



## Vitamin D Status in Saudi Population: A Minireview

### KEYWORDS

Vitamin D, Status, Saudi.

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**ABSTRACT** *Vitamin D plays a major role in growth, development and overall health status. Vitamin D levels in serum are affected by various factors and a wide range of variation is being observed in different populations across the world. It is now believed that genetic factors may also contribute to the vitamin D levels in various ethnic groups. The present review aims at discussing the factors affecting vitamin D levels in Saudi population.*

### Introduction

Vitamin D is considered as a steroid hormone <sup>[1]</sup> and an essential nutrient <sup>[2]</sup> that plays vital roles in growth and development <sup>[3]</sup>. Multiple factors are involved in vitamin D status. Its status is influenced by level of sun light exposure, exposure to ultraviolet-B radiation 290-315 nm <sup>[4]</sup>, latitude, season of year (higher in summer months), weather condition (lower in cloudiness), time of day <sup>[5-7]</sup> as well as race and sex <sup>[6]</sup>. Skin pigmentation also plays a major role and hence is more in blacks than other populations <sup>[4-5]</sup>. Moreover, life style is an important determinant; it is lower in indoors versus outdoors people, urban versus rural, clothing habits <sup>[6-7]</sup>, lower with using sun protection cream <sup>[4,7]</sup>, lower in decreased physical activity and low social status <sup>[6,8]</sup>, lower in obese people <sup>[7]</sup>. Furthermore, diet such as fish, eggs and fortified foods influence individual vitamin D status <sup>[5]</sup>.

The objective of this article is to stress the importance of vitamin D in metabolic processes and overall health status and to compare the concentration of fibroblast growth factor and increased levels of inflammatory cytokines also control circulating calcitriol.

### Vitamin D Sources

The main sources of vitamin D are ergocalciferol (vitamin D2) obtained from plant sources and yeast and cholecalciferol (vitamin D3) produced in the skin by exposure to ultraviolet radiation (UV) B (290–315 nm) <sup>[4, 9-10]</sup>. Cholecalciferol is formed through converting provitamin D (7-dehydrocholesterol) in the skin to previtamin D3 by sun exposure to ultraviolet-B radiation <sup>[11]</sup>. A whole body exposure to UVB radiation of 15 to 20 minutes daily is able to produce up to 250 µg vitamin D (10,000 IU) which usually contributes 80%-90% to vitamin D supply in free-living persons <sup>[4]</sup>.

Dietary sources such as fatty fish, fish oils, milk, eggs, fortified foods and vitamin supplements are considered sources of vitamin D <sup>[5]</sup>. Vitamin D is also found naturally in small amounts in milk and eggs, and in relatively large amounts in fatty fish such as herring and mackerel <sup>[4]</sup>.

Circulating [25(OH)D] concentrations in healthy young adults usually lie between 30–80 nmol/L, dietary vitamin D intake is usually below 5 µg daily, and 1 µg vitamin D increases circulating [25(OH)D] concentrations by approxi-

mately 1–3 nmol/L <sup>[4]</sup>.

Established determinants of vitamin D status are exposure to sunlight and intake of vitamin D either from foods or vitamin supplements <sup>[8]</sup>. In adults, an average of 20-25 ug/day is required to reach a serum [25 OH] level of 75 nmol/L [12]. The Institute of Medicine currently sets the adequate intake as 15 µg vitamin D/day (200 IU/day) for women 15–50 years of age. This amount is believed to be adequate regardless of the amount of sunlight exposure <sup>[5]</sup>.

### Vitamin D Metabolism

Metabolism of Vitamin D is summarized as the following; provitamin D, 7 hydrocholesterol, is converted to previtamin D3 by skin absorption of UV radiation. Previtamin D3 and previtamin D2 are hydroxylated in the liver to 25-hydroxyvitamin D [25(OH)D] which is considered as an indicator of vitamin D status. The latter is metabolized in the kidney to 1,25 dihydroxyvitamin D ([1,25(OH)D], calcitriol) which is the active form of vitamin D <sup>[2,9,11]</sup>.

PTH controls the circulating calcitriol; Reduced number of viable nephrons, increased serum fibroblast growth factor concentrations and increased levels of inflammatory cytokines also affect circulating calcitriol <sup>[4]</sup>.

### Function of Vitamin D

Vitamin D plays a significant role in the homeostasis of calcium and phosphorus and is also recognized as playing a vital role in bone mineralization, skeletal growth, and bone health <sup>[13]</sup>. Bone metabolism and calcium homeostasis are also controlled by parathyroid hormone (PTH) <sup>[10]</sup>.

Furthermore, vitamin D modulates a wide range of molecular and cellular functions such as <sup>[1]</sup>, cell cycle transcription, cell proliferation and differentiation <sup>[14]</sup> that have beneficial effects on musculoskeletal parameters and intestinal calcium transport <sup>[1]</sup> through the active form of vitamin D which is regulated by the transcription of a number of vitamin D-dependent genes coding for calcium-transporting proteins and bone matrix proteins <sup>[14]</sup>. In addition, vitamin D also exerts benefits on immune system <sup>[1]</sup> through cell differentiation and immuno-modulatory properties <sup>[14]</sup>. Moreover, vitamin D is essential for muscle contraction, nerve conduction <sup>[14]</sup>, fuel metabolism, cardiovascular sys-

tem diseases<sup>[1]</sup>, type 2 diabetes aetiology, reduced insulin sensitivity and compromised  $\beta$ -cell function<sup>[15]</sup>, since vitamin D repletion improves insulin sensitivity and insulin secretion<sup>[10]</sup>. Vitamin D is also thought to play a role in protection against cancer (prostate, breast and colon), heart disease and conditions that account for over 60% of deaths in the western world<sup>[2]</sup>.

### Genes involved in Vitamin D

Many genes are involved in Vitamin D; Vitamin D receptor (VDR) is a member of the steroid hormone receptor sub-family which has been found in >30 cell types, including fat cells<sup>[16]</sup>. Cellular vitamin D actions are mediated by a membrane-bound and a cytosolic VDR; about 3% of the human genome is directly and/or indirectly regulated by the vitamin D endocrine system<sup>[4]</sup>.

Genetic variations may phenotypically appear as inter-individual variations in limiting rates of vitamin D synthesis in the skin, hydroxylation in the liver and in the kidney, transport metabolism and degradation that would ultimately influence individual vitamin D status<sup>[17]</sup>. Shimada *et al.*<sup>[18]</sup> suggested that FGF-23 is a potent regulator of phosphate and vitamin D homeostasis.

Several polymorphisms on the VDR gene, three SNPs near at the 3' untranslated region (UTR) are identified by restriction enzymes namely Taq1, Bsm1 and Apa1. These SNPs are non functional but are considered to influence mRNA stability<sup>[17]</sup>.

Common genetic variants that influence circulating [25(OH)D] levels could be important for associations between vitamin D status and several diseases<sup>[19]</sup>. Vitamin D status is affected by variants proximal to genes involved in synthesis of cholesterol, hydroxylation and transport of vitamin D. Individuals with genetic variation in loci 4p12, 11q12 and 11p15 have raised risk of vitamin D deficiency<sup>[20]</sup>. Vasilopoulos *et al.*<sup>[17]</sup> suggested VDR and FTO genes are potential key players in the pathogenetic mechanism of obesity. Yousef<sup>[16]</sup> supported also the association between [1,25(OH)D] and VDR that influence adipocyte differentiation. This association is explained by series of gene-gene, gene-diet and gene-environment that effect on obesity and/or type 2 diabetes mellitus<sup>[17]</sup>.

### Vitamin D Deficiency

High prevalence of vitamin D deficiency was reported in the global population<sup>[2]</sup>. Table 1 is summarized the [25(OH)] level mean (nmol/L) below cut-off (divide by 2.496 to convert into ng/ml).

To classify different stages of vitamin D inadequacy, the following cut-offs are used: <25 nmol/L for deficiency, 25-49.9 nmol/L for insufficiency, 50-74.9 nmol/L for hypovitaminosis/suboptimal supply<sup>[4]</sup>.

Adequate vitamin D is essential for normal human growth and development whereas vitamin D insufficiency/deficiency increases the risk of chronic disease<sup>[6]</sup>. Moreover, vitamin D correlates inversely with body mass index (BMI); inverse correlation exists in overweight and obese subjects<sup>[7, 21]</sup>. Furthermore, vitamin D deficiency is related to cardiovascular disease, hypertension, autoimmune disease, infection, cancer<sup>[13]</sup>.

### Worldwide Vitamin D Status

Vitamin D Status is assessed globally in many researches; Yetley<sup>[22]</sup> reported vitamin D status of the US population in

2008. He found males have higher vitamin D intakes and [25(OH)D] concentrations than do females. Children tend to have higher vitamin D status than adults. He demonstrated that increasing use of multivitamin-mineral dietary supplements in younger to older adults is not associated with a corresponding increase in serum [25(OH)D] concentrations. He also found leaner individuals have higher circulating concentrations of [25(OH)D]. The study confirmed that non-Hispanic whites tend to have higher vitamin D status than do non-Hispanic blacks and Mexican Americans<sup>[22]</sup>.

Mithal and his colleagues (2009) reported global vitamin D status and determinants of hypovitaminosis D across the world. They indicated that hypovitaminosis D is widespread and is re-emerging as a major health problem globally<sup>[23]</sup>.

In a comprehensive review by Zittermann and Gummert<sup>[4]</sup> in (2010), they summarized human vitamin D status according to region of the world. Six regions of the world were reviewed - Asia, Europe, Middle East and Africa, Latin America, North America, and Oceania-through a survey of published literature. Based on the articles referred to in this review, it was concluded that insufficient vitamin D status is prevalent in each of the six regions studied. Depending on the region, between 50% and more than 90% of people had [25(OH)D] concentrations below 50 nmol/L. Low vitamin D status is most common in regions such as South Asia and the Middle East. Some of the important factors contributing to reduced levels of vitamin D are life styles such as indoor leisure time activity and covered clothing in Saudi, with very little exposure to sun., Moreover there is no significant contribution of vitamin D from diet, thus leading to childhood rickets, which is on the increase in many developing countries. Urbanization has therefore significantly been affecting the serum vitamin D levels in these populations<sup>[4]</sup>.

Van Schoor and Lips<sup>[24]</sup> confirmed in (2011) that vitamin D deficiency in adults is highly prevalent in the Middle-East and Asia. Young children, pregnant women and elderly are the major risk groups, the major risk factors being low sun exposure, pigmentation of skin, diet low in sea food and dairy products and covering of the skin<sup>[24]</sup>.

### Studies on Vitamin D status in Kingdom of Saudi Arabia (KSA)

Vitamin D status was reported in Saudi Arabia in many studies; Qari *et al.*<sup>[25]</sup> firmly established in (2010) the relation between vitamin D status and bone health in healthy Saudi women. They found that vitamin D deficiency is highly prevalent among healthy Saudi pre- and postmenopausal women and largely attributed the condition to obesity, poor exposure to sunlight, poor dietary vitamin-D supplementation and age<sup>[25]</sup>.

Ardawi *et al.*<sup>[26]</sup> investigated the 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 and reported similar findings to Qari *et al.*, (2011). Another study by Ardawi *et al.*<sup>[27]</sup> established the association between vitamin D receptor gene polymorphisms and fracture risk among Saudi postmenopausal women. They found a significant association between the *Bsm1* polymorphism and the risk of falling among Saudi postmenopausal women, which may explain the high fracture risk associated with VDR genotypes (*Apal*, *Bsm1*, *Taq1* and *FokI*).

Al-Mazidi *et al.* [28] studied in (2011) the vitamin D status and its correlation with blood pressure and plasma renin levels in pre-menopausal Saudi women. They found no correlation between blood pressure and vitamin D level despite the high prevalence of vitamin D deficiency. They suggested that any underlying relationship was obscured by the relatively young age group or due to the narrow blood pressure range of the studied population [28].

Yousef [16] studied in (2011) the vitamin D status and breast cancer in Saudi Arabian women to see if vitamin D status as assessed by serum concentrations of [25(OH)D] would be lower in breast cancer cases as compared to controls. This study demonstrated statistically a significant relationship between higher serum concentrations of [25(OH)D] and lower risk of breast cancer [16].

Hussein *et al.* [29] reported in (2012) the extent of obesity in Saudi women and the association between vitamin D status and different measures of adiposity. They found that a total of 30.7% of the women were overweight with BMI 25-<30 kg/m<sup>2</sup> and 38.5% were obese with BMI ≥30 kg/m<sup>2</sup>. Obesity was more prevalent among the postmenopausal women. The authors suggested that obesity associated vitamin D insufficiency was likely due to the decreased bio-availability of vitamin D3 because of its deposition in body fat compartments. They recommended that intentional loss in body weight might improve vitamin D status [29].

Another study done in Saudi Arabia in 2012 by Ardawi *et al.* [30] studied the effect of vitamin D nutritional status on muscle function and strength in healthy women aged ≥60 years. The findings suggested serum [25(OH)D] levels ≥ 50 nmol/L for better muscle function and strength. It was suggested that evaluating vitamin D nutritional status in women aged ≥ 60 years would allow correcting hypovitaminosis D and improve muscle function and strength tests [30].

Elshafie *et al.* (2012) studied the comparison of vitamin D deficiency in Saudi married couples. They found that vitamin D deficiency was higher among Saudi married couples, especially wives. They demonstrated that female gender, sedentary lifestyle and low milk consumption were independent predictor of lower vitamin D level [31].

Another study was done by Akbar *et al.* reported severe vitamin-D deficiency associated with decreased circulating endothelial progenitor cells and endothelial dysfunction in patients with Type 2 diabetes mellitus. Severe vitamin-D deficiency was significantly associated with decreased brachial artery flow-mediated dilatation and circulating CD133<sup>+</sup>/kinase insert domain-containing receptor (KDR<sup>+</sup>) endothelial progenitor cells (EPCs). These findings suggest that severe vitamin-D deficiency may contribute to lowered circulating EPCs and endothelial dysfunction in patients with Type 2 diabetes mellitus [32].

#### Awareness Programs and supplementation

Due to an increase in public awareness of the association of vitamin D deficiency with the diseases mentioned earlier, there has been a vast increase in the number of vitamin D orders received by clinical chemistry laboratories [21].

Strategies to raise the store of vitamin D have to apply as a routine measurement through effective sunlight exposure, vitamin D supplementation, calcium supplementation, increased dairy intake and potentiated loss of fat should be taken in calorie-restricted dieters [21].

A study done 2006 showed that calcium with vitamin D supplementation resulted in a small but significant improvement in hip bone density among healthy postmenopausal women [33]. Another study done in 2007 recommends minimum doses of 1200 mg of calcium, and 800 IU of vitamin D (for combined calcium plus vitamin D supplementation) to prevent fractures and bone loss in people aged 50 years or older [34].

#### Conclusions

In conclusion, from the above report we clearly understand the vital role played by vitamin D in overall health status and that the levels of serum vitamin D show significant variation in different ethnic groups. The factors that play a key role in absorption and utilization of vitamin D have also been outlined. Hence close monitoring of serum vitamin D levels in populations would help in developing supplementation programs that would in turn result in amelioration of overall health status.

**Table 1. [25(OH)] Levels in Middle East Countries**

Country	[25(OH)] level mean (nmol/L) below cut-off
UAE	20.27
Lebanon	24.21
Saudi Arabia	24.96
Jordan	< 29.95
Tunisia	30.45
Iran	31.45
Occupied Palestine	33.95
Morocco	39.44
Qatar	51.04

(Adopted from Bassil *et al.* [1])

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