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Vitamin D Status Among Women in Middle East

Abdulrahman Al-Mohaimeed*, Nauman Zafar Khan, Zahid Naeem, Ebtehal Al-Mogbel

Family and Community Medicine Department, College of Medicine, Qassim University, Saudi Arabia

Abstract Of the vitamins that help maintain health, vitamin D holds a very important place. Its deficiency is a major global health problem and affects both genders at all stages of life. Lack of exposure to the sunlight is among the foremost of the causes of vitamin D deficiency. However, contemporary literature reveals an interesting paradox in the Middle East where abundant sunshine and vitamin D deficiency coexist. The conundrum acquires further complexity when we consider the so far unresolved debate on the right reference range, dietary recommendations, the difference of assessment methods and ranges in the various different laboratories worldwide, continuously emerging new and more accurate methods of serum vitamin D assessment though with limited availability and the debate regarding the most accurate method currently available for measuring its serum levels. Furthermore, the literature on the Middle East reveals that women are affected more than men. Generally, vitamin D level estimations have been found to be quite low across all age groups in this region. Old age, female gender, multi-parity, winter season, clothing style, low socioeconomic status and urban living have consistently been associated with low levels of vitamin D in the literature. Almost similar deficiency levels are found in regions with different socio-cultural norms but comparable weather. Further studies are needed to establish the correct reference range, dietary recommendations, the risk-benefit ratio of exposure to the sunshine and the most accurate laboratory method of its serum level assessment for the population in this region.

Keywords Vitamin D, Women, Middle East

1. Introduction

Vitamin D deficiency is considered a major public health problem that affects individuals across all life stages including otherwise healthy men and women, pregnant women, neonates, infants, children, adolescents, adults and the elderly even in sunny countries. The Middle Eastern countries, which get bright sunlight almost all year round, are a case in point. Availability of sunlight in this region fails to give adequate protection against vitamin D deficiency, especially to women. Vitamin D deficiency is now recognized as a worldwide health problem, associated with poor dietary intake and inadequate exposure to sunshine, affecting upwards of a billion people.[1, 2]

Vitamin D is a fat-soluble substance that plays an important role in bone metabolism, controls calcium absorption, mediate skeletal mineralization with parathyroid hormone (PTH), maintains calcium and phosphorous homeostasis and sustains a wide variety of metabolic and physiological functions.[3, 4, 5]

Two major forms of vitamin D exist, vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). The former comes from plant sterols "ergosterol", and the latter is obtained from fish oils (also called liquid sun rays) and by skin synthesis following exposure to short wavelength ultra violet rays (UVB) from the sun. Confusion abounds about the right reference range and which vitamin D test to order. Presently, there is no consensus in the scientific community about the appropriate reference range and cut-off points for ascertaining deficiency or insufficiency, as well as optimal and possible toxicity status. However, studies have identified various ranges for disease risk reduction. Laboratories use a variety of ranges. The Clinical Lab News' survey (July 2009) amply reflects that. Reported deficiency levels for 25-OH-D started at ≤8 ng/mL and went all the way up to ≤30 ng/mL.[6, 7, 8, 9, 10]

Although a matter of controversy and continuous debate in the current literature[11, 12] the current recommendations for the Dietary Reference Intake of vitamin D in the United States by the Institute of Medicine are: 5 μg/day (200 IU/day) for newborns, children and adults up to age of 50 years, 10 μg/day (400 IU/day) for adults aged (51-70) years and 15 μg/day (600-800 IU/day) for individuals >70 years.[13, 14, 15, 16, 17]

A common cause of vitamin D deficiency is inadequate dietary intake, especially in the face of increased bodily requirements. Other important causes include decreased absorption states in diseases such as cystic fibrosis, celiac disease, and conditions that reduce cholesterol absorption, increased catabolism with chronic use of certain drugs such as anticonvulsants, glucocorticoids, highly active antiretroviral drugs, rifampicin and some immunosuppressants.[1, 18]

* Corresponding author:
armoh@qumed.edu.sa (Abdulrahman Al-Mohaimeed)
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2. Vitamin D Deficiency among Middle East women

Numerous studies have been performed worldwide to evaluate the prevalence of vitamin D deficiency in different populations. Its inadequacy constitutes a largely unrecognized epidemic in many populations worldwide. It has been reported in healthy children, young adults, especially African Americans, middle-aged and elderly adults from diverse countries around the world including the UK, France, Greece, China, Finland and Canada.[19-47] However, the Middle East (15°- 36°N) offers an inspiring but challenging research grounds regarding vitamin D deficiency. Despite plenty of sunshine, the population here has one of the highest rates of rickets in the world. This is explained by limited exposure to the sun due to cultural practices and prolonged breast feeding without vitamin D supplements.[47] A large proportion of adolescent girls, up to 70% in Iran and 80% in Saudi Arabia, had 25(OH)D levels below 25nmol/L. The reported proportions were 32% in Lebanese girls and between 9-12% in Lebanese adolescent boys. Diarrhea and maternal vitamin D status in infants, gender, clothing style, season, and socioeconomic status were found to be the independent risk factors for low 25(OH) D levels.[47, 48]

The first vitamin D estimation study in the Middle Eastern region in adult women included university students and the elderly women from Saudi Arabia which revealed a mean 25(OH)D level ranging between 10-30nmol/L. Interestingly, the mean 25(OH)D level was near 25nmol/L in Lebanese, Saudi, Emirati and Iranian women. A similar mean was recorded in the elderly Lebanese women.[47] The proportion of subjects with vitamin D levels below specific cut-off limit varied. It was between 60-65% in Lebanon, Jordan and Iran; and was 48% for a cut-off less than 37.5nmol/L in subjects from Tunisia. In the elderly Lebanese, 37% of men and 56% of women had vitamin D levels below 25nmol/L; the corresponding proportions were 8% for men and 14% for elderly subjects participating in the Longitudinal Aging Study in Amsterdam. In a similar international study conducted in women with osteoporosis, the highest proportion of hypovitaminosis D was noted in the Middle East. Inadequate vitamin D intake, urban dwelling, female gender, wearing the veil and abaya, winter season, age and high parity were independent predictors of low vitamin D levels.[47]

Studies from Saudi Arabia, Kuwait, United Arab Emirates and Iran reveal that 10-60% of mothers and 40-80% of their neonates had undetectable to low vitamin D levels (0-25nmol/L) at delivery[30-33]. In contrast higher socio-economic status, proper antenatal care, and vitamin D intake were associated with higher vitamin D levels.[47]

In summary, vitamin D deficiency is endemic in the Middle East. It impacts all age groups and both genders. However, women are at a higher risk which calls for further studies and intervention programs

2.1. Women in Middle East

Although a global issue, hypovitaminosis D is especially emphasized in the literature covering the Middle East due to a number of interesting paradoxes. Middle East receives abundant sunlight all year round. However, contemporary studies show a high prevalence of hypovitaminosis D among women of different age-groups. These finding are attributed mainly to inadequate exposure to sunlight,[49] either because of the dressing style[50-55]or avoidance of extremely hot sun.[56, 57] Additionally, inadequate sun exposure as one of the major causes of vitamin D deficiency could also be related to the living conditions. For instance those living in multi-storey apartments in cities hardly ever get any direct sunlight.[57]It could also be due to skin pigmentation that reduces the penetration of ultra-violet light. Other causes mentioned in the literature are inadequate diet lacking vitamin D.[54, 58]

Interestingly, Arab women and other women of Middle Eastern origin living in Europe, whose exposure to sunshine is limited, have been shown to have low serum concentrations of 25-(OH)D, a high prevalence of hypovitaminosis D, and consequently vitamin D deficiency. Serum concentrations of 25-(OH)D and dietary vitamin D intake of 60 veiled Arab women living in Denmark, randomly selected from patients attending Primary Health Centers for reasons not related to vitamin D deficiency, were compared with those of 44 age-matched Danish women.[17] The mean serum 25-(OH)D concentration in veiled Arab women was 7.1±1.1 nmol/L compared with 47.1±4.6 nmol/L in Danish women. Ninety-six percent and 85 % of the veiled Arab women had serum 25-(OH)D concentrations <20nml/L and <10nmol/L, respectively. None of the Danish women in that study had serum 25-(OH)D values < 10nmol/L and only 9% of the Danish women had values < 20nmol/L.[59] This eminently highlights the role of sunshine in preventing vitamin D deficiency.

The frequency and duration of skin exposure to UVB sunlight is a primary factor determining the vitamin D status. The housebound and those who spend little time outdoors have few opportunities for exposure to sunshine. In addition, sunshine that passes through glass or plexiglas does not contain UVB and is therefore ineffective for skin synthesis of cholecalciferol. Individuals who wear clothes that cover most of the body, including the face, head, and arms, or who liberally use sunscreen, have minimal sunshine exposure. Current campaigns on skin cancer prevention often emphasize the importance of protecting the skin from sunshine without promoting the importance of safe sunshine exposure for the skin synthesis of vitamin D. Customary dress that conceals much or all of the body is associated with a high prevalence of low vitamin D status, even in sunny areas of the world at low latitudes (e.g., Beirut and Bekaa Valley Lebanon)[60]

Conversely, a number of other studies state that covering face with the veil may not be the real cause. Gannage`-Yared et al[51] found there were other factors which were responsible for low vitamin D levels than the veil itself. Recently, Islam et al[61] compared vit D level in veiled and non-veiled women in Bangladesh and did not find any differences. It would therefore be prudent to consider other relevant aspects whilst establishing a relationship between veil and customary dressing, and lower levels of vitamin D.

Most of these studies suggest that Arab women have lower serum 25-(OH)D concentrations than the generally accepted lower limit of normal range (25.0-37.5 nmol/L). In some of the studies nearly all of the subjects had serum 25-(OH)D concentrations lower than 50nmol/L, which has been suggested as a lower conservative cutoff point in recent studies. Therefore, hypovitaminosis D and in particular, vitamin D deficiency, seem to be public health problems in Arab women and other women of Middle Eastern origin. However, lack of standardized definition of hypovitaminosis D, vitamin D deficiency and community-based data prevent any meaningful international comparison of the magnitude of the problem. Therefore, community-based studies using a generally accepted definition are urgently needed to provide baseline data to evaluate the impact of future interventions on the prevalence of vitamin D deficiency in Arab countries.[59, 62] These studies would lay the foundation of preventative programs that can improve the quality life in the Middle East, on the one hand, and reduce health expenditure, on the other.

2.2. Saudi Arabia

A cross-sectional study was carried out in the Royal Guard Primary Health Care Center in Riyadh, Saudi Arabia on a consecutive sample of 50 Saudi married couples attending the center without complaints related to vitamin D deficiency. Data were collected through an interview questionnaire addressing the risk factors and dietary habits. Men had higher sun exposure (P=0.001), wore light colored clothes at home (P=0.002) and consumed more milk (P=0.023) and soft drinks (P=0.001). Vitamin D level was higher in men with the mean difference of about 9 nmol/l (P<0.001). The prevalence of vitamin D deficiency (<25 nmol/l) was 70% in women, compared with 40% in men (P=0.001). Multivariate analysis identified male gender, physical activity and the intake of milk as statistically significant positive independent predictors of vitamin D level, adjusted for factors such as age, sun exposure, clothing, skin color, body mass index (BMI), and consumption of soft drinks and animal protein.[63]

A cross-sectional study carried out in the Royal Guard Primary Health Care Center in Riyadh, Saudi Arabia on a consecutive sample of 50 Saudi married couples attending the center for non-vitamin D deficiency related complaints found out that vitamin D level was higher in men with the mean difference of about 9 nmol/l (P<0.001). The prevalence of vitamin D deficiency (<25 nmol/l) was 70% in women, compared with 40% in men (P=0.001). Multivariate analysis identified male gender, exposure to sun, physical activity and the intake of milk as statistically significant positive independent predictors of vitamin D level.[63]

Another sample (n=200) comprising two groups (group 1, 25- 35 years and group 2, above 50 years) of healthy women studied in Al Khobar, Eastern Saudi Arabia reported that vitamin D deficiency was 30% in group 1 and 55% in group 2. Life style and sun exposure were studied. (OH)DIn this study, even though all women were veiled, their vitamin D levels were comparable to those reported from the west of the country.[64]

A pilot study conducted to investigate the effect of sun exposure at recommended levels on the vitamin D status of Arab women sampled eight healthy Arab women of childbearing age who consented to expose their faces, arms and hands for 15 minutes per day twice a week for 4 weeks within the privacy of their courtyard. Serum 25-hydroxyvitamin D[25(OH)] levels were measured pre- and post-intervention. Although vitamin D levels remained sub-optimal, median serum 25(OH)D levels were significantly higher post-intervention (23.0 nmol/L) than pre-intervention (17.6 nmol/L). Extending sun exposure, therefore, for more than 4 weeks should be investigated as part of strategies to improve vitamin D status in high-risk Arab women who lack direct exposure to sun.[62]

A recent random survey of 1,172 healthy Saudi pre-and postmenopausal women measured anthropometric parameters, socioeconomic status, sun exposure index together with serum levels of 25(OH)D, calcitriol, intact PTH, Ca, PO4, Mg, creatinine, albumin, and biochemical BTMs. 80% of the sample exhibited vitamin D deficiency (serum 25(OH)D< 50 nmol /L) with only 11.8% of the sample having adequate vitamin D status (serum 25(OH)D>75 nmol/L). Obesity, poor exposure to sunlight, poor dietary vitamin D supplementation, and age were largely found to be the incriminating factors.[65]

A sample of medical students studied for serum 25(OH)D levels showed that the entire group (100%) had low vitamin D levels. The prevalence of vitamin D deficiency was 96.0% (92.64% in males and 99.03% in females), while the remaining 4% had vitamin D insufficiency. The mean 25(OH)D level was 26.83 ± 12.60 nmol/l in males and 16.03 ± 8.28 nmol/l in females (P-value = 0.0001. There was no difference between the two groups in terms of exposure to the sun.[66]

2.3. Qatar

A study conducted between 15 Jan 2007 to 15 Jan 2008 on healthy volunteers (n=340) showed an overall vitamin D level of 11.7 ng/ml. Their exposure to the sun and vitamin D supplements were monitored. Serum levels were lower in females (10.3 ng/ml) than in males (13.7 ng/ml). Ninety-seven percent of all participants had a mean level <30 ng/ml whilst87% had a mean level of <20 ng/ml.[67]

2.4. United Arab Emirates (UAE)

Low serum 25-(OH)D in female Arab subjects, which may predispose their infants to hypocalcaemia, has been suggested to be due to inadequate exposure to sun, but may include other socio-biological factors. The effects of duration of sunshine exposure--weighted against the magnitude of clothing (UV exposure) and other socio-biological variables such as age, education and living accommodation--on serum 25-(OH)D and mineral status of 33 UAE women of childbearing age were compared with those of 25 non-Gulf Arabs and 17 Europeans. Serum concentrations of calcium, phosphorus, alkaline phosphatase and intact parathyroid hormone among the groups were not significantly different. The serum concentration of 25-(OH)D in UAE nationals was 8.6 ng/ml (4.5-17.4), mean +/- 1 SD, and in non-Gulf Arabs 12.6 ng/ml (6.0-26.4); both these values were significantly lower ($p = < 0.0001$) than the 64.3 ng/ml (49-84.3) found in Europeans. Compared with Europeans, the UAE and non-Gulf Arabs in this study were younger, had fewer years of education and had significantly lower clothing and UV scores ($p < 0.0001$). Furthermore, there was a positive correlation between serum 25-(OH)D and UV score, but not with length of exposure. After adjusting for other confounding variables, nationality, clothing and UV scores remained major determinants of serum 25-(OH)D ($p < 0.0001$). Therefore, limited skin exposure to sunlight appears to be an important determinant of vitamin D status in subjects. Strategies to increase vitamin D stores should include vitamin D supplementation or advice on effective sunlight exposure.[62]

2.5. Kuwait

Four cases of unexplained vitamin D deficiency-related osteomalacia in otherwise healthy veiled Kuwaiti women triggered the study of a group of 50 veiled volunteer Kuwaiti women between 14 and 45 years, who had three children or less, and 22 unveiled volunteer Kuwaiti women with matching age and number of children as control. Renal and hepatic diseases were ruled out.

Results showed subclinical vitamin D deficiency among veiled women. Additionally, two cases of clinically overt osteomalacia were discovered among the veiled volunteers suggesting a high prevalence of the disease among veiled Kuwaiti women.[68]

2.6. Oman

The objective of this study was to investigate serum 25-hydroxyvitamin D[25(OH)D] levels and its relationship to biochemical bone profile, exposure to sunlight and vitamin D intake amongst Omani women of childbearing age. 41 apparently healthy women working at the Royal Hospital, Muscat, Oman and aged 18-45 years, with mean ± SD of 29 ± 6 years, were included in this study conducted in December 2006. They completed a questionnaire regarding the duration of sun exposure, food intake and type of clothing worn. Serum 25(OH)D, calcium, phosphate, alkaline phosphatise and parathyroid hormone level were analysed. Results indicated that all women had a 25(OH)D level <50 nmol/L as the cut-off for deficiency. 25(OH)D levels were strongly correlated with the lack of sun exposure ($P < 0.001$). The study concluded that subclinical 25(OH)D deficiency may be prevalent amongst Omani women. Risk factors such as poor sunlight exposure should be addressed in women of childbearing age. If increased sunlight exposure is not possible, oral supplementation should be considered to avoid all possible consequences and complications of vitamin D deficiency.[69]

2.7. Jordan

In a study of serum 25–hydroxyvitamin D (25(OH)D) status and factors associated with deficiency in a nationally representative survey of 2013 Jordanian women of reproductive age in spring 2010 was evaluated by liquid chromatography-tandem mass spectrometry. The objective of study was to see prevalence ratios for deficiency associated with skin covering and other factors. Results showed 60.3% deficiency and 95.7% insufficiency among women. Prevalence of deficiency was 1.60 times higher for women who covered themselves with a scarf or a hejab. The study concluded that vitamin D deficiency and insufficiency pose significant public health problems to Jordanian women. Prevalence of deficiency was significantly higher among urban women and among those who covered themselves with a scarf or hejab or niqab.[70]

2.8. Iran

A cross-sectional study conducted to determine the prevalence of vitamin D deficiency among the adult population of Isfahan, Central Iran(243 men and 868 women; mean age 41.4 years), showed mild, moderate and severe vitamin D deficiencies as 19.6%, 23.9%, and 26.9% respectively. Vitamin D deficiency was more prevalent among women ($p = 0.001$) and younger age-group ($p = 0.001$). Medians of 25-(OH)D in spring-summer and autumn-winter were 21 ng/mL and 18 ng/mL, respectively ($p = 0.005$). 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.

The prevalence of severe vitamin D deficiency was higher in autumn-winter period than the spring-summer period. As elsewhere in the Middle East, the prevalence of vitamin D deficiency was high in the sunny city--Isfahan--especially among women. The high prevalence of vitamin D deficiency in this city emphasizes the necessity of vitamin D supplementation as exposure to the sun is limited due to the type of clothing required by the prevalent legal environment.[71]

2.9. Turkey

A cross-sectional study among Turkish adolescent girls demonstrated that (43.8%) of them had vitamin D insufficiency and (21%) were deficient at the end of the winter season. The findings were more striking in girls who wore concealing clothing.[50]

3. Areas of Uncertainty and Future Research Needs

All clinicians, investigators, and public health officials interested in vitamin D biology, photo carcinogenesis, or skin biology and pathophysiology would probably agree that more research in overlapping areas is needed. Perhaps the most clinically important issues are:

• The Middle East needs further studies to establish the correct reference range, dietary recommendations, and the most accurate laboratory method for vitamin D serum level assessment for its population (regional relevance).

• The longstanding controversy has led many responsible professional groups to wonder whether to recommend a safe or prudent amount of unprotected sun exposure to the public concerned about their skin and overall health. The risk-benefit ratio of sun exposure, and probably of high 25(OH) D concentrations, varies enormously within the populations. Moderate or even generous sun exposure might have little effect on a darkly pigmented person's risk of subsequent photo-aging and skin cancer while promoting higher 25(OH)D concentrations. But a similar exposure could promote development of precancerous and even cancerous lesions in already photo-damaged fair skin individuals without increasing the already maximized vitamin D photosynthesis.

• Solar UVB intensity varies enormously with latitude, altitude, time of the day, and time of the year, among many other variables. UVA radiation varies far less in intensity and is far more abundant in sunlight than UVB radiation, so unprotected late-summer-afternoon or midday-winter exposure might involve almost no UVB exposure and hence no vitamin D synthesis, but might still contribute to photo-aging and photo-carcinogenesis. A rule of thumb might be that any sunburn dose is too much by a factor of ≥3, because maximal vitamin D synthesis is achieved after approximately one-third of a minimal erythema dose. Individuals, who never had sunburn or who live in climates that never allow them to experience sunburn are relatively safe from the damaging effects of unprotected sun exposure. People with light complexions or whose living circumstances are associated with the possibility of frequent sunburns probably have no safe minimum unprotected exposures, because these exposures would be only for a few minutes and would almost certainly be exceeded cumulatively on a daily basis during the course of routine activities. Research data has established UV radiation as a carcinogen responsible for more than 1 million skin cancers per year in the United States alone, as well as for photo-aging, an essentially universal problem among middle and old aged whites. These data also show that lifelong safe sun practices minimize both risks. With continued goodwill and enhanced communication, one can hope that the "controversy" surrounding the "sunshine vitamin" will, one day, become a thing of the past.[72]

• Does an inverse cause-effect relation exist between higher 25(OH) D concentrations and cancer incidence, hypertension, diabetes, multiple sclerosis, and other conditions for which research has noted inverse epidemiologic associations? Implicit in these issues and questions is the fact that one cannot construct cause and effect relations from epidemiologic studies, which are inevitably confounded by indirect and group-averaged measures of key variables, socioeconomic factors, racial and genetic factors, and lifestyle associations. In contrast with these understudied areas, randomized, prospective controlled trials among frail elderly groups strongly suggest that such individuals benefit from daily oral supplementation of ≥800 IU of vitamin D, which enhances muscle strength and decreases falls, reducing risk of bone fracture. These data imply that the present recommended daily allowance (600 IU/d) for vitamin D in those ≥70 years old is probably inadequate and that increasing vitamin D intake in frail older individuals, particularly those who are housebound or institutionalized, would probably confer a health benefit.[3]

• Does having a higher than conventionally recommended serum 25(OH) D concentration produce any health benefit, or even a prospective health benefit, in healthy children and adults? If such a benefit exists, what is the minimum duration required for maintaining high 25(OH) D concentrations (e.g., throughout life or only for a period of months or years)?

4.Conclusions

The review shows a widespread prevalence of low levels of vitamin D measured by serum 25(OH)D in the Middle East and in people of Middle Eastern origin living outside the region. Although hypovitaminosis D affects men, women and children, women are particularly susceptible and demonstrate lower levels of vitamin D compared to men. The degree of hypovitaminosis though varies from country to country. Female gender and paucity of exposure to sunlight coupled with cultural practices, especially the dressing style, could be seen as major risk factors. More research is needed to establish the regionally relevant reference range or ranges which would help on the diagnostic side on the one hand and will help inform public health interventions in the region.

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