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Review

Clinical practice guidelines for vitamin D in the United Arab Emirates

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ABSTRACT

In the UAE and the Gulf region in general, there are several intricate public health issues in the context of vitamin D deficiency that needs to be addressed. Changes in lifestyle such as diet, lack of exercise, cultural habits, avoiding sun exposure due to excessive heat, and other risk factors predispose those who live in GULF countries, such as Emiratis likely to becoming vitamin D deficient. Consequently, the prevalence of vitamin D deficiency is high, and new guidelines are needed to overcome this major public health issue. Peer-reviewed papers related to guidelines and those vitamin D-related papers relevant to the Middle-Eastern region were extracted from multiple research databases using key words according to the general guidelines from the Preferred Reporting Items for Systematic Analysis. This guideline was prepared focusing on the United Arab Emirate and the Gulf populations, to overcome the high incidence of vitamin D deficiency and to improve overall health. We recommend the following vitamin D supplementations for different groups of people: (A) Breastfed infants supplement with 400 IU/day up to age 6 months, and 400–600 IU/day between 6 and 12 months, depending on daily intake of total vitamin D and sun exposure; (B) for children and adolescents of age 1–18 years supplement with 600–1000 IU/day depending on the body weight; (C) adults greater than 18 years', supplementation with 1000–2000 IU/day is recommended, while, (D) the elderly (over 65 years) should be supplemented with 2000 IU/day, throughout the year; (E) pregnant and breast feed women, 2000 IU/day from the first trimester of pregnancy. (F) Premature infants, supplementation of 400–800 IU/daystart from the first days of life. (G) For obese, individuals and those with metabolic syndrome, supplementation of 2000 IU/day (H) For individuals with dark skin complexions and for night workers, supplementation of 1000–2000 IU/day (25–50 μg/day), throughout the year, depending on body weight. The goal of supplementation is to achieve and longer term maintenance of serum 25(OH)D concentration of 30–50 ng/mL.

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1. Introduction

The awareness of the significance of optimal vitamin D status and consequences of vitamin D deficiency for human health at all stages of life must be markedly improved among physicians, health policy makers and the general public health. The research studies that we and others had conducted highlighted the high prevalence of vitamin D deficiency and its implications on general health of the UAE population countrywide [1,2]. Maintaining a good vitamin D status requires adequate sun exposure or sufficient intake from diet and supplements. Biomarkers of vitamin D status are also affected by season and geographic latitude.

We have successfully launched Vitamin D deficiency awareness programs in the form of conducting annual International conferences and seminars where researchers, doctors/scientists, technologists in the field of vitamin D research from all over the world are invited. This awareness program has successfully completed 5 years in continuation under the patronage and support of H.E. Sheikh Nahayan Mabarak Al Nahayan, Minister of Culture and Knowledge Development, Govt. of United Arab Emirates (UAE).

Involvement of the food industry by encouraging private enterprises operating at the national and local level is required. Support in terms of technical expertise pertaining production of fortified food items, availability of standardized vitamin D formulation(s) and information on the marketing potential of the fortified items should be made available. Moreover, affordable and widely accessible testing facilities for vitamin D levels should be made available to individuals who are at risk of clinical vitamin D deficiency with easy accessibility, throughout UAE.

Till this date, effective legislation to ensure good quality and regulation of vitamin D fortified foods at minimal cost to the end consumer is not yet in place within the UAE. To this extent, there is room for remarkable initiatives like mandating the distribution of vitamin D fortified foods at midday meals within schools.

Vitamin D sufficiency status may not be treated as a “feel good status” for the affluent who can afford medical expenses and expensive vitamin D supplements. Vitamin D is prevalent across all socioeconomic strata. It is imperative that policymakers understand the gravity of the situation pertaining to vitamin D status and as a consequence—the untold burden on the healthcare system in the UAE.

This guideline is based on both the recent clinical practice guidelines published by The Endocrine Society [3] and The Institute of Medicine guidelines [4]. It is intended to be used as guidelines for physicians in the UAE and the Gulf Cooperation Council (GCC) member states.

2. Definitions

2.1. Vitamin D

Vitamin D is a steroidal hormone similar to estrogen or testosterone. It stands alone as the only ‘vitamin,’ the body can produce. Vitamin D is called the “Sunshine Vitamin” because the body naturally produces it through exposure of Ultra Violet B (UVB) rays from the sun through the skin [5,6]. There are two major forms of vitamin D- ergocalciferol (D2) and cholecalciferol (D3). Vitamin D3 can be synthesized under the UVB irradiance or could be absorbed via the intestine from salmon fish and other seas foods and fortified foods or from cholecalciferol containing supplements.

The source of vitamin D2 (ergocalciferol) is mushroom and plants. The 25- hydroxyvitamin D [25(OH)D] level (calcidiol), a biochemical marker of vitamin D status, is used to indicate the sum of 25(OH)D3 and 25(OH)D2 levels, and both compounds are hydroxylated in the liver by 25-hydroxylase [CYP27A1, CYP2R1]. 25(OH)D undergoes further hydroxylation by the enzyme 1α-hydroxylase [CYP27B1] to become the active metabolite 1α,25-dihydroxyvitamin D3 [1α,25 (OH)2D3](calcitriol); this process takes place predominantly in the proximal tubule cells of the kidney, but also in many tissues and organs (extra-renal sites, paracrine pathway).

2.2. Vitamin D deficiency

Vitamin D deficiency is defined as not having enough vitamin D that the body needs to function physiologically. Vitamin D deficiency is a widespread epidemic and is a major preventable health issues, worldwide. While it contributes or aggravates several common chronic diseases such as osteoporosis, autoimmune diseases, certain cancer, cardiovascular diseases (CVD), viral and bacterial infections (e.g., tuberculosis, influenza), and diabetes; it primarily causes rickets in children and osteomalcia in adults [7–11].

2.3. What is an optimal 25(OH)D level?

Proposed "optimal" range for 25(OH)D is broad (25–80 ng/mL). In addition, there are differences of opinion as to the definitions of vitamin D insufficiency; reported as <30 ng/mL versus 20 ng/mL, and deficiency reported as <20 ng/mL versus 10 ng/mL [3,4]. Mild-to-modest deficiency can be associated with osteoporosis and secondary HPT. Whereas, severe deficiency may lead to failure to mineralize newly formed osteoid in bone, resulting in rickets in children and osteomalacia in adults. Thus, an optimal vitamin D level might depend on the health outcome in question. While mineralization of the skeleton needs lower levels (at least ≥20 ng/mL), prevention of non-communicable diseases may need a higher threshold of vitamin D (at least ≥30 ng/mL) [3,10–12]. The public need to be educated about the skeletal versus non-skeletal benefits of vitamin D and the thresholds for both in order to make an informed decision about improving their vitamin D status.

We recommend to use the American Endocrine Society Vitamin D guidelines/cutoff points of serum 25(OH)D adequacy and deficiency (3). Table 1 shows the vitamin D recommendation of daily allowance (RDA) for the population of UAE and GCC for all age groups and conditions. The infant dose of vitamin D supplement is 400–600 IU per day depending upon the use of formula fed infants. For all age groups the dose also depends upon the body weight, seasonal variation, and exposure to the sun.

2.4. 25-Hydroxyvitamin D [25(OH)D]

25(OH)D is the main storage form in the human body. It is also the main form of vitamin D circulating in the blood and is amenable to measure accurately. Thus, the 25(OH)D is the form that needs to be measured in serum to assess the vitamin D adequacy (i.e. sufficiency, insufficiency, deficiency or toxicity). The 25(OH)D level (calcidiol), a biochemical marker of vitamin D status, is used to indicate the sum of 25(OH)D3 and 25(OH)D2 levels, and both compounds are hydroxylated in the liver by 25-hydroxylase [CYP27A1, CYP2R1]. Subsequently, 25(OH)D undergoes further hydroxylation predominantly in the proximal tubule cells of the kidney, but also in many tissues and organs (extra-renal sites) by the enzyme 1α-hydroxylase [CYP27B1] to become the active metabolite 1α,25-dihydroxyvitamin D3 [1α,25-(OH)2D3] (calcitriol) [5,6].

2.5. Vitamin D_2 (Ergocalciferol)

Primarily derived from plant sources, such as mushrooms, plants and yeast; marketed as vitamin D_2 (ergocalciferol). This primary form, hydroxylate at position 25, converting to 25(OH)D in the liver. This storage form of vitamin D has independent biological activities. Following intestinal absorption, its 1α hydroxylation occurs in kidneys with the end product – the active hormone – 1,25 (dihydroxy)vitamin D [1,25$(OH)_2$D].

2.6. Vitamin D_3 (Cholecalciferol)

Cholecalciferol is generated in animals and is the naturally occurring form of vitamin D in humans. Following exposure to UVB rays in the skin, ergosterol is converted to pre-vitamin D with 7-dihydroxy cholesterol (7-DHC) precursor of cholesterol in the skin [13,14] *In vitro*, lanolin is often used as a raw material for commercially producing vitamin D_3. Vitamin D_3 is present in oily fish (salmon, sardine, etc.) and few other sea foods.

Table 1
Vitamin D intake recommendation guidelines for the UAE and GCC.

Life Stage	Recommended Daily Allowance (RDA)		Tolerable Upper Intake Levels per day	Remarks
Group	International Units	micrograms	International Units/ micrograms	
Neonates and Infants				
0–6 months	400 IU	10 μg	1000 IU/25 μg	RDA even if formula fed
6–12 months	400–600 IU	10–15 μg	1000 IU/25 μg	RDA even if formula fed
Children and Adolescents				
1–18 yrs	600–1000 IU	15–25 μg	2000 IU/50 μg at age range 1–10 yrs; 4000 IU/100 μg at age range 11–18 yrs	RDA dose depends on body weight and season
Adults and Seniors				
>18–64 yrs	800–2000 IU	20.0–50.0 μg	4000 IU/100 μg	RDA dose depends on body weight and season
65 yrs and older	1000–2000 IU	25.0–50.0 μg/day	4000 IU/100 μg	RDA throughout the year
Recommended intake for groups at risk of vitamin D deficiency				
Pregnancy & Breastfeeding	1500–2000 IU	37.5–50.0 μg	4000 IU/100 μg	Females should consider starting supplementation before pregnancy
Premature infants until 40 gestational weeks	400–800 IU	10–20 μg	1000 IU/25 μg	RDA dose depends on body weight; 400-800 IU daily until accomplishing the corrected gestational age of 40 weeks should be warranted; thereafter, as for normal-term infants
Obese children and adolescents	1200–2000 IU	30–50 μg	2000 IU/50 μg at age range 1–10 yrs; 4000 IU/100 μg at age range 11–18 yrs	RDA dose depends on body weight, season and sensible sun exposure
Obese adults and elderly	1600–4000 IU	40–100 μg	10000 IU/250 μg	RDA dose depends on body weight, season and sensible sun exposure
Adults who are night workers or with dark-skin complexion	1000–2000 IU	25–50 μg	4000 IU/100 μg	RDA dose depends on body weight; RDA dose recommended throughout the year

Because of the longer half-life and the ability to achieve higher serum levels, vitamin D_3 is considered to be more potent than vitamin D_2 [15–18], but others disagree with this concept [16]. The body is equipped with a rescue metabolic path, both in the liver and in the kidney to prevent excess production of 25(OH)D and $1,25(OH)_2D$ by diverting the synthesis process into producing inactive vitamin D metabolites. Thus, though excessive sun exposure could increase the risk of developing skin cancer, it would not result in vitamin D toxicity [5,6].

2.7. 1,25-Dihydroxyvitamin D [$1,25(OH)_2D$](Calcitriol)

1,25-Dihydroxyvitamin D (calcitriol) is the biologically active form of vitamin D. Due to multiple reasons calcitriol is not considered as a marker of overall vitamin D status for several reasons [17]. First, the circulating half-life of calcitriol is short, only 4–6 h [17]. It is responsible for maintaining serum ionized calcium level tightly, thus the importance of having a short half-life. Second, the concentrations of calcitriol in serum and plasma are about 1000-fold less than 25(OH)D and, thus, is not easy to measure accurately. Third, and perhaps most important, overall vitamin D deficiency leads to decreased intestinal calcium absorption and a lower ionized calcium level, which in turn, stimulates increased secretion of PTH. Increased PTH, enhances blood ionized calcium level through increased renal production of calcitriol, enhances intestinal calcium absorption and renal tubular reabsorption, and increases bone resorption [13,19].

Thus, overall vitamin D deficiency generally leads to increased serum calcitriol concentration, which does not reflect the body's storage of vitamin D. Nevertheless, the measurement of serum calcitriol is useful in certain clinical circumstances, including renal failure (failure to 1α-hydroxylase enzyme), granulomatous disease (e.g., sarcoidosis, histoplasmosis, tuberculosis), and workup of rare inborn errors of vitamin D metabolism. In granulomatous disease, there is increased conversion of 25(OH)D to $1,25(OH)_D$ that occurs in extra-renal tissues, potentially leading to hypercalcemia [20].

2.8. Vitamin D receptor (VDR)

The calcitriol receptor, also known as the vitamin D receptor (VDR) is a member of the nuclear receptor family of transcription factors [21]. Upon activation by vitamin D, the VDR forms a heterodimer with the retinoid-X receptor and binds to hormone response elements on DNA resulting in expression or repression of specific gene products. The VDR not only regulates transcriptional responses but also involved in microRNA-directed post transcriptional mechanisms [22]. In humans, the vitamin D receptor is encoded by the VDR gene which has more than 200 polymorphism sequences [23]. VDR is expressed in most tissues of the body including the pancreatic β-cells, which are involved in the regulation of glucose metabolism, intestinal transport of calcium, Iron and other minerals [24].

3. International guidelines for vitamin D

3.1. The Endocrine Society/American Endocrine Society (TES)

The endocrine society guideline [3] is recommendations for individual patients, but not necessarily for special or vulnerable groups. It suggests that infants and children aged 0–1 yr require at least 400 IU/d (IU = 25 ng) of vitamin D and children 1 yr and older require at last 600 IU/day to maximize their bone health. To raise the blood level of 25(OH)D consistently above 30 ng/mL (75 nmol/L) may require at least 1000 IU/day of vitamin D.

3.2. 3.2. The Institute of Medicine (IOM)

The Institute of Medicine (IOM) recommendations [4] are not for individual persons but for making Public Health Policies for the United States and Canadian Governments. Therefore, IOM recommendation are NOT applicable for (A) outside north America, (B) individual patients, and (C) groups of vulnerable persons. Considering the above, we recommend that IOM recommendations are not to be used for GULF countries for individual patient management or for public health policy making.

3.3. Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe

The key opinion leaders established ranges of serum 25-hydroxyvitamin D concentration indicating vitamin D deficiency [<20 ng/mL (<50 nmol/L)], suboptimal status [20–30 ng/mL (50–75 nmol/L)], and target concentration for optimal vitamin D effects [30–50 ng/mL (75–125 nmol/L)]. General practical guidelines regarding supplementation and updated recommendations for prophylactic vitamin D intakes in Central European neonates, infants, children and adolescents as well as in adults (including recommendations for pregnant and breastfeeding women and the elderly) were developed, keeping in mind a target/optimal 25(OH)D level to be obtained and maintained.

Improving the Vitamin D status of children, adolescents, adults and the elderly must be included in the priorities of physicians, healthcare professionals and healthcare regulating bodies. The Central European Guidelines offer elaborated consensus on vitamin D supplementation guidance and population strategies for eradication of vitamin D deficiency in general population and groups at increased risk of low vitamin D supply [25].

3.4. Recommended Vitamin D intake for the general population—supplementation strategy for UAE

3.4.1. Neonates and infants (0–12 months)

Vitamin D supplementation should be introduced from the first days of life, irrespective of whether the infant is breastfed or formula-fed. Exclusively breastfed infants are at increased risk of vitamin D deficiency with its health consequences, therefore exclusively breastfed infants should be considered as a target group for implementation of vitamin D supplementation. We recommend, supplementation of 400 IU/day (10.0 μg/day) up to age 6 months, and 400–600 IU/day (10.0–15.0 μg/day) between 6 and 12 months of age depending on daily oral total vitamin D intake.

3.4.2. Children and adolescents (1–18 years)

We recommend supplementation of 600–1000 IU/day (15.0–25.0 μg/day), depending on body weight, between May and October (high season) each year; and supplementation of 600–1000 IU/day (15.0–25.0 μg/day), depending on body weight, remainder of the year, if sufficient sun (UVB) exposure is not ensured. Since the weather in the UAE is sunny almost all days of the year, increased sun exposure happens during winter (low season) because the temperatures are lower. People avoid sun in the summer (high season) due to excessive heat but increase their outdoor activities significantly in winter. Sensible exposure to sunlight taking into account time of the day, season, body weight, age and skin complexion is highly recommended. Adolescents, due to their habits (indoor activities, computer, mobile phone, social media, TV, gaming) are at the increased risk of vitamin D deficiency.

3.4.3. Adults (>18 years) and the elderly

We recommend, depending on body weight, supplementation of 800–2000 IU/day (20.0–50.0 μg/day), throughout the year, if sufficient skin synthesis of vitamin D is not ensured in winter. The elderly (65 years and above) should be supplemented with 1000–2000 IU/day (25.0–50.0 μg/day) throughout the year, because of the reduced efficacy of vitamin D synthesis in the skin and altered metabolism. Sensible exposure to sunlight is recommended.

3.4.4. Pregnant and breastfeeding women

We advise women who plan for pregnancy to start Vitamin D supplementation prior to pregnancy and maintain as recommended for adults. Adequate Vitamin D intake before pregnancy should be ensured for optimal growth of the infant. Vitamin D supplementation of 1500–2000 IU/day (37.5–50.0 μg/day) should begin, preferably from the first trimester of pregnancy. We recommend that together with other commonly recommended supplements, the obstetricians consider starting their patients on vitamin D supplementation ideally before becoming pregnant (once they are planning a pregnancy) or at least, soon after pregnancy is confirmed. Measurement of serum 25(OH)D concentration should define the optimum dosage (based on whether the patient is vitamin D deficient or insufficient) with approved supplementation. The goal of supplementation is to achieve and maintain serum 25(OH)D concentration of 30–50 ng/mL (75–125 nmol/L).

3.5. Recommended Vitamin D intakes in groups at high- risk of vitamin D deficiency

3.5.1. Premature infants

We recommend that vitamin D supplementation is introduced from the first days of life (as soon as enteral feeding is possible).

Supplementation of 400–800 IU/day (10–20 μg/day) until accomplishing the corrected gestational age of 40 weeks and; thereafter, the recommendations as for normal-term infants.

3.5.2. Obese children and adolescents (BMI >90th percentile for age and gender using local reference in a given country)

We recommend supplementation of 1200–2000 IU/day (30–50 μg/day), depending on severity of obesity. Sensible exposure to sunlight is recommended. Supplementation of 1200–2000 IU/day (30–50 μg/day), depending on severity of obesity, is recommended throughout the year, if sufficient skin synthesis of Vitamin D is not ensured in the winter (low season).

3.5.3. Obese adults and the elderly (BMI 30+ kg/m2)

We recommend supplementation of 1600–4000 IU/day (40–100 μg/day), depending on severity of obesity, is recommended throughout the whole year. Sensible exposure to sunlight in the context of additional oral vitamin D intake is safe.

3.5.4. Night workers and adults with dark-skin complexion

We recommend supplementation of 1000–2000 IU/day (25–50 μg/day), depending on body weight; throughout the year for both individuals who have dark skin complexion and for night workers.

3.5.5. Persons with intellectual and developmental disability

People with neurodevelopmental disorders and intellectual disabilities have much greater health care needs and also higher minimum serum vitamin D levels [26,27]. The Vitamin D Task Force of the American Academy of Developmental Medicine and Dentistry (AADMD) recommended the year-long serum 25(OH)D concentrations for optimal health in this vulnerable group between 30 and 50 ng/mL (75–125 nmol/L) [26,27]. Oral vitamin D can be administered, daily, weekly, every other week, or monthly. Administration vitamin D less than once monthly leads to marked fluctuations of serum 25(OH)D levels, which is not beneficial [27].

To achieve vitamin D levels of 30–50 ng/mL needs intakes of 2000–5000 IU/day vitamin D_3, depending on individual factors including body weight, skin color, time spent out of doors, and age. These values are also supported by the U.S. Endocrine Society guidelines [3].

3.6. Frequency of 25(OH)D testing

Frequency of ordering the test should be limited to baseline, the pretreatment screening. Subsequent measurements should not be performed prior to 8 weeks from the start of high-dose oral vitamin D supplementation, or 4–6 months after supplementation with the standard doses of vitamin D (i.e. allow time to achieving steady levels in the blood). Further testing is not indicated after reaching the target therapeutic levels, except for most vulnerable persons, where the optimal levels are difficult to be achieved and/or maintained, the 25(OH)D levels can be repeated between 9 or 12 months to assure the maintenance of vitamin D at physiological levels.

These group of individuals, not only need higher doses of oral supplements of vitamin D, but also tend to have altered

Table 2
The following 4 platforms are used in hospitals within Abu Dhabi for the measurement of total 25(OH)D.

Hospital/Laboratory at Abu Dhabi	Company/ country	Platform and method	Standardization	LOD nmol/ L	Linearity nmmol/ L	Imprecision
SKMC Hospital, Lifeline Hospital, Cleveland Clinic, Burjeel Hospital, NRL, ICLDC, Lifecare Hospital, L.L.H., Ahlia Hospital, Medsol Lab, Al Salama Hospital, NMC Hospital, Proficiency Lab	Chromsystems, Germany	HPLC system with UV detection	UV (verified by LC–MS/MS)	2.7	3.5–925	0.8–4.6%
Gulf Diagnostics Hospital, Al Noor Hospital	Roche Diagnostics, Switzerland	Cobas E601, 1-step competitive binding chemiluminescence against vitamin D binding protein	NIST SRM 2972	7.5	7.5–175	2.2–6.8%
Life Medical Centre, Zayed Military Hosp, NMC Hospital	Abbott, USA	Architect i System, 1-step competitive binding chemilu-minescence against 25OHD	UV (verified by LC–MS/MS)	7.7	20–400	2.8–4.6%
Life Mwdical Centre, NMC Hospital, Zayed Military Hospital	DiaSorin Liaison Immuno Assay System,Italy	The LIAISON® analyzer	Chemiluminescence technology (CLIA)	N/A	10–375	2.3–10.1

metabolism of it. Therefore, it is important to assure normal serum vitamin D levels and not having either hypo- or hypervitaminosis D. A routine yearly checkup is recommended for those apparently healthy individuals not taking any supplements.

3.7. We recommend 25(OH)D testing in:

- patients with rickets, osteomalacia, musculoskeletal pain, propensity to falls, idiopathic and secondary osteoporosis, patients with osteoporotic fractures, and history of low-energy fractures
- patients with abnormalities of calcium and/or phosphate metabolism
- patients with hyperparathyroidism
- patients with prolonged glucocorticoid therapy at the dose of 5 mg of prednisone per day or higher
- patients taking anticonvulsant medications, patients taking ketoconazole
- patients taking anti-AIDS medications (anti-retroviral medication)
- patients with malabsorption syndromes (coeliac disease, Crohn's disease, past gastrointestinal bypass surgery, cystic fibrosis, inflammatory bowel disease)
- patients treated with long-lasting elimination diets
- allergy, lactose intolerance/hypolactasia, total parenteral nutrition, eating disorders
- patients with chronic kidney disease stage 3–5 and kidney transplant recipients
- patients with hepatic failure and/or cholestasis
- patients with granulomatous disorders (tuberculosis)
- patients with cancer
- patients with cardiovascular diseases, especially hypertension
- patients with metabolic syndrome, obesity, type 2 diabetes
- patients with some chronic autoimmune diseases (multiple sclerosis, psoriasis, rheumatoid arthritis, dermatomyositis, systemic lupus erythematosus)
- hospital admissions secondary to infectious diseases (hepatitis C, recurrent acute lower respiratory tract infection)
- chronic or recurrent allergic diseases such as atopic dermatitis or atopic asthma
- Institutionalized persons
- Those with disabilities; especially those with developmental and intellectual disabilities.

4. Materials and methods

Multiple methodologies for 25(OH)D measurement exist, including RIA, HPLC, and liquid chromatography tandem mass spectroscopy. Current methodologies are sufficient for routine clinical practices. It is important to use the same laboratory for follow-up of serum 25(OH)D assays. The comparability of 25(OH)D results seems likely to improve as uniform standards available through the National Institute of Standards and Technology (NIST) become widely implemented. There are 4 main platforms used in various hospitals at Abu Dhabi to measure the total 25(OH)D levels as shown in Table 2.

All clinical assays, including 25(OH)D measurements are subject to significant assay variability. This can be reduced by using internal and external quality controls (QAs) in each assay. Therefore, to assure the quality of the data, we recommend to use laboratories that are participating in external QA programs (like Vitamin D External Quality Assessment Scheme-DEQAS) and are certified (ACP) for this particular analysis. Such variability confounds attempts to define a single "cut point" value set to be indicative of low vitamin D status. Some of the labs use ng/mL units to report results while others use nmol/L Multiply ng/mL by 2.5 to convert it to nmol/L or divide nmol/L by 2.5 to get into ng/mL.

4.1. Recommended 25(OH)D level

Keeping in mind the evidence on both extra-renal and renal activity of CYP27B1 as well as on skeletal and pleiotropic action of vitamin D and numerous health benefits related to proper vitamin D supply [10–12], the recommended 25(OH)D level, that should be obtained and maintained in general population of otherwise healthy Emiratis' of all ages, is at least 30 ng/mL and 60 ng/mL.

4.2. Revision of RDA

Recommended Daily Allowance values for vitamin D and calcium intake should be revised.

4.3. Educational programs

There is a great need for awareness among physicians and the general public at large regarding vitamin D health implications. Vitamin D deficiency is prevalent worldwide and particularly predominant in the UAE. It is the most under-diagnosed and under-treated, but easily treatable disease. In fact, vitamin D deficiency is often misdiagnosed. Adequate investment and effort are much needed to develop, launch and sustain public awareness programs in the UAE and Middle-Eastern countries. The curricula of medical colleges need to be updated pertaining vitamin D status, nutrition, and bone metabolism of the general population. Inclusion of pertinent and updated information pertaining to vitamin D, and its skeletal and extra skeletal benefits is required.

Table 3
Recommendations to alleviate high prevalence of vitamin D deficiency.

Item	Recommendation
1	Educators should teach the need for vitamin D sufficiency and benefits of a healthy lifestyle.
2	Mandatory distribution of vitamin D fortified foods at midday meals in schools is an important suggestion that might help in reducing D-deficiency. Eliminating high-caloric (fructose-containing) soft drinks and cheap, unhealthy food from school cafeterias and menus is necessary.
3	Mandate, daily outdoor physical activities in schools.
4	Make available, affordable and widely accessible vitamin D testing facilities to all who are at high risk of clinical vitamin D deficiency.
5	A reliable, cost-effective, and sensitive technology such as DXA should be made available at minimal cost for screening bone mineral density and body composition in individuals at high risk, throughout the UAE.
6	Government as well as the private sector should extend support for research, so that the impact of supplementation programs and fortification strategies in actual practice may be studied and monitored and more efficacious ways are developed.
7	Nationwide, surveys are to be commenced to identify and document nutritional status including vitamin D of UAE residents.
8	Continued research and epidemiological studies are needed to demonstrate the status of vitamin D deficiency and its implications on general health of UAE nationals, and residents countrywide, that can be sued for policy making for the country. Deficiency and 'desirable' 25(OH)D serum levels.

Table 4
Recommended safety upper limits of vitamin D for various groups.

Specific group of people	Recommended Upper Limit for vitamin D supplementation
Neonates and infants	1000 IU/day (25 μg/day)
For children aged 1–10 years,	2000 IU/day (50 μg//day)
Children and adolescents aged 11–18 years	4000 IU/day (100 μg/day)
Adults and the elderly with normal body weight	4000 IU/day (100 μg/day)
Obese adults and obese elderly people	10,000 IU/day (250 μg/day)
both pregnant and breastfeeding women	4000 IU/day (100 μg/day)
Institutionalized people	5000 IU/day (125 μg/day)

Making bone and mineral health a priority: All healthcare facilities, including all primary health care facilities should institute awareness programs to educate the local residents about the need for vitamin D sufficiency. Active participation of social organizations. Social workers, healthcare workers, and school teachers need to be informed and educated with regards to basic nutrition including requirement of nutrition and physical activities. This educational effort would allow spreading the word about the needs for vitamin D sufficiency and the means to achieve it.

Government sponsored mass media programs, with the aid of tele-media and print media are required to educate the masses about the grim vitamin D deficiency status in the UAE and the GULF countries. The masses should be educated on the benefits of a combination of sun exposure, vitamin D fortified food items, supplements and regular physical exercise.

A need for sufficient calcium intake along with vitamin D must be emphasized.

4.4. Vitamin D supplements

Since food is not a rich source of vitamin D, affordable, good quality and readily available vitamin D supplements for the masses are needed [28]. Vitamin D supplements should be made available at all primary care health centers to children, pregnant women and lactating women. Exclusively breastfed newborns and exclusively breastfed infants as well as adolescents are at high risk of vitamin D deficiency, therefore, these risk groups require special attention and implementation of vitamin D deficiency prevention strategies. In the UAE now more than 2 dozen brands of vitamin D are available as supplements (personal survey conducted by Prof. Afrozul Haq in February 2016).

These supplements are from various manufacturers of Europe, USA, Switzerland and UAE in the form of injections, tablets and capsules with varying potency. Recently, there is introduction of an exciting supplemental vitamin D in the solution form (Colemed 50,000 IU/mL) which is already in use at the National Health Services (NHS), UK. This product is currently launched in the UAE with the name Colemed from MYMED Pharma Ltd, Birmingham Science Park, England, UK. Colemed 50,000 IU/mL is the only solution form of high potency to treat vitamin D deficiency and healthcare professionals around UAE and Saudi Arabia have shown great interest in this product.

4.5. Fortification of foods with vitamin D

Expansion of the efforts invested by different organizations such as VPS Healthcare in the importance of vitamin D deficiency should be considered. This includes educating children and school-teachers, conducting annual International conferences in the UAE where leaders in the field of vitamin D research are invited. This effort needs to be extended to food fortification and other nutritional supplemental programs [29].

Food industry should be encouraged to develop private-public partnerships operating at local and the national level. Support in terms of technical expertise pertaining to the production of fortified food items, availability of standardized vitamin D formulation(s) and information on the marketing potential of the fortified items should be made available.

Effective legislation to ensure safety, good quality and regulated vitamin D fortified foods at minimal or no increase of cost to the consumer is required. Implementing policies for fortification is very important and selecting the right food items to be fortified is of utmost relevance because of differences in food preferences based on ethnicity and culture. Interventions needed to benefit school children. Table 3 illustrates the recommended public health interventions to alleviate high prevalence of vitamin D deficiency in UAE and GULF countries.

There is no consensus on optimal levels of 25-hydroxyvitamin D, although experts define deficiency as levels of <20 ng/mL (50 nmol/L). Using these levels, one billion people worldwide have vitamin D deficiency [4]. Vitamin D intoxication is defined as 25 (OH) D levels >375 nmol/L). This rare and only found in individuals taking in excess of 40,000 IU per day for a prolonged period [5,6].

4.6. Adverse effects of vitamin D

Table 4 illustrates the Tolerable Upper Intake Levels (ULs) of vitamin D for population groups in UAE and GCC/GULF countries. This encompass the highest average daily vitamin D intakes that likely to pose no risk of adverse effects.

Vitamin D toxicity is very rare and should not be diagnosed solely on the basis of an elevated 25(OH)D level; instead, it should be recognized as a clinical syndrome in the presence of hypercalcemia, suppressed PTH, hypercalciuria and markedly elevated serum 25(OH)D levels (>150 ng/mL). This syndrome is commonly associated with hyperphosphatemia. The main manifestation of vitamin D toxicity is the clinical signs and symptoms of hypercalcemia (e.g., nausea, dehydration, and constipation) and hypercalciuria (e.g., polyuria and kidney stones).

Hypervitaminosis D in the absence of hypercalcemia may prompt further investigation to evaluate the etiology of increased vitamin D levels; however, unlike hypercalcemia, it is not a medical emergency. Once observed, in either case, it is important to stop all vitamin D and supplements. It may be appropriate to stop multivitamins as may have vitamin A and is likely to enhance to the negative effects of hypercalcemia. Most patients with vitamin D toxicity have levels greater than 150 ng/mL.

Multiple reports indicate that vitamin D supplementation with 1600 IU/d or 50,000 IU monthly was not associated with laboratory parameters of toxicity [such as, 25(OH)D, PTH, bone alkaline phosphatase, and 24-h urine calcium] and even failed to increase total 25(OH)D levels above 30 ng/mL in 19% of participants, confirming its safety [28–31]. In a recent study of 11 cases of hypervitaminosis D who developed symptoms of hypercalcemia due to excess intake of vitamin D supplements in the form of high dose (600,000 IU injectable) for back pains, osteoarthritis, osteoporosis, diabetes, for several weeks. It is concluded that before prescribing vitamin D supplements, we should properly

look into the background history of the patient along with biochemical parameters to know the status of vitamin D so that toxicity is prevented [32].

5. Conclusion

In conclusion, the health authorities within the UAE have started serious action towards improving health among the population. To this extent, numerous awareness programs had been initiated to address the problem of vitamin D deficiency as a major public health burden. The effort should now focus on releasing specific vitamin D guidelines for the population within the country and implementing new policies for food fortification. All healthcare facilities, including primary health care centers should institute awareness programs to educate the physicians and the local residents about the need for vitamin D sufficiency.

Frequency of ordering the test for 25(OH)D should be limited to baseline, the pretreatment screening. Subsequent measurements should not be performed prior to 8 weeks from the start of high-dose oral vitamin D supplementation, or 4–6 months after supplementation with the standard doses of vitamin D. The masses should be educated on the benefits of a combination of sun exposure, vitamin D fortified food items, supplements and regular physical exercise. A need for sufficient calcium intake along with vitamin D must be stressed at all times. Affordable, good quality and readily available vitamin D supplements for the masses are needed. Vitamin D supplements should be made available at all primary care health centers to pregnant women, lactating women and for all age group patients at risk of vitamin D deficiency.

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