#### An Alarming High Prevalence of Vitamin D Deficiency Among Healthy Adults

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Abstract: Background and objectives: Vitamin D is critically important for the development, growth and maintenance of healthy bones from birth to death. This research is designed to study the prevalence of vitamin D deficiency among healthy adults, and to assess the demographic features, sunlight exposure, dietary habits and other risk factors. Methods: A cross sectional study including 365 subjects above the age of 18 years, randomly selected from five healthy care (early case detection) clinics. The study was conducted from April to October 2012. Participants completed detailed questionnaires regarding their demographic data, average daily sunlight exposure, dietary habits, multivitamins use and regular exercise. Height and Body mass index (BMI) and circulating levels of 25-hydroxyvitamin D [25(OH) D] were measured. **Results:** A total of 365 eligible participants included in the study. 25.2% were deficient and 36.2% were insufficient in vitamin D level. Vitamin D deficiency and insufficiency were significantly more frequent among female and age group 60 years and more (p<0.05). After adjustment of age and gender, a highly significant association was found between duration of exposure to sunlight and vitamin D deficiency. The risk to develop vitamin D deficiency is nearly 5 times more in participants exposed to sunlight less than 5 Minutes/Day, when compared with participants exposed to sunlight >30 minutes/Day, OR=5.13 (95% CI=3.14-7.90). Consumption of vitamin D rich food, occupation, BMI and exercise were found to be strong predictors of vitamin D deficiency, OR=4.38, 2.88, 2.46 & 2.74 respectively. Multivitamins use was significantly associated with vitamin D deficiency in univariate analysis (p < 0.05), but this was weakened somehow when adjusted in multivariate analysis, adjusted OR=1.17 (95% CI=0.74-2.55). Conclusion & Recommendations: Interventions should be taken to increase consumption of vitamin D rich foods such as fortified milk, fish, liver and cheese, taking a vitamin D supplement, physical exercises, increasing sun exposure to the extent needed for adequate vitamin D production and/or periodic medical examination of healthy adults for early case detection and intervention.

[Gaafar M. and Badr S. An Alarming High Prevalence of Vitamin D Deficiency Among Healthy Adults. *Life Sci J* 2013; 10(1):3292-3298]. (ISSN: 1097-8135). <u>http://www.lifesciencesite.com</u>. 416

Key words: Vitamin D deficiency, prevalence, risk factors, healthy adults.

#### 1. Introduction

Vitamin D deficiency is an unrecognized epidemic and a common health problem worldwide <sup>(1)</sup>. It has been reported from many countries, including those with a lot of sunshine that the prevalence of vitamin D deficiency ranges from 15-80% <sup>(2)</sup>. Studies from Saudi Arabia, Kuwait, United Arab Emirates, and Iran reveal that 10-60% of mothers and 40–80% of their neonates had undetectable low vitamin D levels at delivery <sup>(3-5)</sup>.

Vitamin D is a prohormone that is essential for normal absorption of calcium from the gut, and deficiency of vitamin D is associated with rickets in growing children and osteomalacia in adults <sup>(6, 7)</sup>. Various studies had identified potential associations between vitamin D deficiency and a variety of diseases, including type 1 and 2 diabetes, metabolic syndrome, cancer, cardiovascular disease, multiple sclerosis, rheumatoid arthritis, hypertension, and neuromuscular malfunction <sup>(8-10)</sup>. Mental health has also been shown to be affected by vitamin D deficiency <sup>(11)</sup>.

Vitamin D is primarily made in the skin by cutaneous synthesis under the action of ultraviolet radiation (UVR) after exposure to sunlight (80-90%) and (10-20%) is derived from dietary sources <sup>(12, 13)</sup>. This significant role of sunlight in vitamin D synthesis suggests a low prevalence of vitamin D deficiency in tropical and Middle East countries, where sunshine is abundant. However, studies carried out in Hawaii, Turkey, India, Iran and Saudi Arabia had shown a high prevalence of vitamin D deficiency <sup>(14-16)</sup>. Several factors have contributed to this dangerously low vitamin D levels, respondents' behavior of avoiding sunlight due to extreme of temperature, people mostly remain inside and clothing which prevented sunlight exposure. Moreover, the dietary habits are also blamed, as food with high level of vitamin D level is not being consumed (17-19)

Vitamin D deficiency can result from inadequate irradiation of the skin, insufficient dietary intake of the vitamin, or impairments in metabolic activation (hydroxylation) of the vitamin <sup>(20)</sup>. Other factors potentially affect vitamin D status include genetic factors, adiposity and factors affecting the cutaneous synthesis of vitamin D such as skin pigmentation, age, season, latitude, melanin concentration, clothing and use of sunscreens<sup>(21)</sup>.

Studying the problem of vitamin D deficiency will affect the prevention strategies including life style modification, mainly proper exposure to UV light (especially sunlight), better dietary intake, activity and compliance to medicines <sup>(22)</sup>. The objectives of this study are to *investigate the prevalence of vitamin D deficiency among healthy adults in Kuwait, and also assess the demographic features, sunlight exposure, dietary habits and other risk factors of vitamin D deficiency among study participants.* 

# 2. Subjects and methods: Study design and subjects

This analytical cross-sectional clinic-based study is carried out in the State of Kuwait. This sunny country was divided into five health regions, from each one a healthy care (early case detection) clinic was randomly selected: Alrumaithya (Hawalli), Abdalla Elabdelhadi (Capital), Alnahda (Farwaniya), Fahaheel and Al-Ahmadi. These clinics were designed for regular check up of healthy population for early case detection. The study was conducted from April to October 2012.

A total sample of 410 Kuwati subjects attending the clinic for routine check-up, both males and females above the age of 18 years were randomly selected and approached by physicians, out of them 375 subjects (91.5%) agreed to enroll and gave samples. Ten subjects, who were complaining of hepatic or renal diseases or were taking drugs that could influence vitamin D status as steroids and anti epileptics, are excluded from the study, and so, 365 subjects were eligible for the study. Participants completed detailed questionnaires regarding their demographic data, average daily sunlight exposure, dietary habits, multivitamins use and regular exercise.

Height was measured without shoes and weight was recorded while wearing indoor clothing. Body mass index (BMI) (weight in Kg, divided by height in meters squared) was calculated. The WHO classification for BMI was used to estimate the degree of obesity <sup>(23)</sup>.

# Biochemical parameters (25-hydroxyvitamin D measurement)

Circulating levels of 25-hydroxyvitamin D [25(OH)D] are considered to be the most reliable measure of overall vitamin D status <sup>(6)</sup>. In the present

study, the serum 25 (OH) D levels were measured by a direct enzyme-linked immunosorbent assay with the 25-Hydroxy Vitamin D Direct EIA kit purchased from Immunodiagnostic Systems Ltd. (Fountain Hills, Arizona, USA). This assay has been shown to reliably measure both 25-hydroxyvitamin D isoforms (D2 and D3)<sup>(24)</sup>.

Mild, moderate and severe vitamin D deficiencies were defined as 25-OHD values of 20-30 ng/mL, 10-<20 ng/mL, and <10 ng/mL respectively. As per recently available literatures <sup>(25, 26)</sup>, there is another classification for vitamin D deficiency: the combination of moderate and severe vitamin D deficiencies is considered vitamin D deficiency (25-OHD <20 ng/mL) and mild vitamin D deficiency (25-OHD 20-30 ng/mL) as vitamin D insufficiency. **Statistical analysis** 

#### Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (version 17). The association between vitamin D deficiencies and risk factors was determined using the x2 test. Statistical significance implies P value <0.05. The degree of risk was determined by Odds Ratio (OR) and 95% Confidence Interval (CI). The multivariate logistic regression analysis was performed; the dependent variables were: normal vitamin D (0) and vitamin D deficiency (1). The independent variables (covariates) were: age, gender, occupation, duration of exposure to sunlight, consumption of vitamin D rich food, multivitamins use, BMI and exercise.

**Ethical issues**: All the study subjects gave voluntary informed consent before participation. The protocol of the study was reviewed and approved by an ethics committee at the study centers.

# 3. Results:

A total of 365 participants included in the study, 92 (25.2%) were deficient and 132 (36.2%) were insufficient in vitamin D level. Among them 165 (45.2%) were males and 200 (54.8%) were females. Vitamin D deficiency and insufficiency were significantly more frequent among female and age group 60 years and more (p<0.05). A higher proportion of participants with vitamin D deficiency and insufficiency were involved in indoor work or were house wives or not working; The difference was statistically significant when compared with others involved in field (outdoor) work (p<0.0001). No statistical significant association was found between vitamin D level and other covariates, including level of education and marital status (p>0.05); Most (74.3%) of study participants were married, rest of them were single, widow or divorced (Table 1).

		Vitamin D Status			
Socio-demographic characteristics	<b>Deficient</b> (n=92=25.2%) (<20 ng/ml)	<b>Insufficient</b> (n=132=36.2%) (20 to 30 ng/ml)	<b>Normal</b> (n=141=38.6%) (>30 ng/ml)	Total (n=365)	P-Value
Age (Yrs):					
18 - 39	32 (34.8%)	42 (31.85%)	84 (59.6%)	158 (43.3%)	<0.0001
40 – 59	12 (13.0%)	18 (13.6%)	24 (17.0%)	54 (14.8%)	<0.0001
60+	48 (52.2%)	72 (54.6%)	33 (23.4%)	153 (41.9%)	
Gender:					
Male	33 (35.9%)	54 (40.9%)	78 (55.3%)	165 (45.2%)	< 0.05
Female	59 (64.1%)	78 (59.1%)	63 (44.7%)	200 (54.8%)	
Level of education:					
Primary school or less	28 (30.4%)	39 (29.5%)	43 (30.5%)	110 (30.1%)	>0.05
Intermediate and secondary school	50 (54.4%)	73 (55.3%)	76 (53.9%)	199 (54.5%)	~0.03
University and above	14 (15.2%)	20 (15.2%)	22 (15.6%)	56 (15.4%)	
Marital Status:					
Married	70 (76.1%)	103 (78.0%)	98 (69.5%)	271 (74.3%)	>0.05
Unmarried	22 (23.9%)	29 (22.0%)	43(30.5%)	92 (25.7%)	~0.03
(Single, divorced or widow)					
Occupation/ work:					
Field (outdoor)	32 (34.8%)	31 (23.5%)	92 (65.2%)	155 (42.5%)	<0.0001
Office( indoor)	34 (36.9%)	71 (53.8%)	21 (14.9%)	126 (34.5%)	~0.0001
House wife/ not working	26 (28.3%)	30 (22.7%)	28 (19.9%)	84 (23.0%)	

#### Table (1): Socio-demographic characteristics of the study participants (n=365)

Table (2): Nu	umber and	percent	distribution	of the	study	participants	by	vitamin	D status	and	average	daily	sunlight
exposure													

Average daily sunlight exposure	<b>Deficient</b> (n=92) (<20 ng/ml)	<b>Insufficient</b> (n=132) (20 to 30 ng/ml)	<b>Normal</b> (n=141) (>30 ng/ml)	Total (n=365)	P-Value
	(20 119 111)		( 50 lig/lil)		
Less than 5 Minutes/Day	47 (51.1%)	48 (36.4%)	8 (5.7%)	103 (28.2%)	
5-15 Minutes/Day	28 (30.4%)	62 (46.9%)	12 (8.5%)	102 (27.9%)	<0.0001
15-30 Minutes/Day	12 (13.1%)	16 (12.1%)	57 (40.4%)	85 (23.3%)	<0.0001
>30 minutes/Day	5 (5.4%)	6 (4.6%)	64 (45.4%)	75 (20.6%)	

Average daily sun exposure makes an impact on the amount of vitamin D synthesized and that is available for cellular processes. Highly significant negative correlation was found between duration of daily sunlight exposure and vitamin D deficiency and insufficiency (p<0.0001) (**Table 2**).

Table (3): A	Association between	consumption	of vitamin D	) rich food and	d vitamin D status
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		Vitamin D Status			
Vitamin D rich food	<b>Deficient</b> (n=92) (<20 ng/ml)	Insufficient (n=132) (20 to 30 ng/ml)	<b>Normal</b> (n=141) (>30 ng/ml)	Total (n=365)	P-Value
Milk (>2cups=>400ml/week)	26 (28.3%)	52 (39.4%)	132 (93.6%)	210 (57.5%)	<0.0001
Eggs (>2 eggs/ week)	42 (45.7%)	62 (47.0%)	86 (61.0%)	190 (52.1%)	0.02 (<0.05)
Fish (>2serving/week)	20 (21.7%)	38 (28.8%)	98 (69.5%)	156 (42.7%)	< 0.0001
Liver (>2 serving/week)	16 (17.4%)	29 (22.0%)	83 (58.9%)	128 (35.1%)	<0.0001
Cheese (>2 serving/week)	38 (41.3%)	57 (43.2%)	80 (56.7%)	175 (48.0%)	0.03 (<0.05)
Margarine (>2 serving/week)	22 (23.9%)	33 (25.0%)	45 (31.9%)	100 (27.4%)	0.3 (>0.05)

The study subjects who consuming milk, eggs, fish, liver and cheese, were having normal vitamin D level. While those not consuming these food items,

were insufficient or deficient in vitamin D levels (p<0.05) (Table 3).

Table (4): Distrib	ution of the study nar	rticinants by multivita	amins use. BML exer	rise, and vitamin D status
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Variable	<b>Deficient</b> (n=92) (<20 ng/ml)	Insufficient (n=132) (20 to 30 ng/ml)	<b>Normal</b> (n=141) (>30 ng/ml)	Total (n=365)	P-Value
Multivitamins use:	18 (19.6%)	35 (26.5%)	50 (35.5%)	103 (28.2%)	< 0.05
Body Mass Index (BMI):					
Under weight (<18.5)	7 (7.6%)	12 (9.1%)	10 (7.1%)	29 (7.9%)	<0.0001
Normal (18.5–24.99)	38 (41.3%)	42 (31.8%)	117 (83.0%)	197 (54.0%)	<0.0001
Overweight & Obese (>25)	47 (51.1%)	78 (59.1%)	14 (9.9%)	139 (38.1%)	
Exercise:					
No exercise	45 (48.9%)	76 (57.6%)	7 (5.0%)	128 (35.1%)	<0.0001
3-7 hours/week	39 (42.4%)	43 (32.6%)	45 (31.9%)	127 (34.8%)	<0.0001
>7 hours/week	8 (8.7%)	13 (9.8%)	89 (63.1%)	110 (30.1%)	

The 25OHD level was significantly higher in multivitamin users (P<0.05). Highly significant positive association was found between overweight, obese and vitamin D deficiency and insufficiency

(p<0.0001). There was an inverse correlation between exercise and vitamin D deficiency and insufficiency (p<0.0001) (Table 4).

Table (5): Multivariate analysis of predictors for vitamin D deficiency and insufficiency using stepwise logistic regression

Variable	Adjusted OR	95% CI	p-value
Sunlight exposure:	5.13	(3.14-7.90)	< 0.0001
Consumption of vitamin D rich food:	4.38	(2.57-6.68)	< 0.0001
Indoor work:	2.88	(1.84-3.92)	< 0.05
Multivitamins use:	1.17	(0.74-2.55)	>0.05
Overweight & Obese:	2.46	(1.64-3.24)	< 0.05
Exercise:	2.74	(1.83-3.74)	< 0.05

OR: Odds Ratio, CI: Confidence Interval.

Multiple logistic regression analysis was performed on a number of predictors that might independently be associated with development of vitamin D deficiency and insufficiency. After adjustment of age and gender, a highly significant association was found between duration of exposure to sunlight and vitamin D deficiency. The risk to develop vitamin D deficiency is nearly 5 times more in participants exposed to sunlight less than 5 Minutes/Day when compared with participants exposed to sunlight >30 minutes/Day, OR=5.13 (95% CI=3.14-7.90).

Consumption of vitamin D rich food, occupation, BMI and exercise were found to be strong predictors of vitamin D deficiency, OR=4.38, 2.88, 2.46 & 2.74 respectively. Multivitamins use was significantly associated with vitamin D deficiency in univariate analysis (p<0.05), but this was weakened somehow when adjusted in multivariate analysis, adjusted OR=1.17 (95% CI=0.74-2.55) (Table 5).

# 4. Discussion:

Vitamin D is critically important for the development, growth and maintenance of healthy bones, from birth to death. Determining vitamin D status of a population can be a challenging task <sup>(27)</sup>. Many research studies had found correlation between low vitamin D levels and a wide range of illnesses, including cancer, autoimmune diseases and cardiovascular disorders <sup>(28)</sup>. Unfortunately, and up to our knowledge no study had evaluated the level of vitamin D among adult healthy Kuwati population.

The results of present study confirmed the high prevalence of vitamin D deficiency and insufficiency. 92 subjects (25.2%) were having deficient, 132 (36.2%) were insufficient and 141 (38.6%) subjects having normal value of 25hydroxyl-vitamin D (25OHD) in their serum. Studies in the sunniest areas in the Middle East as Saudi Arabia, United Arab Emirates, Iran and Lebanon indicates 30 to 50% of children and adults had 25(OH)D under 20 ng/ml and other studies indicated that 73% of women and 80% of their infants were vitamin D deficient at the time of birth  $^{(3-5, 29)}$ .

In this study, the prevalence of vitamin D deficiency was much higher among elderly people (60 years and above) (p<0.0001), and this was similar to other studies <sup>(30-32)</sup>. This may be explained by the fact that elderly people remain homebound and do not receive as much sunlight exposure as those who are younger <sup>(33)</sup> and also, when the elderly population receive sun exposure, vitamin D production is hindered by decreased capability of the skin to utilize the sunlight received because of decrease of 7dehydrocholesterol in the skin, which leads to decreased absorption of UVB rays that convert precaliciferol to cholecalciferol <sup>(34)</sup>. However, other studies reported the higher prevalence of vitamin D deficiency among young adult people (2, 35) and referred this to supplementation of vitamin D among elderly people, especially women, who are getting used to taking multivitamin tablets and decline of milk consumption in the adolescent population, milk is being replaced with other beverages including soda and juice, which provide little benefit to bone health (36)

The findings showed that women were more likely to be vitamin D-deficient and insufficient than men, especially for severe vitamin D deficiency (p<0.05). Although Kuwait is a sunny state, direct female exposure to sun is however limited, most women wear a scarf and long-sleeve clothes. This also may be impact of teenage pregnancy outcomes ( $^{37}$ ). This was in agreement with other studies ( $^{4, 28}$ )

The two main sources of vitamin D are sunlight and diet. The skin synthesizes a steroid, 7dehydrocholesterol, which is capable of absorbing specific wavelengths of light. When the skin is exposed to certain wavelengths of ultraviolet B (UVB) rays from the sun, the stored 7dehydrocholesterol is converted to previtamin D3 or precalciferol <sup>(38, 39)</sup>. Results of current study shows that study subjects who exposed to sunlight for longer duration of time has adequate level of vitamin D which is statistically significant (OR=5.13). Avoidance of sunlight might be a contributing factor to the high prevalence of low vitamin D in Kuwati population. The cultural practice of wearing long sleeves and head cover among males and veil/ Abaya/ Hijab and extensive clothing among females may be contributing factors.

The amount of vitamin D received in the diet also has an impact on serum levels. Given the body's ability to absorb vitamin D is not compromised, increased intake of foods rich in vitamin D, will lead to increased serum levels <sup>(34)</sup>. Study subjects who were consuming milk, eggs, fish, liver and cheese had significantly higher level of

vitamin D (OR=4.38). But those who consumed margarine had no significant effect on serum vitamin D levels (p>0.05). This was in agreement with other studies <sup>(31, 32)</sup>

This study revealed that sedentary lifestyle in the form of decreased physical activity and exercise, increases the risk of vitamin D deficiency (OR=2.74) due to the fact that, a sedentary lifestyle in which weight-bearing exercise is not used to maintain bone density leads to an increased need for vitamin D  $^{(40,41)}$ . On the other hand, vitamin D is a fat-soluble vitamin and is thus stored in adipose tissue. Participants with deficient and insufficient vitamin D status had higher odds for metabolic syndrome after adjustment for age and sex (OR=2.46). It becomes difficult for the body to retrieve stored vitamin D because it is less bioavailable when it is imbedded in deeper adipose stores <sup>(8, 42)</sup>. This was convenient with other studies <sup>(43, 44)</sup>.

#### 5. Conclusions and Recommendations:

Due to the increasing prevalence of vitamin D deficiency in apparently healthy Kuwaiti population, it is suggested that interventions be taken to increase intake among high risk population. Such interventions include increasing consumption of vitamin D rich foods such as fortified milk, fish, liver and cheese, taking a vitamin D supplement, physical exercises, increasing sun exposure to the extent needed for adequate vitamin D production and/or periodic medical examination of healthy adults for early case detection and intervention.

# Limitations of the study:

The study sample was small and it would be useful if participants were evaluated at different times of the year to study the seasonal variations.

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