Vitamin D deficiency: A single centre analysis of patients from 136 countries

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Review

Vitamin D deficiency: A single centre analysis of patients from 136 countries

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ABSTRACT

Vitamin D deficiency is a global problem, thought to be related to lack of sunlight exposure, and usually accompanied by reduced dietary intake. This study was designed to determine vitamin D status of 60,979 patients admitted to the Burjeel Hospital of VPS healthcare in Abu Dhabi, United Arab Emirates (UAE) from October 2012 to September 2014. The total concentrations of vitamin D [25(OH)D] of all the studied patients were measured in a single laboratory. Of the studied patients, 57.5% were female and 42.5% were male. Serum 25(OH)D (total) measurements showed 82.5% of the studied patients have vitamin D deficiency to insufficiency. 26.4% of females and 18.4% of males have extreme deficiency of 25 (OH)D. There was higher variability of vitamin D in group of females then males according to coefficient of variation. In our studied cohort teenagers (13–19 years) have shown the lowest levels of serum vitamin D (data not shown and will be communicated as a separate publication). The prevalence of hypovitaminosis D is significantly high among population of UAE, Saudi Arabia and many Middle Eastern countries, especially among women, despite abundant sunshine. 86.1% UAE nationals and 78.9% visitors of other nationalities were found <75 nmol/L of 25(OH)D. 28.4% of UAE nationals and 17.5% of visitors of other nationalities have extreme deficiency of 25(OH)D. Our results are significant, as all of our patients are residing permanently in the UAE or visitors that has yearlong sunlight. In addition, measuring 25(OH)D concentrations in a single laboratory minimized test level variations. Our current study formed the basis of further studies to determine if vitamin D deficiency and insufficiency can aggravate systemic diseases, including hypertension, diabetes or obesity that are also wide-spread in the Middle Eastern region.

Contents

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1. Introduction

The active form of vitamin D, 1,25$(OH)_2$D can act as a hormone to exert diverse functions, ranging from influencing bone mineralization to mineral ion metabolism. It is believed that more than half of the world population lacks adequate sun exposure to maintain adequate vitamin D [1–3]. An association between inadequate vitamin D and aging related complications, including osteoporosis, cancer, diabetes, autoimmune disorders, hypertension, atherosclerosis, muscle weakness, and neuronal disorders has been reported [4–7]. Severely deficient/insufficient levels of 25 (OH)D are also detected in the populations of Middle-Eastern countries, including UAE, possibly related deliberate avoidance of sunlight exposure [8–11]. To minimize such inadequacy, many kinds of food & drinks are widely fortified with vitamin D. This study was designed to determine vitamin D status in individuals who reside in a country that has yearlong bright sunlight, and have the access with vitamin D fortified food. To minimize test level variations, vitamin D status of all individuals (n = 60,979) were measured in a single laboratory.

2. Subjects

This was a retrospective study, designed to determine vitamin D status of all the patients admitted to the Burjeel Hospital in Abu Dhabi, UAE from October 2012 to September 2014. Burjeel Hospital is a tertiary care hospital under the auspices of the new standards put in place by the Health Authority of Abu Dhabi (HAAD). Equipped with the most advanced facilities in the treatment, and diagnosis, with a team of renowned specialists and medical personnel at the helm. Burjeel hospital Pathology lab is a CAP accredited state of the art facility where the 25(OH)D is routinely measured.

A total of 60,979 patients tested 25(OH) D concentration during the suggested timeframe. All the subjects included in this study were either permanent residents of UAE or visitors from various countries. These patients admitted to the hospital for unspecified vitamin D deficiency, unspecified hypothyroidism, rickets, osteoporosis, osteopenia, pain in soft tissues of limb, myalgia, hypocalcemia, dizziness and giddiness and other malaise and fatigue etc. Patients found deficient were treated with vitamin D supplements as various forms and preparations of vitamin D supplements are available in the UAE hospital pharmacies. Ethical approval for the study was obtained from the Institutional Review Board/Ethics Committee of VPS Healthcare/Burjeel Hospital, and was in accordance with the Helsinki Declaration. Consent from the patients was taken during their 1st visit to the hospital which states" I grant permission for my medical data to be used for clinical research, if needed, with the understanding that my identity shall remain confidential and privacy respected.

3. Study design and methods

Data was extracted from the files involving 60,979 patients using computerized database. Serum vitamin D measurement was carried out as described earlier [12]. Vitamin D total assay is a competitive electrochemiluminescence (ECL) protein binding assay intended for the quantitative determination of total 25(OH)D in human serum and plasma. The patented ECL method by F. Hoffman-La Roche AG (Basel, Switzerland) for the cobas platform offers a 25-hydroxy vitamin D assay. The test is available for use on all of the Roche cobas modular analyzer platforms; it received FDA clearance in July 2012 [13]. The assay was validated in our laboratory following clinical laboratory standards [14]. Between day precision was CV = 4.9% and 1.9% at mean concentrations of 43.3 and 105 nmol/L respectively using quality control material provided by Roche Diagnostics. External quality controls from college of American Pathologists(CAP) were used periodically to maintain the quality and precision of 25(OH)D testing.

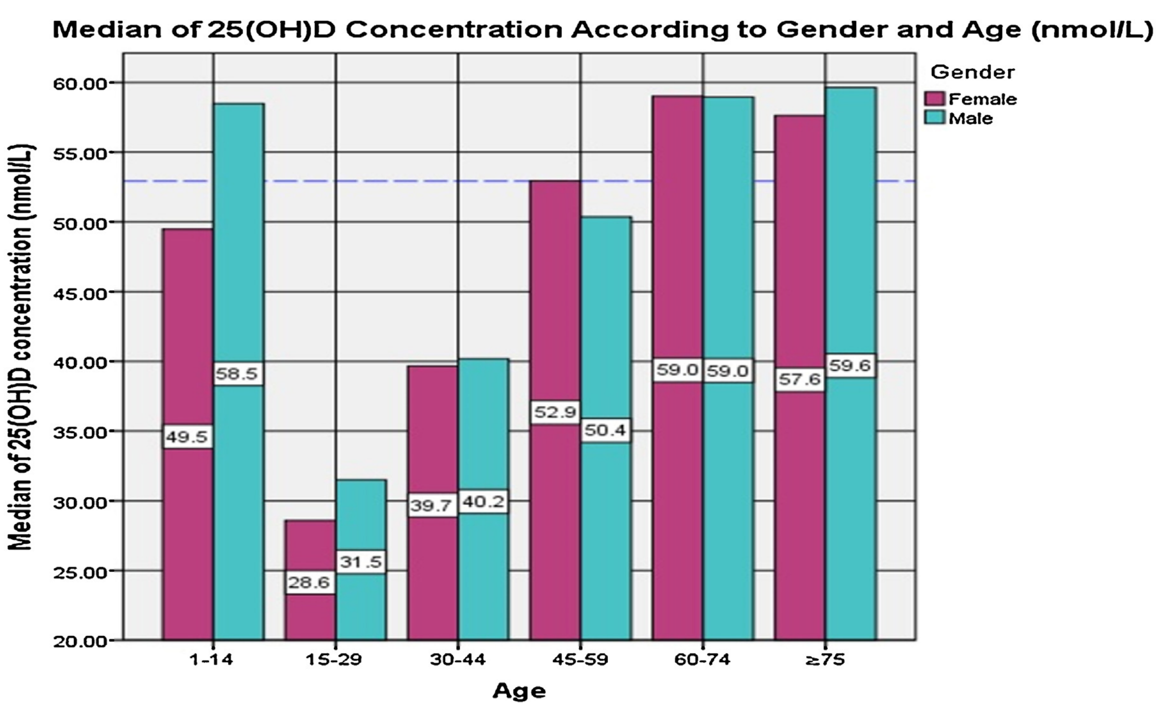

Fig. 1. Bar Chart showing median of 25(OH)D concentration according to age and gender. (For interpretation of the references to colour in the text, the reader is referred to the web version of this article.)

Table 1
Age and gender distribution of 60,979 patients included in the study.

Age (Years)	Gender: Female	Male	Total
1–14	3173	3039	6212
15–29	9720	5167	14,887
30–44	13,958	9678	23,636
45–59	6153	5652	11,805
60–114	2062	2377	4439
Total	35,066	25,913	60,979

Table 2
Patients (%) with extreme deficient, mild deficient, insufficient or optimal concentration of 25(OH)D(nmol/L) according to gender.

		Extreme deficiency (≤24.99) (%)	Mild deficiency (25–49.99) (%)	Insufficiency (50–74.99) (%)	Optimal (75–250) (%)
Gender	Female	26.4	35.0	21.6	17.0
	Male	18.4	39.9	23.6	18.1
Total		23.0	37.0	22.5	17.5

Reference ranges used in this study are based upon the recommendations of the Endocrine Society [15] and the Institute of Medicine (IOM). The 25(OH)D concentration recommended as 'cutoffs' to define vitamin D deficiency differ between the US IOM report and the US Endocrine Society guideline. The US Endocrine Society guidelines [15] defines vitamin D deficiency as 25(OH)D less than 20 ng/mL (50 nmol/L), vitamin D insufficiency as 25(OH)D between 21 and 29 ng/mL, and the safety margin to minimize the risk of hypercalcemia as 25(OH)D equal to 100 ng/ml (250 nmol/L). On the other hand, the US IOM report [16] concluded that 25(OH)D equal to 16 ng/mL (40 nmol/L) covers the requirements of approximately half the population, 25(OH)D equal to 20 ng/mL (50 nmol/L) covers the requirements of ≥97.5% of the population, and 25(OH)D >50 ng/ml (125 nmol/L) should raise concerns about potential adverse effects. The difference in these recommendations reflects different views on current evidence. The US IOM Committee placed heavy emphasis on data from RCTs when there was discordance between results from RCTs and observational studies [17]. Although evidence from multiple observational studies and meta-analysis, as reviewed above, suggested additional health benefit with serum 25(OH)D above 20 ng/mL up to 30 ng/mL, this body of evidence was not taken into consideration by the US IOM report.

4. Data analysis

Statistical software SPSS IBM Statistics 22 and SAS 9.4 have been used for the analysis of data for the vitamin D. There were 60,979 cases of patients considered from October 2012 to September 2014. Normality was tested by Anderson-Darling test, where is confirmed that there is not normal distribution in the data on significance level of alpha 0.05. In the data of vitamin D, skewness was found, therefore the median was used to describe the data and non-parametric tests, for instance two-tailed Mann-Whitney, multidimensional Kruskal-Wallis non-parametric test and Chi-Square test. The power analysis was used to reduce sample size before testing of hypothesis.

5. Results and discussion

All the patients admitted to the Burjeel Hospital in Abu Dhabi, UAE, tested for vitamin D status, were included in this study, irrespective of age, sex, and country of origin; of particular importance, all the vitamin D measurements were done in a single laboratory that minimized test level variations. In our studied population (n = 60,979), analyzed cases consists of 35,066 females (57.5%) and 25,913 males (42.5%). When the levels of vitamin D sorted by gender, the maximum number falls under the category of 21–30.99 nmol/L of vitamin D with 16.4% of female and 17.4% of male. The next category for male was 31–40.99 nmol/L (16.4%) and for female was 11–20.99 nmol/L (15.4%) (Fig. 1).

The age of our studied cohort ranged from 1 year to more than 100 years, but the most frequent categories were age 30–44 years

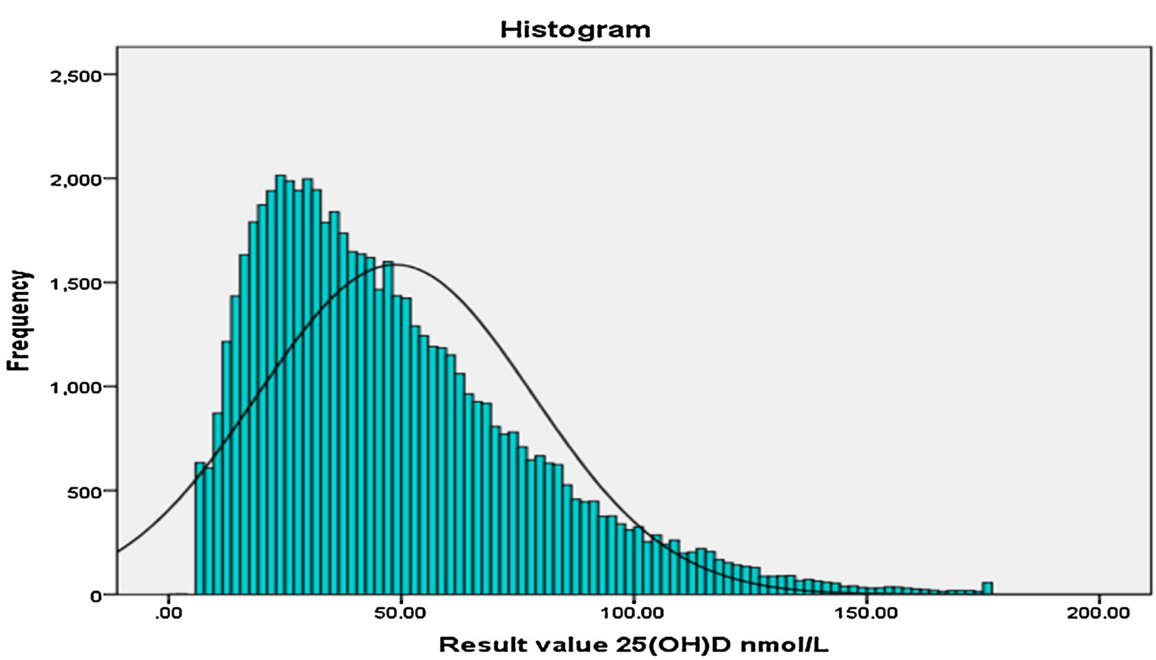

Fig. 2. Frequency distribution of the 25(OH)D measurements. 25(OH)D concentration is shown as a skewed distribution, and most of the values are less than 50 nmol/L.

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Table 3
Differences in 25(OH)D concentration according to gender.

Gender	Mean	Median	Std. deviation	Minimum	Maximum	Coefficient of variation (%)
Female	47.41	40.80	30.00	1.35	175	63.28
Male	50.37	43.91	28.75	2.48	175	57.08

[23,636 (38.8%) cases], age 15–29 years [14,887 (24.4%) cases], and age 45–59 years [11,805 (19.4%) cases] (Table 1).

Although analyzed patients were from of 136 different countries, the maximum cases were from UAE 30,640 (50.2%), followed by India 5602 (9.2%) and Egypt 3692 (6.1%). In addition to UAE, India, and Egypt, other top ten of countries, among top 10 in terms of numbers, were Jordan, Pakistan, Philippines, Yemen, Syria, Palestine and Sudan. All these patients visited hospital in Abu Dhabi, but they are originally from 135 other countries, therefore, in this study we compared only two groups of patients, UAE nationalities and visitors of other nationalities. Patients who visited the UAE not bring vitamin D supplements with them. Vitamin D supplements from various manufacturers are available in the UAE and deficient patients were treated.

When 25(OH)D concentration was sorted into intervals the most frequent categories were in interval of 21–30.99 nmol/L [10,262 (16.8%) patients], in the category of 31–40.99 nmol/L [9247 (15.1%) patients] and then in the category of 11–20.99 nmol/L [8030 (13.2%) patients. The main results of extreme deficiency, mild deficiency, insufficiency and optimal levels of 25(OH)D for both males and females are shown in Table 2.

The coefficient of variation for females was 63.28% indicative of a higher variability in group of female patients. The coefficient of variation for males was 57.08%, however this variability found higher in group of female patients. In Fig. 1 the blue dotted line depicts the median. Median of 25(OH)D concentration for females was 40.80 nmol/L and 43.91 nmol/L for males. The highest difference in median was found between genders in kids (1–14 years). In this age group the medians for females was 49.5 nmol/L while for males was 58.5 nmol/L. The frequency distribution of 25 (OH)D concentrations are shown as a skewed distribution, and most of the values are less than 50 nmol/L. Skewness right distribution of 25(OH)D concentration of patients with median of 42.25 nmol/L (Fig. 2).

For variables normality was tested by Anderson-Darling test. The null hypothesis was rejected on significance level of alpha 0.05, that's why non-parametric test was used. Genders in result value of 25(OH)D were tested by two-tailed Mann-Whitney test. Gender affected the result value of 25(OH)D, with a statistically significant difference between male and female (Sig. = 0.000). According to the recommended range of the Endocrine Society [15] low serum 25(OH)D concentration (below the cut off line 75 nmol/L) was found in 83% of the females and 81.9% of the males. Extreme deficiency was found in 26.4% in females and 18.4% in males. Differences in 25(OH)D concentration according to gender is shown in Table 3.

Extreme deficiency was found in 28.4% cases of UAE nationals and 17.5% visitors of other nationalities. The percentage of patients with deficient, insufficient or adequate levels of 25(OH)D for UAE nationals and other nationals are shown in Table 4.

The National Health and Nutrition Examination Survey III showed that people with vitamin D levels in the lowest quartile had a mortality rate ratio of 1.26 (95% CI, 1.08–1.46) [18]. The prevalence of hypovitaminosis D is significantly high among population of UAE, Saudi Arabia and many Middle Eastern countries, especially among women, despite abundant sunshine. In this retrospective study including 60,979 patients samples, we found that most of the patients having insufficient levels of vitamin D. In the UAE (30,640 number of patients), 86.1% were found $<$75 nmol/L and only 13.9% having sufficient levels $\geq$75 nmol/L of 25(OH)D. There is potentially a great upside (in terms of improving overall health and well-being) to increasing serum 25(OH)D concentrations above 30 ng/mL or 75 nml/L [19]. Functional indices of vitamin D status have been proposed in which serum 25(OH)D concentrations above 32 ng/ml (80 nmol/L) are necessary to improve calcium absorption [20].

Vitamin D deficiency is highly prevalent, even in countries with abundant sunshine, when skin exposure to UVB sunlight is limited by lifestyle and other factors. Our results from a relatively large cohort suggest that an effective strategy to prevent vitamin D deficiency and insufficiency is necessary. The following steps are important and should be implemented at the population level to help in reducing such wide-spread vitamin D inadequacy around the globe.: (1) promote safe skin exposure to UVB sunlight; (2) ingesting foods that contain vitamin D; (3) intake of vitamin D supplements and (4) increase awareness among policy makers, health professionals, and the general public about the importance of vitamin D and its role in health. The reasons for the high prevalence of vitamin D insufficiency during adolescence are unclear. Future research will be focused on kids and teens who were found with the lowest levels of vitamin D in our studied cohort.

Conflict of interest

The authors have declared no conflict of interests.

Funding source

This study was supported by VPS Healthcare, Dr. Afrozul Haq is working as a Research Director for this international health organization.

Table 4
Patients (%) with extreme deficient, mild deficient, insufficient or optimal 25(OH)D concentration (nmol/L) according to nationality.

		Extreme deficiency (≤24.99) (%)	Mild deficiency (25–49.99) (%)	Insufficiency (50–74.99) (%)	Optimal (75–250) (%)
Nationality	UAE	28.4	37.6	20.1	13.9
	Visitors of other nationalities	17.5	36.5	24.9	21.1
Total		23.0	37.0	22.5	17.5

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