Italy, and Ireland) and in American populations, and it was often accompanied by elevated PTH levels. [9-13] Despite a year-long abundant sunlight in several countries in the Middle East and Asia, vitamin D deficiency is very common among different populations in different age groups. It was reported in Saudi Arabia, Jordan, Morocco, Lebanon, China, and Thailand as well as the Indian subcontinent region. [12, 14-22] Avoidance of sunlight and poor dietary intake are probably the main risk factors for vitamin D deficiency. To our knowledge, there is a lack of recent studies addressing vitamin D status among young Saudi females in the Riyadh region in Saudi Arabia, we undertook this study to assess vitamin D status and secondary hyperparathyroidism among young healthy females visiting primary health care clinics in the Riyadh area of Saudi Arabia.

Subjects and Methods

This is a cross-sectional study. Data and blood samples collection took place over a 4-month period between January 1st, 2011 and April 30th, 2011. The study was approved by the research and ethical committee of King Abdullah International Medical Research Center. Sample size was guided by previous study in Saudi Arabia (Al-Khobar), it was estimated to be 369 plus 131 = 500 participants might be needed for the study with CI of 95% and desired precision of ± 5%. Adjusting sample size for response rate, problems of patient compliance with lab test and errors in data collection. In total, 465 young adult Saudi females aged 19 to 40 years old were selected from family medicine and primary care clinics at King Fahad National Guard Hospital (King Abdulaziz Medical City) in Riyadh, Saudi Arabia. Exclusion criteria included chronic diseases or other health conditions that may affect the vitamin D level in blood (parathyroid gland disease, liver diseases, renal diseases, epilepsy, cancer, inflammatory bowel disease, malabsorption, celiac disease, gastric bypass, bowel surgery, pregnancy or lactation), use of vitamin D supplements or any medication that can affect vitamin D level (anticonvulsants, osteoporosis drug therapy, chemotherapy, antituberculosis drugs) and inability to provide informed consent. All patients who visited primary health care and employee health clinic were invited by the head nurse or by their general practitioner to participate in the study. Subjects' medical records were first reviewed by the attending physician to confirm their eligibility. Each eligible patient received an invitation letter that contained brief information about vitamin D, its importance, common health consequences of vitamin D deficiency and detailed study explanation. Subsequently, informed written consent was obtained from candidates before undertaking the interview to complete the study questionnaire. Data from participants were obtained through an interviewer-administered questionnaire that included socio-demographic information such as age, marital status, educational level, occupation and information about dietary intake and sun exposure habits. BMI data were collected from all participants. Blood samples were collected from participants to assess serum 25-hydroxy vitamin D [25(OH)D] concentration, PTH, calcium, phosphorous, alkaline phosphates and albumin. There were no restrictions on diet or requests to discontinue any medication before testing.

Serum 25-OH- vitamin D_2/D_3 was measured in King Fahad National Guard Hospital by the LIAISON 25 OH vitamin D total assay using chemiluminescent immunoassay (CLIA) technology, a more recently developed automated immunoassay by DiaSorin that has largely replaced the RIA. Serum 25-OH-vitamin

D was considered normal if ≥ 75 nmol/L, deficient < 25 nmol/L and insufficient if between 25-75 nmol/L. Serum PTH, calcium, alkaline phosphates and phosphorous were measured with standard laboratory procedures. Data were entered in a computer and analyzed using Statistical Package for Social Sciences (SPSS) version 18 software. A chi-squared test was used to assess statistically significant associations between vitamin D level in blood and different variables. A P-value of ≤ 0.05 was considered as a significant cutoff point with a 95% confidence interval.

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Results

A total of 465 females were included in the analysis. The mean age was 28.62 ± 6.57, and the majority of participants were married (63.7%) and housewives (51.8%). The socio-demographic information and BMI data are shown in **table (1).** All of our participants had low vitamin D levels (serum 25-OH-vitamin D < 75 nmol /L), with a mean level of 18.34 ± 8.2 nmol/L as shown in **table (2).**

Of all the participants, 79.1% (n=368) exhibited severe vitamin D deficiency (serum 25-OH-vitamin D less than 25 nmol /L). **Table (3)** shows that females who were younger than 30 years old were more vitamin D deficient compared to females older than 30 years old (P-value <0.001, (X2) = 15.3). There was a statistically significant relationship between vitamin D level and marital status and between vitamin D level and educational level. Mean 25 (OH) D level was low in single participants compared to married (P=0.014, odds ratio [OR] = 1.893 95% CI= 1.130 – 3.17). In contrast, housewives were less vitamin D-deficient (72.6%) compared to working participants (86.1%) (P-value <0.001 X2 = 12.905 [OR] = 0.426, 95% CI (0.265-0.684). In addition, participants with higher levels of education (secondary school and above) showed lower vitamin D levels compared to participants with lower levels of education (P-value <0.001, X^2=21.29).

Table (1). Socio-demographic characteristics:

Characteristics	**No**(n=465)	**%**
Age group		
19-24	156	**33.5**
25-29	103	**22.2**
30-35	115	**24.7**
36-40	91	**19.6**
Marital status		
Single	156	**33.5**
Married	296	**63.7**
Divorced	12	**2.6**
Widowed	1	**0.2**
Educational level		
Illiterate	29	**6.2**
Primary school	47	**10.1**
Intermediate	49	**10.5**
Secondary school	131	**28.2**
University and above	209	**44.9**

Occupation		
Housewife	241	**51.8**
Unemployed	63	**13.5**
Student	64	**13.8**
Educational field	45	**9.7**
Health field	36	**7.7**
Administrative field	16	**3.4**
Occupation status		
Working	161	**34.6**
Non-Working	304	**65.4**
Dressing style		
Niqab	358	**77.0**
Complete cover (including eyes and hands)	97	**20.9**
Hijab	10	**2.2**
BMI group		
Low weight (less than 18.5)	19	**4.1**
Normal (18.5-24.9)	124	**26.7**
Overweight (25-29.9)	159	**34.2**
Obese (30 and above)	163	**35.1**

Table (2). Levels of serum vitamin D among participants

Vitamin D in group	**No.**	**(%)**	**Mean nmol/L**	**±Std.**
Normal	0	(0%)	0	
Deficiency	368	(79.1%)	14.92	±4.534
Insufficiency	97	(20.9%)	31.31	±5.600
Total	465	(100.0%)	18.34	±8.197

BMI did not have a statistically significant association with vitamin D level. The majority of participants with vitamin D deficiency were symptomatic. Back pain and generalized body aches were the most common complaints (60.6%), but that was not statistically significant. **Table (4)** shows a statistically significant relationship between serum 25 (OH) D concentrations and amount of milk intake, cod liver oil and multivitamin supplementation. In this sample, 85.2% of participants women who reported that they never or rarely drank milk had severe vitamin D deficiency compared to 56.3% who reported drinking almost the daily requirement of milk (more than 2 cups) (P value = 0.013 and X^2 = 10.67). No significant relationship was observed between serum vitamin D and average sun exposure, except that participants who tried to avoid sun exposure were more likely to have a vitamin D deficiency (P value= 0.020, X^2 = 7.861). Observing the relationship between serum 25(OH) D and times of sun exposure per week showed that participants who were exposed three or more times per week had high levels of vitamin D, but it was not statistically significant. As shown in **table (5),** secondary hyperparathyroidism (PTH > 7.2 Pmol/L) was evident in 56.8% of the participants. The inverse relationship between vitamin D and intact PTH was observed in 61.4% of participants with severe vitamin D deficiency compared to 39.2% of participants with vitamin D insufficiency (P value ≤ 0.001 [OR]= 0.405, CI(0.256-0.640).

Table (3). Vitamin D level in relation to Socio-demographic Data.

Socio-demographic Data	Categories	Vitamin. D Level		Total	Chi-Squared Value (X^2)	P Value
		Deficient No. %	Insufficient No. %			
Age Group	Below 30	222 (85.7)	37 (14.3)	259(100)	15.307	.000
	30 and above	146 (70.9)	60 (29.1)	206(100)		
	Total	368 (79.1)	97 (20.9)	456(100)		
Marital Categories	Single	133 (85.3)	23 (14.7)	156 (100)	6.008	0.014
	Married	223 (75.3)	73 (24.7)	296 (100)		
	Total	356 (78.8)	96 (21.2)	452 (100)		
Educational level	Low Education	81 (64.8)	44(35.2)	125 (100)	21.294	.000
	High Education	287 (84.4)	53(15.6)	340 (100)		
	Total	368 (79.1)	97 (20.9)	465 (100)		
Occupation Categories	Housewife	175 (72.6)	66 (27.4)	241 (100)	12.905	.000
	Other	193 (86.1)	31 (13.8)	224 (100)		
	Total	368 (79.1)	97 (20.9)	465 (100)		

Table (4). Vitamin D level in relation to average diet.

Diet Consumption Pattern	Categories	Vitamin D Level		Total	Chi Square Value (X^2)	P Value
		Deficiency No. %	Insufficiency No. %			
Times of 1 cup milk intake per day	Never or rarely	161 (85.2)	28 (14.8)	189 (100)	10.67	0.013
	Once	154 (76.2)	48 (23.8)	202 (100)		
	Twice	44 (75.9)	14 (24.1)	58 (100)		
	More than 2 times	9 (56.3)	7 (43.8)	16 (100)		

	Total	368 (79.1)	97 (20.9)	465 (100)		
Milk type	Raw milk	40 (83.3)	8 (16.7)	48 (100)	1.898	0.387
	Commercial milk	259 (76.4)	80 (23.6)	339 (100)		
	Both	13 (86.7)	2 (13.3)	15 (100)		
	Total	312 (77.6)	90 (22.4)	402 (100)		
Average seafood (fish, tuna, shrimp) consumption per week	Never or rarely	217 (74.1)	76 (25.9)	293 (100)	13.316	0.011
	Once	113 (89.0)	14 (11.0)	127 (100)		
	Twice	23 (82.1)	5 (17.9)	28 (100)		
	3 times	11 (91.7)	1 (8.3)	12 (100)		
	More than 3 times	4 (80.0)	1 (20.0)	5 (100)		
	Total	368 (79.1)	97 (20.9)	465 (100)		
Cod liver Oil Intake	No	349 (80.4)	85 (19.6)	434 (100)	8.518	0.004
	Yes	14 (56.0)	11 (44)	25 (100)		
	Total	363 (79.1)	96 (20.9)	459 (100)		
multivitamin Intake	No	278 (82.7)	58 (17.3)	336 (100)	7.473	0.006
	Yes	71 (70.3)	30 (29.7)	101 (100)		
	Total	349 (79.9)	88 (20.1)	437 (100)		

Table (5). Relationship between vitamin D deficiency and Parathyroid hormone levels.

VITAMIN D LEVEL	PARATHYROID HORMONE IN GROUPS (Pmol/L)		Total	Odds Ratio (CI)	P Value
	Normal	**High**			
	No. % mean ± SD	No. % mean ± SD			
Insufficient	59 (60.8) 5.2 ± 1.2	38 (39.2) 10.1 ± 2.4	97 (100)	0.405 (0.256 - 0.640)	0.000
Deficient	142 (38.6) 5.5 ±1.2	226 (61.4) 10.8 ±3.1	368 (100)		
Total	**201 (43.2)**	**264 (56.8)**	465 (100)		

Discussion

Vitamin D plays an important role in diverse physiological functions in addition to its role in bone homeostasis. In addition to musculoskeletal complications, epidemiological studies revealed an association between vitamin D levels and a wide range of chronic diseases that include "cardiovascular diseases, metabolic diseases, such as diabetes mellitus; autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis; neoplastic diseases, such as colon cancer and breast cancer". [1, 21-24]

There is a debate in the literature regarding cutoff values and criteria that appropriately define suboptimal vitamin D levels. The proposed criteria to define an optimal level of 25(OH) D include maximum suppression of circulating PTH concentration and greatest calcium absorption. The level of 25(OH) D that is associated with maximal suppression of PTH has been reported to range from 12 to 40 ng/ml, with most studies reporting 25(OH) D values of approximately 30 to 32 ng/ml. [20]

Vitamin D deficiency has become a global public health problem. Several studies have drawn attention to the prevalence of vitamin D deficiency worldwide. Most of these studies focused on elderly people, with few reports on the prevalence of vitamin D deficiency in young adults. The most recent statistics demonstrated that more than 90% of non-white and approximately 75% of white population groups in the United States now suffer from vitamin D insufficiency (25- hydroxyvitamin D < 30 ng/ml). [25] In Europe, the prevalence of vitamin D deficiency varies. It is highly prevalent in the UK, where 25(OH) D < 75 nmol /L were found in 87% of participants in winter and in 60% of participants in summer. [26] Some European countries showed moderate risk of deficiency, where 25(OH) D< 20 ng/ml) was found in 51% in Ireland, 50% in Germany and approximately 40% in Spain. [13, 26] In France, suboptimal vitamin D levels are rare and are reported as 14% among healthy adult individuals. [10] Despite the abundant sunshine in the Middle East and Asia, some countries in these regions report the highest rate worldwide of hypovitaminosis D. In Thailand, the prevalence was determined as 77% of premenopausal females, and the prevalence reached up to 90% in India. [21, 27] In Qatar, 97% of all health care professionals were vitamin D deficient (mean level of 25(OH) D<75 nmol /L). [28] A similar rate was noted in a cross-sectional study of Jordanian women of childbearing age, where 97% had serum vitamin D levels <50 nmol/L. [29] In Morocco, 91% of healthy adult females aged 24 to 77 years had serum 25(OH) D<75 nmol /L, and approximately 72% of adult Lebanese had serum level of vitamin D <12 ng/ml. [18,19] A study from Tunisia reported a low prevalence of vitamin D deficiency in 47% of participants. [30] Such differences in the prevalence of vitamin D deficiency worldwide might be related to different populations studied or different cutoff levels of serum 25(OH) D that were used. Other factors that may drive these differences include inadequate vitamin D fortification in dietary products (milk, cereal, and drinks such as orange juice), difference in clothing style, latitude and seasonal variations where vitamin D levels are highest in September at the end of summer and lowest in winter. [13, 31]

Our study aimed to determine the prevalence of vitamin D deficiency and secondary hyperparathyrodism among young adult females at the age of peak bone mass (19-40 years). The study was conducted in the central region of Saudi Arabia and included women who were visiting primary health care centers. Surprisingly, hypovitaminosis D (serum 25(OH) D Level ≤75 nmol/L (30 µg/L), was prevalent in 100% of participants. Of all participants, 79.1% had severe vitamin D deficiency (25(OH) D< 25 nmol/L), while 20.9% showed vitamin D insufficiency or mild to moderate deficiency (serum 25(OH)D between 25-50 nmol/L) with a mean level of 31.3 ± 5.6.

At the national level, our study reported the highest prevalence rate of suboptimal vitamin D3 levels compared to reported data in other areas of Saudi Arabia. In Jeddah, a recent survey of 1,172 randomly selected healthy Saudi women showed that 80% of them exhibited vitamin D deficiency (serum 25(OH)D< 50 nmol /L). [32] Another study that was conducted in the Eastern region of Saudi Arabia reported a lower prevalence and showed that only 30% of young females aged 25 to 35 years were vitamin D deficient. [33] The widespread hypovitaminosis D in the Riyadh area could be explained by many factors, including limitations of the study sample and the very hot and dry weather of the Riyadh area, which may restrict outdoor activities during the daytime. Most females intentionally avoid sun exposure for cosmetic purposes, which may contribute to the findings of the study. The Riyadh region is remotely located from the seacoast compared to the Eastern and Western regions of the Kingdom, which may drive the population dietary habits to depend mainly on cattle and poultry meat rather than sea food, which is known as a good source of vitamin D.

The influence of socio-demographic characteristics on serum 25-OHD concentration has been observed in our study. Younger women (<29 years) have more vitamin D deficiency than older women (P ≤ 0.00); however, in contrast, other studies showed that vitamin D level decreases as age increases. [(26, 33)] Educational levels and employment status had a large impact on vitamin D level in our study, where hypovitaminosis D was more common among highly educated and working females (P value= 0,014 and 0,000, respectively). This finding could be explained by the fact that most highly educated females are employed. Most of this population is employed indoors with less sun exposure, compared to housewives who have more free time for sun exposure. The diet for those in the workplace comprises mainly fast food, which lacks many important vitamins and minerals. In contrast, a study in Tunisia reported that vitamin D deficiency is common among housewives. [(30)]

Although Saudi Arabia enjoys a sunny climate throughout the year, direct exposure to sunlight by the local population is limited due to high daytime temperature, as observed in our study. The duration of sunlight exposure necessary to maintain adequate stores of vitamin D has always been a controversial issue, but recently, it was recommended to be 10-15 minutes of mid-day sun (10:00 am- 3:00 pm) and approximately 1 minimal erythemal dose (MED). MED refers to the amount of sun exposure that produces a faint redness in the skin of an adult with light pigmentation and is comparable to taking 10,000-20,000 IU of vitamin D3 orally if the whole body is exposed. Based on this, exposure of hands, face and arms (approximately 15% of the body surface area and approximately 1/3 MED) should produce approximately 1000 IU of vitamin D3. Individuals with darker pigmentation would require 5-10 times more exposure to generate a similar amount of vitamin D. [(34, 35)] In our study, we did not find any significant relationship between vitamin D concentration and duration and time of sun exposure. However, by using multiple linear regression analysis, we found that times of sun exposure per week is one of the predictor variables that are statistically correlated with serum 25(OH)D concentration (P-value = 0.057) (R= 0.369).

Secondary hyperparathyroidism is a well-known complication of vitamin D deficiency. Many studies found that there was an inverse relationship between vitamin D level in serum and parathyroid hormone level, which can precipitate cortical bone loss and increase bone turnover. [(28, 36-38)] Similarly, our study found that secondary hyperparathyroidism (PTH > 7.2 pmol/L) was present in 56.8% of participants who had hypovitaminosis D with a mean level of 10.73 pmol/L. The inverse association between serum 25(OH) D and intact PTH was more evident in 61.4% of participants with severe vitamin D deficiency compared to 39.2% of participants with vitamin D insufficiency (P-value ≤ 0.001 OR= 0.405). Levels of serum calcium, phosphorous and alkaline phosphate normally reflect bone turnover, and they are usually abnormal in severe osteomalacia. Despite low vitamin D levels among the participants, our study showed that serum calcium, phosphorous and alkaline phosphate levels were within the normal range in approximately 97% of participants. This finding might be attributed to compensatory high parathyroid hormone levels. The finding of normal serum biochemical parameters in most cases is interesting and at the same time alarming, as many osteomalacia and osteoporosis cases could be missed if serum 25-(OH) D were not measured.

We recognize some limitations to our study. Although the sample size was appropriate, it was relatively small, and it was not population-based. Therefore, the findings might not reflect the actual prevalence of vitamin D deficiency in the general population as a whole, but it could be significant. The blood samples were collected only once during the months of January through April. It would have been useful if patients were evaluated at different times of the year to determine the effects elicited by seasonal changes on vitamin D levels.

In conclusion, regardless of age, race or geographic location, suboptimal vitamin D status seems to be an important issue facing the world today. However, inter-laboratory variation of serum 25(OH) D measurements may hinder comparisons between different populations. The etiology of the high prevalence of vitamin D deficiency in our study is multifactorial, where lack of sunlight exposure and inadequate diet are the most important factors. To prevent an increase in incidence, raising awareness of the importance of vitamin D and health education should be enhanced. Because there is a problem with obtaining vitamin D from natural sources, it is important to encourage combined calcium and vitamin D supplements (tablet or drop form) for all Saudi females regardless of risk level as maintenance dose after correcting deficiency and follow-up are crucial. This intervention is both simple and inexpensive, and it may lead to improvement in bone structure and protect from non-musculoskeletal complications.

Ethical statement

This research study was reviewed and approved by the Institutional Review Board (IRB) ethical committee of King Abdullah International Medical Research Center. Informed consent was obtained from all participants before the study. All participants were given a follow-up appointment for results discussion, counseling and treatment initiation if indicated.

Abbreviations

KAMC………… King Abdul-Aziz Medical City
PTH…………… Parathyroid Hormone
BMI…………… Body Mass Index
MED………….. Minimal Erythemal Dose

References:

1. Teresa Kulie, Amy Groff, DO, Jackie Redmer, Jennie Hounshell and Sarina Schrager. Vitamin D: An Evidence-Based Review. (J Am Board Fam Med. 2009 Nov-Dec; 22(6):698 –706.
2. Michael F Holick *and Tai C Chen*. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008; 87(4):1080S– 6S.
3. Bodo Lehann and Michael Meurer. Vitamin D Metabolism. Dermatologic Therapy 2010; 23:2–12.
4. Mark A. Moyad. Vitamin D: A Rabid Review. Dermatology Nursing Jan-Feb 2009; 21(1):25-30.
5. P. Lips. Vitamin D Physiology. Progress in Biophysics and Molecular Biology .2006; 92: 4–8.
6. Bischoff-Ferrari HA, Kiel DP, Dawson-Hughes B, Orav JE, Li R, Spiegelman D, et al**.** Dietary calcium and serum 25-hydroxyvitamin D status in relation to BMD among U.S. adults. J Bone Miner Res.2009; 24:935–942.
7. Cauley JA, Lacroix AZ, Wu L, Horwitz M, Danielson ME, Bauer DC, et al. Serum 25 hydroxyvitamin D concentrations and risk for hip fractures. Ann Intern Med.2008; 149:242–250.
8. Mir Sadat-Ali, Abdulmohsen AlElq, Hifa Al-Turki, Fatma Al-Mulhim, Amein AlAli. Vitamin D level in healthy men in eastern Saudi Arabia. Ann Saudi Med.2009; 29(5): 378-382.
9. Nava Stoffmana and Catherine M. Gordonb. Vitamin D and adolescents: what do we know? Current Opinion in Pediatrics 2009, 21:465–471.
10. M. Z. Erkal , J.Wilde , Y. Bilgin , A. Akinci , E. Demir, R. H. Bödeker , et al. High prevalence of vitamin D deficiency, secondary hyperparathyroidism and generalized bone pain in Turkish immigrants in Germany: identification of risk factors. Osteoporos Int. (2006) 17: 1133–1140.
11. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. Diabetologia 2005; 48:1247–1257.
12. P. Lips. Vitamin D status and nutrition in Europe and Asia. Journal of Steroid Biochemistry & Molecular Biology.2007; 103: 620–625.
13. M. O'Sullivan, T. Nic Suibhne, G. Cox M. Healy, C. O'Morain. High prevalence of vitamin D insufficiency in healthy Irish adults. Ir J Med Sci (2008) 177:131–134.
14. Saleh H Sedrani, Abdel Wahab TH Elidrissy, and Kamal M ElArabi,. Sunlight and vitamin D status in normal Saudi subjects. Am J Clin Nuir I983Jul; 38(1):129-132.

15. V. Fonseca, R. Tongia, M. El-hazmi. ABu-Aisha. Exposure to sunlight and vitamin D deficiency in Saudi Arabian women. Postgrad Med J. 1984 Sep; 60(707):589-91.
16. Siddiqui AM, Kamfar HZ. Prevalence of vitamin D deficiency rickets in adolescent school girls in western region, Saudi Arabia. Saudi Med J. 2007; 28(3):441–444.
17. Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. Osteoporos Int. 2001; 12: 931–5.
18. Fadoua Allali, Sihame El Aichaoui, Hamza Khazani, Boubker Benyahia, Bouchra Saoud, Saâd El Kabbaj. et al. High Prevalence of Hypovitaminosis D in Morocco: Relationship to Lifestyle, Physical Performance, Bone Markers, and Bone Mineral Density. Semin Arthritis Rheum.2009 Jun; 38(6):444-451.
19. Gannage-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. J Bone Miner Res. 2000; 15(9):1856–62.
20. Wat WZ, Leung JY, Tam S, Kung AW. Prevalence and Impact of Vitamin D Insufficiency in Southern Chinese Adults. Ann Nutr Metab 2007; 51:59–64.
21. Soontrapa S, chailurkit LO. Hypovitaminosis D in Thailand. J Med Assoc Thai.2009 Sep; 92 Suppl5:S26-9.
22. David R. Fraser. Vitamin D-deficiency in Asia.J steroid Biochem mol Biol 2004 May; 89-90(1-5):491-5.
23. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab 2007; 92:2017–29.
24. Natasha Khazai, Suzanne E. Judd, and Vin Tangpricha, Calcium and Vitamin D: Skeletal and Extraskeletal Health. Curr Rheumatol Rep. 2008 April; 10(2): 110–117.
25. John S. Adams and Martin Hewison. Update in Vitamin D. (*J Clin Endocrinol Metab, February 2010*, 95(2):471–478.
26. González-Molero I, Morcillo S, Valdés S, Pérez-Valero V, Botas P, Delgado E, et al. Vitamin D deficiency in Spain: a population-based cohort study. European Journal of Clinical Nutrition 2011; 65:321-328.
27. R. Goswami, S.K. Mishra & N. Kochupillai. Prevalence & potential significance of vitamin D deficiency in Asian Indians. Indian J Med Res, March 2008; 127: 229-238.
28. Salah M. Mahdy, Samer A. Al-Emadi, Izzat A.Khanjar, Mohammed M. Hammoudah, Housam A. Sarakbi, Abdul-Rahim M. Siam et al. Vitamin D status in health care professionals in Qater. Saudi Med j 2010;31(1):74-77
29. Gharaibeh MA, Stoecker BJ. Assessment of serum 25 (OH) D concentrations in women of childbearing age and their preschool children in Northern Jordan during summer. Eur J Clin Nutr. 2009 Nov; 63(11):1320-6.
30. N. Meddeb, H. Sahli, M. Chahed, J. Abdulmoula, M. Feki, Hadj Salah, et al. Vitamin D deficiency in Tunisia. Osteoporos Int 2005; 16:180-183.
31. Joseph W. Diehl, Melvin. Chiu. Effect of ambient sunlight and photoprotection on vitamin D status. Dermatologic therapy 2010;23:48-60
32. Ardawi MS, Qari MH, Rouzi AA, Maimani AA, Raddadi RM. Vitamin D status in relation to obesity, bone mineral density, bone turnover markers and vitamin D receptor genotypes in healthy Saudi pre- and postmenopausal women. Osteoporos Int. 2011; 22:463-475.
33. Hifa A. Al-Turki, Mir Sadat-Ali, Abdulmohsen H. Al-Elq, Fathma A. Al-Mulhim, Amein K. Al-Ali. 25-Hydroxyvitamin D level among healthy Saudi Arabian women. Saudi Med J 2008; 29(12): 1765-1768.
34. Patricia T. Alpert, Ulfat Shaikh. The Effects of Vitamin D Deficiency and Insufficiency on the Endocrin and Paracrine Systems. Biological Research Nursing. 2007; 9(2): 117-12.
35. V.H. Ekbote, A.V. Khadilkar, M.Z. Mughal, N. Hanumante, N. Sanwalka,V.V. Khadilkar, et al. Sunlight exposure and development of rickets in Indian Toddlers. Indian Journal of Pediatrics 2010; 77:61-65.
36. 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. Clinical Endocrinology. 2010; 73(5):573-580.

37. Rodrigo Moreno-Reyes, Yvon A. Carpentier, Marleen Boelaert, Khadija El Moumni, Ghislaine Dufourny, Christine Bazelmans, et al. Vitamin D deficiency and hyperparathyroidism in relation to ethnicity: a cross-sectional survey in healthy adults. Eur J Nutr 2009; 48:31–37.
38. Holic MF: Vitamin D status, measurement, interpretation and clinical application. Ann Epidemoil 2009; 19: 73-78.