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ORIGINAL PAPER

Vitamin D Deficiency in the Middle East and its Health Consequences for Children and Adults

Ghada El-Hajj Fuleihan

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Abstract Despite its abundant sunshine the Middle East, a region spanning latitudes from 12°N to 42°N allowing vitamin D synthesis year round, registers some of the lowest levels of vitamin D and the highest rates of hypovitaminosis D worldwide. This major public health problem affects individuals across all life stages including pregnant women, neonates, infants, children and adolescents, adults, and the elderly. Furthermore, while rickets is almost eradicated from developed countries, it is still reported in several countries in the Middle East. These observations can be explained by limited sun exposure due to cultural practices, dark skin color, and very hot climate in several countries in the gulf area, along with prolonged breast feeding without vitamin D supplementation, decreased calcium content of diets and outdoor activity, obesity, and lack of government regulation for vitamin D fortification of food, in several if not in all countries. The lack of population based studies renders estimates for the prevalence and incidence of rickets in the Middle East difficult, but several series from the region illustrate its dire consequences on growth and development. Furthermore, it is reported that 20–80% of apparently healthy individuals from several countries in this region have suboptimal vitamin D levels, depending on the cut-off used for defining hypovitaminosis D, the country, season, age group, and gender studied. Suboptimal levels have been associated with compromised skeletal health across age groups, and with poor muscular function and increased fall risk and osteoporotic fractures in the elderly. Studies detailing associations between low vitamin D levels and musculoskeletal health in the Middle East, and the impact of various treatment regimens are reviewed. Current recommendations for vitamin D derived from data in western subjects may not be sufficient for subjects from the Middle East, therefore suggestions for vitamin D replacement doses based on evidence available to-date are provided. Hypovitaminosis D is a major public health problem across all life stages in the Middle East with deleterious immediate and latent manifestations. Long term strategies to address this often silent disease should include public education, national health policies for screening and prevention through food fortification, and treatment through vitamin D supplementation.

Keywords Rickets · Hypovitaminosis D · Middle East · Calcium · Nutrition · Neonates · Infancy · Adolescence · Elderly · Culture · Socioeconomic · Veiling

G. El-Hajj Fuleihan (✉)
Calcium Metabolism and Osteoporosis Program, American University of Beirut, Beirut, Lebanon
e-mail: gf01@aub.edu.lb

Introduction

The Middle East region is a sub-continent that does not have precisely defined borders, and definitions vary from one source to the other. Traditionally the Middle East region includes western Asia and some parts of North Africa (Fig. 1). A commonly used modern definition includes the following countries: Bahrain, Egypt with its Sinai Peninsula in Asia, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, the United Arab Emirates, and Yemen [1, 2]. The Middle East has a hot and arid climate and the latitudes it spans, from 12° to 42°N, allow vitamin D synthesis from ultraviolet B (UVB) rays for almost all months of the year, for more than 8 h a day [3].

While rickets is almost eradicated in western northern developed countries, excluding Asian immigrants, the

Fig. 1 Middle East in the context of major continents and regions. Definition of Middle Eastern countries varies; countries discussed in the chapter are labeled above. Countries considered in the chapter include: Bahrain, Egypt with its Sinai Peninsula in Asia, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, the United Arab Emirates, and Yemen

Middle East is a region that registers some of the highest rates of rickets worldwide. This is in large part explained by limited sun exposure, cultural practices, and by dark skin color and low calcium intake rather than vitamin D deficiency in several countries in Africa [4]. In addition, hypovitaminosis D, the latency disease of osteoporosis, constitutes a major public health problem in this region. Low vitamin D levels have also been associated with autoimmune disorders, certain cancers, and with the metabolic syndrome and type 2 diabetes, for which some of the highest rates reported arise from the Middle East. Despite the skin ability to synthesize vitamin D from exposure to UVB rays throughout the year, both rickets and hypovitaminosis D are more prevalent across all age groups in this region compared to the western populations.

Rickets, a symptomatic disease with overt clinical consequences, and hypovitaminosis D, a subclinical disorder with subtle and latent outcomes, will be discussed separately. Relevant articles were identified by performing a PubMed search entering the key terms rickets and Middle East, and a separate search was performed entering the key terms hypovitaminosis D and Middle East. Both searches had no restrictions on date, language, gender, or type of article. Another search was conducted by entering the individual names of the countries of interest detailed above with the terms rickets or hypovitaminosis D. The abstracts of all identified articles were screened. Studies that could be retrieved and that discussed the presentation and manifestations of rickets, risk factors for its development, or the prevalence and presentations of hypovitaminosis D and its clinical consequences were included. Osteomalacia results from severe hypovitaminosis D in adults and presents with isolated or generalized skeletal pain. Case reports illustrate that this condition still exists in the Middle East, but the magnitude of the problem is unclear. Indeed, unless specifically searched for, it can be misdiagnosed as fibromyalgia, chronic fatigue syndrome, or depression, and therefore it is not discussed as a separate entity. The origin of many affected kindreds with vitamin D dependant rickets type II, an autosomal recessive familial disorder with the unusual feature of alopecia, is concentrated in the Mediterranean region. However, studies reporting non-nutritional rickets, including vitamin D dependant rickets type II, were excluded [5]. Additional articles were obtained from the author's library or from the reference list of the search identified articles.

Nutritional Rickets

Nutritional rickets is a disease resulting from impaired bone mineralization due to insufficient calcium or phosphorus at the growth plate in growing children. It ranks as one of the five commonest diseases in children from developing countries and is still quite common in the Middle East [4, 6]. Although nutritional rickets in infants had been traditionally thought to be exclusively secondary to vitamin D deficiency, increasing evidence over the last several years points to a pivotal role of calcium deficiency in its pathogenesis as evidenced from studies conducted in older children from South Africa, Nigeria, and Egypt [4, 7]. Thus, nutritional rickets can be the result of severe nutritional deficiencies in calcium or vitamin D, or even as likely if not more likely a combination of less severe deficiencies in both [4, 8]. However, the relative contribution of deficiency in either calcium or vitamin D to the disease has not been adequately investigated, and is only reported in limited studies from certain countries.

Nutritional Rickets in the Middle East

The prevalence of nutritional rickets in the Middle East is not known due to the lack of population based figures. The prevalence of rickets was estimated at 27% in a sample group of 197 children under 5 years of age attending a health center in a rural area in North Yemen [9]. Similarly, population-based incidence rates for rickets are lacking, however, annual incidence rates derived from selected studies report a rate of 10% in an older field survey conducted in a maternity and child welfare center of a rural community of 6000 inhabitants in Egypt [10], of 1% between 1981 and 1986 in a study of Kuweiti children less than 2 years of age [11], of 0.5% between 1997 and 1999 in a study of Saudi infants less than 2 years [12], and of less than 0.1% in 2007–2008 (down from 6%) in children 0–3 years from Turkey due to a national vitamin D campaign [13]. These figures, albeit based on selected samples of children, are nevertheless at least 100 folds higher than the reported annual incidence rates of 3–7.5 cases/100,000 children in western developed countries [14]. Furthermore, rickets accounts for a substantial number of pediatric hospital admissions in the region. A report of 500 cases of rickets admitted at the Suleimania hospital in Riyadh between 1986 and 1988, estimated that the diagnosis accounted for 1.8% of all hospital admissions for that period [15], it was estimated at 1% in a hospital based study conducted in Saudi Arabia [16], and at 6.5% in a similar study of newborns from Kuwait [17]. Rickets accounted for 10.6% of all admissions for infants presenting with an acute illness to a hospital in Jordan [18]. Limited sun exposure due to cultural practices, dress styles, limited time spent out-doors, and prolonged breast feeding without vitamin D supplementation account in large part for the persistence of rickets in the Middle East despite its plentiful sunshine [4, 6], as detailed below. This is probably more relevant in infants, whereas the pathophysiology is likely to be mixed in older children with variable contributions of concomitant low calcium intake. Finally, genetic factors such as possible resistance to vitamin D and polymorphisms in the vitamin D receptor (VDR) may modify the clinical manifestations of nutritional rickets [7]. In a recent study of 98 rachitic children from Egypt and Turkey, increased frequency of the F (Fok1) VDR allele was noted in patients from Turkey, and the BB (Bsm) polymorphism was associated with a lower vitamin D in patients and controls and with the severity of rickets [7]. Maternal vitamin D deficiency during pregnancy is an established risk factor for rickets presenting neonatally or in early infancy [13, 17, 19, 20].

Turkey

Turkey, specially its Eastern part, had been accepted as an endemic region for vitamin D deficiency rickets, with substantial improvement due to a national vitamin D campaign on most recent estimates [13]. A small retrospective study of 42 infants less than 3 months of age presenting with seizures, and a mean 25-hydroxy vitamin D [25(OH)D] of less than 15 ng/ml, identified exclusive breast feeding, low maternal sun exposure, and concealed maternal clothing as risk factors for vitamin D deficiency in these infants [21]. They presented mostly in winter and spring, and lacked the classical skeletal manifestations of rickets. Two additional studies revealed a similar risk profile. A survey conducted on 39,133 children aged 0–3 years presenting to outpatient clinics in Erzurum between March 2007 and Feb 2008, revealed that the 39 infants presenting with nutritional rickets, at a mean age of 10 months, and with a mean 25(OH)D level of 6 ng/ml, were more likely to come from larger families, of lower socioeconomic and educational level, and that both infants and their mothers spent less time outdoors and were less likely to take vitamin D supplementation compared to controls [13]. Similarly, a recent study of 68 rachitic children, aged 6 months–4 years, revealed that household crowding, lower parental socioeconomic status and educational level, suboptimal prenatal care, time spent outdoors during pregnancy, exclusive breast feeding of the infant, and lower calcium intake to be risk factors for developing rickets [7].

Iran

In a review of records of 30,000 admissions in a pediatric ward in Shiraz, Iran, between 1958 and 1967, 25 cases were diagnosed with vitamin D deficiency rickets [22]. The majority of cases ($N = 18$) were below age three, and had clinical findings consistent with rickets such as rachitic rosary, pigeon breast deformity, widening of the wrists, Harrison's groove, and lower extremity deformities. All patients had been exclusively breast fed, had not received vitamin D supplementation, belonged to a group with a lower socioeconomic status, suffered from protein–calorie malnutrition, and were below the third percentile for height and weight and presented with an acute infection.

Iraq

In a study of 50 infants presenting with two or more clinical signs of rickets in a children's outpatient department in Mosul, mean age was 18 months, and all children were breast fed, at least for the first 6 months of their life [23]. Clinical signs included delayed closure of the fontanelle, bossing of the head, delayed teething, beading of the ribs or rosary, widening of the wrists and bowing of the legs, and the majority of children suffered from growth failure, few were marasmic and hypoalbuminemic, invalidating the notion that rickets occurs in growing children who are not wasted [23]. Rickets was 2.5 folds more common in infants presenting with wheezy bronchitis compared to controls [24].

Jordan

In a case control study of 47 infants, mean age 8 months, admitted to a hospital with an acute illness and found to have rickets, child family ranking of second or more, large family size, breast feeding, maternal clothing type (wearing head cover) were risk factors associated with rickets [18].

Saudi Arabia

A total of 102 infants with vitamin D deficiency, half of whom were Saudis, and 30 control subjects were studied in a maternity and children's hospital in Makkah between 1993 and 1994 [25]. Exclusive breast feeding and lower maternal educational status were more likely to be present in patients than controls, and families of patients tended to be larger than those of the controls. Similarly, in a study of 61 infants with rickets, mean age of 16.5 months and mean 25(OH)D of 8 ng/ml, conducted between 2004 and 2005 in a major hospital in Ryadh, breast feeding and limited sun exposure were more common in patients than controls [26]. Rickets was linked to vitamin D deficiency in 59% of adolescents, to poor calcium intake in 12%, and to genetic abnormalities in the remaining proportion (25-hydroxylase deficiency in 8.8%, vitamin D dependant rickets type I in 6%, and hypophosphatemic rickets for 12%) [27]. Conversely, both limited sun exposure and poor calcium intake have been estimated to contribute to rickets in two other studies of children and adolescents, mean age 13 years, $N = 42$ and 21 subjects per study, respectively [28, 29]. In these studies, mean 25(OH)D levels were below 10 ng/ml, and mean calcium intake was below 500 mg in one study [29] and between 100 and 300 mg in the other [28]. In adolescents presenting symptoms were more likely to be exclusively musculoskeletal in nature, including aches and pains, tetany, muscle weakness, and limb deformities [27, 29].

Kuwait

A study reported 75 neonates with rickets presenting with rachitic rosary at birth, thus pointing to the development of rickets due to maternal hypovitaminosis D during pregnancy [17]. The mean 25(OH)D was less than 7 ng/ml, and hypotonia, enlarged fontanelles, and widened cranial sutures were other manifestations of the disease [17]. Breast feeding and poor sun exposure were major risk factors for the development of rickets in 250 infants less than 2 years of age [11]. Similarly, exclusive breast feeding, delayed weaning to solids, nutritional quality of semisolids, and low sun exposure were major risk factors in another study of 103 infants with rickets [30]. At diagnosis these infants were shorter, lighter, and had lower 25(OH)D levels than controls, measured at 10 ng/ml and 33 ng/ml, respectively.

United Arab Emirates

Thirty-eight Emirati children with rickets referred to pediatric clinics of two university hospitals and their mothers were compared to 50 non-rachitic children–mother controls. The patients' mean age was 13 months, serum calcium was 8.88 mg/dl, mean 25(OH)D was 3.2 ng/ml, and serum alkaline phosphatase was 834 IU/l, compared to mean 25(OH)D of 17.2 ng/ml in controls. The majority (92%) were breast feeding, 8% were on supplements, and sunshine exposure was nill [20]. However, in another retrospective study of 31 older children with rickets, mean age less than 3 years, only half had 25(OH)D levels below 10 ng/ml, while calcium deficiency contributed to the development of rickets in the other half [31].

Egypt

Fifty-four successive cases of clinically diagnosed rickets presenting at an outpatient clinic in Cairo, and subsequently confirmed radiologically, were compared to 28 controls [32]. Half had signs of the disease in limbs, skull, and chest, and two-third could not stand. Children mostly presented because of failure to thrive before age 2, and they were lighter and shorter than controls. Whereas mean calcium intake was low, estimated at 300 mg/day, both in patients and controls, patients had a lower mean 25(OH)D level of 3.3 ng/ml compared to 10.1 ng/ml in controls. Similarly, in a more recent study of 30 children with rickets a mixed etiology, namely a low calcium intake <500 mg and sub-optimal 25(OH)D levels in mid-teens, was felt to be responsible for the development of rickets [7].

Non-skeletal Manifestations of Nutritional Rickets

In addition to the classical skeletal manifestations of rickets outlined above, the proportion of patients presenting with convulsions varied from 4 to 79%, depending on the study [11, 13, 15, 18, 21, 25, 33–36]. In addition, the studies detailed above illustrate an association between rickets and infectious conditions, in large part respiratory infections and diarrhea. The admitting diagnosis was recurrent chest infections in 66% of 500 cases of rickets in Saudi Arabia [15]; broncho-pneumonia was present in 43% of 200 rachitic Iranian children [33] and 44% of 250 rachitic children from Kuwait [11]. Similarly, an acute infection or respiratory diseases were the presenting manifestation in 20–60% of cases presenting with rickets in smaller studies from Turkey, Egypt, Jordan, and Saudi Arabia [13, 18, 22, 25, 37, 38]. Gastroenteritis accounted for 8–56% of reasons for admission [11, 18, 32, 33].

Dilated cardiomyopathy secondary to hypocalcemia is an unusual manifestation of nutritional rickets [39], 16 such cases were reported from a Children's hospital in London, all were from dark-skinned ethnic minorities, 12/16 were exclusively breast fed, and presented at the end of winter. Dilated cardiomyopathy, as a manifestation of vitamin D deficiency rickets, has been reported in three infants from the Middle East, one from Turkey and two from the United Arab Emirates [40, 41]. All three infants presented with heart failure, had florid skeletal signs of rickets, and had hypocalcemia with 25(OH)D levels below 8 ng/ml. They all experienced rapid clinical improvement within a week of instituting therapy with inotropes, diuretics, in addition to calcium and vitamin D, and had resolution of their cardiomegaly and radiologic healing of rickets within few weeks of therapy initiation. The two infants from the United Arab Emirates were exclusively breast fed, did not receive vitamin D supplementation, had little sun exposure, and their mothers both had 25(OH)D levels of <8 ng/ml [41].

Rickets in Immigrants from Middle East

Several studies have reported high rates of rickets in immigrants from the Middle East to western countries. In a study of 126 patients with rickets or vitamin D deficiency in Australia, 11% originated from the Middle East [42]. Similarly in a study of 41 adolescents diagnosed with rickets in France, 33/41 (80%) were immigrants, of those 15 were from South Africa, 10 from North Africa, 6 from Pakistan, and 2 from Turkey [43].

Hypovitaminosis D

Hypovitaminosis D is a subclinical condition with latent manifestations. There is no consensus on optimal levels of 25(OH)D, but it has recently been re-defined by most experts by a cut-off of less than 20 ng/ml, for both children and adults [14, 44–46]. In recent publications it is often defined as vitamin D insufficiency when the level falls between 10 and 20 ng/ml, and as vitamin D deficiency when the level falls below 10 ng/ml [45]. However, some of the studies detailed below had predated such definitions and have used variable cut-offs (Tables 1, 2, and 3).

Mothers–Neonates–Infants

Neonates born to mothers with low vitamin D levels have lower cord vitamin D levels, and may be at the risk for rickets and other complications [14]. Studies from the region revealed a high prevalence of hypovitaminosis D in pregnant mothers and their neonates (Table 1).

A study of eight Beduin women and 41 Jewish Shepardi women from the Negev Desert, revealed a mean 25(OHD) level of 7.8 ng/ml in the Beduin, and of 3.2 ng/ml in the cord blood of their offsprings, compared with a mean 25(OH)D level of 25 ng/ml in the control mothers and of 12 ng/ml in the cord blood of their neonates [47]. Venous blood obtained from 100 consecutive and unselected Saudi Arabian mothers and their asymptomatic neonates, within 48 h of delivery, revealed that 59 mothers and 70 neonates had 25(OH)D levels below 10 ng/ml, along with asymptomatic hypocalcemia [19]. Similarly, a study of 90 Arab and South Asian mothers and their breast fed infants at 6 weeks, revealed that 61% of mothers and 80% of the offspring had 25(OH)D below 10 ng/ml [48]. The same authors studied a convenient sample of 50 infants admitted at 15 months to the hospital and their mothers and demonstrated that 50% of mothers and 22% of children had 25(OH)D levels below 10 ng/ml [49]. Over two-third were still breast feeding and 40% did not receive vitamin D supplements. In a study of 119 pregnant womans and their newborns from Saudi Arabia, the median 25(OH)D concentration in mothers was 5.7 ng/ml, 50 cord samples had undetectable vitamin D levels, and it was below 4 ng/ml in another 81 cord specimens. Higher socioeconomic status, antenatal care, and vitamin D intake were associated with higher maternal vitamin D levels [50]. A cohort study of 48 Iranian pregnant women revealed that 20% had 25(OH)D levels below 10 ng/ml and 40% had levels below 20 ng/ml [51]. Fifty mothers and their term babies were studied at delivery in Tehran, 80% of the mothers had 25(OH)D below 10 ng/ml, mean cord serum levels were 2 ng/ml [52]; but there was no effect of maternal vitamin D levels on birth weight after adjusting for maternal height, age, and parity.

Table 1 Prevalence of hypovitaminosis D by country in pregnant women and neonates in the Middle East

Author	Year	Country–city	Latitude	*N*	Gender	Age (years) Mean ± SD or range	25(OH)D Mean ± SD (ng/ml)	25(OH)D Cut-off values (ng/ml)	Predictors	Comments
Serenius	1984	Saudi Arabia–Riyadh	24°N	119	Women at term and their neonates	NA	*Median* All: 5.7	*Undetected levels* Mothers: 9% Cord blood: 42% *% <4* Mothers: 16% Cord blood: 26%	High SES[a] Antenatal care Vitamin D supplement	Survey, 75% of subjects selected randomly from hospital
Bassir	2001	Iran–Tehran	35°N	50	Women at term and their neonates	16–40 years	Mothers: 5.1 ± 10.4 Newborns: 2 ± 3.8	*% <10–12* Mothers: 80% Newborns: 82%	Sun exposure	Pilot study, convenience sample from hospital
Molla	2005	Kuwait–Kuwait City	29°N	214	Women at term and their neonates	27.5 ± 4.2	Mothers: 14.6 ± 10.7 Newborns: 8.2 ± 6.7	*% <10* Mothers: 38–41% Newborns: 60–70%	Maternal education	Mothers selected from two hospitals
Ainy	2006	Iran–Tehran	35°N	95	Women 48 Pregnant 47 control	26.2 ± 5.0	1st term: 20.6 ± 12 2nd term: 25.7 ± 16.7 3rd term: 24.5 ± 12.8 Control: 23.0 ± 12.9	*% <10–12* 1st term: 20% 2nd term: 10% 3rd term: 3% Control: 15% *% between 10 and 20* 1st term: 40% 2nd term: 38% 3rd term: 44% Control: 25%	Pregnancy trimester	Cohort study, randomly selected from care centers

[a] *SES* Socioeconomic status, *NA* Data not available

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Table 2 Prevalence of hypovitaminosis D by country in children and adolescents in the Middle East

Author	Year	Country–city	Latitude	*N*	Gender	Age (years) Mean ± SD or range	25(OH)D Mean ± SD (ng/ml)		25(OH)D Cut-off values (ng/ml)		Predictors	Comments
El-Hajj Fuleihan	2001	Lebanon–Beirut	33°N	346	Spring: 81 Boys 88 Girls Fall: 83 Boys 94 Girls	Spring: 13.3 ± 1.6 Fall: 13.3 ± 1.7	Spring: Boys: Girls: All: Fall: Boys: Girls: All:	 19 ± 7 15 ± 8 17 ± 8 24 ± 6 19 ± 7 22 ± 7	*% <10–12* Spring: Boys: 9% Girls: 32% All: 21% *% between 10 and 20* Spring: Boys: 46% Girls: 42% All: 44%	 Fall: Boys: 0% Girls: 8% All: 4% Fall: Boys: 25% Girls: 46% All: 36%	Gender Season SES[a] Clothing	Children selected from three schools of different SES[a]
Bahijri	2001	Saudi Arabia–Jeddah	21°N	935	NA	4–72 months	4–6 months: 6–12 months: 12–24 months: 24–36 months: 36–72 months:	26.2 ± 14.1 24.9 ± 14.1 24.6 ± 14 26.7 ± 11.3 24.2 ± 11.5	*% between 5 and 10* 4–6 months : 14% 6–12 months: 13% 12–24 months: 14% 24–36 months: 4% 36–72 months: 8%		Episodes of diarrhea Dietary intake of vitamin D Sun exposure	Random selection covering all districts and all SES[a]
Moussavi	2005	Iran–Isfahan	32°N	318	153 Boys 165 Girls	14–18	Boys: Girls:	37.3 ± 18.8 16.8 ± 8.4	*% <20* Boys: 18% Girls: 72%		Gender Sun exposure	Cross-sectional, multistage random selection from schools
Dahifar	2006	Iran–Tehran	35°N	414	Girls	11–15	All:	30	*% <10–12* All: 3.6%		Calcium intake Sun exposure	Cross-sectional, random selection from schools
El-Hajj Fuleihan	2006	Lebanon–Beirut	33°N	363	184 Boys 179 Girls	10–17	All:	16 ± 9	*% <10–12* Boys: 12% Girls: 33% *% between 10 and 20* Boys: 66% Girls: 51%		Gender Winter	Convenience sample, from four schools, balanced geographical and socioeconomic presentation

Table 2 continued

Author	Year	Country–city	Latitude	N	Gender	Age (years) Mean ± SD or range	25(OH)D Mean ± SD (ng/ml)	25(OH)D Cut-off values (ng/ml)	Predictors	Comments
Siddiqui	2007	Saudi Arabia–Jeddah	21°N	433	Girls	12–15	NA	*% <10–12* All: 81%	Family income Sun exposure Intake of dairy products	Randomly selected from different schools
Rabbani	2008	Iran–Tehran	35°N	963	424 Boys 539 Girls	7–18	Boys: 21.6 Girls: 18.4	*% <20* Boys: 11% Girls: 54% *% <8* Boys: 0.9% Girls: 11%	Gender, age in girls	Random cluster sampling

[a] *SES* Socioeconomic status, *NA* Data not available

Conversely, in a more recent study from Tehran, 449 apparently healthy women and their newborns were studied at the time of delivery [53]. Only one-third of women had adequate calcium and vitamin D intakes as determined by the Institute of Medicine [54]. Mean length at birth and 1 min Apgar scores in the neonates correlated with maternal calcium and vitamin D intake, and neonates of mothers with adequate calcium and vitamin D intake were 0.9 cm taller and had a higher Apgar at birth than those who consumed sub-optimal levels [53].

Several studies from the Middle East report that 10–60% of mothers and 40–80% of their apparently asymptomatic neonates have undetectable to low vitamin D levels (0–10 ng/ml) at delivery [18, 47, 48, 50–52, 55]. Socio-economic status, educational level, antenatal care, and sun exposure were predictors of vitamin D levels.

Children and Adolescents

Hypovitaminosis D does not spare the pediatric age (Table 2) [14, 46]. A large proportion of adolescent girls, up to 70% in Iran [56] and 80% in Saudi Arabia [57] have 25(OH)D levels below 10 ng/ml. The proportions reported were lower, measured at 32% in Lebanese girls and, between 9 and 12% in Lebanese adolescent boys [58, 59]. In a study of a random sample of 433 Saudi girls, ages 12–15 years, 81% had 25(OH)D levels below 10 ng/ml and 61% had no symptoms or rickets [57]. Similarly, a study of 318 adolescent Iranians reported that 25(OH)D levels were below 20 ng/ml in 46% of students, and in 72% in girls and 18% of boys [56]. The most recent cross-sectional, random sampling survey of 963 students from Tehran, ages 7–18 years, revealed that the 25(OH)D level was below 20 ng/ml in 54% of girls (all of whom were veiled) and in 11% of boys (see Table 2 for mean levels) [60]. In contrast, the mean 25(OH)D level was higher, calculated at 30 ng/ml in another study of 414 Iranian girls [61], only a subset of whom ($N = 15$, 3.63%) had low 25(OH)D levels and hypocalcemia, unexpected findings in view of a reported mean vitamin D intake of 119 IU/day and sun exposure of 10 min/day [61]. A cross-sectional study of apparently healthy 458 Qatari children revealed a mean 25(OH)D of 13.4 ng/ml, and vitamin D deficiency (defined as a 25(OH)D level less than 30 ng/ml) was reported in 315 of the children (68%); the highest proportions recorded were in adolescents, and the lowest were in children below age 5 years [62]. Fractures, delayed milestones, rickets, and gastroenteritis were more common in vitamin D deficient children than in control subjects [62]. The mean 25(OH)D (±SD) level in 346 adolescent Lebanese children was 17(8) ng/ml at the end of winter and 22(7) ng/ml at the end of summer [58]. Girls had lower sun exposure than boys, 9% of boys and 32% of girls had a level below 10 ng/ml,

Table 3 Prevalence of hypovitaminosis D by country in adults in the Middle East

Author	Year	Country–city	Latitude	*N*	Gender	Age (years) Mean ± SD or range	25(OH)D Mean ± SD (ng/ml)		25(OH)D Cut-off values (ng/ml)	Predictors	Comments
El-Sonbaty	1996	Kuwait–Kuwait City	21°N	72	Women: 50 veiled 22 non-veiled	14–45	Veiled: Non-veiled:	5.8 ± 2 12 ± 3.3	*% <8* Veiled: 86%	Veiling	Case control study, convenience sampling
El-Hajj Fuleihan	1999	Lebanon–Beirut	33°N	465	Women	15–60	All:	11 ± 14	*% <10–12* All: 60% *% between 10 and 20* All: 35%	Veiling	Random sample from a village in central Lebanon
Ghannam	1999	Saudi Arabia–Riyadh	24°N	321	Women	10–50	All:	10 ± 8	*% <10–12* All: 52%	Lactation Parity	Convenience sampling through advertisements
Alagol	2000	Turkey–Istanbul	41°N	48	Premenopausal women	26 ± 8	By dress style: Western: Partial cover: Full cover:	 22 ± 16 13 ± 10 4 ± 2	*% <16* By dress style: Western: 44% Partial cover: 60% Full cover: 100%	Dress style	Convenience sampling
Gannage	2000	Lebanon–Beirut	33°N	310	99 men 217 women	30–50	Men: Women: All:	14.3 ± 7.5 7.6 ± 5.8 9.7 ± 7.1	*% <12* Men: 48% Women: 84% *% <5* Men: 41% Veiled: 62%	Vitamin D intake Urban dwelling Veiling High parity	Convenience sampling, from different rural and urban centers
Mishal	2001	Jordan–Amman	31°N	146	22 men 124 women	18–45	Summer: Men: Women by dress style: Western: Hijab[a]: Niqab[b]: Winter: Men: Women by dress style: Western: Hijab[a]: Niqab[b]:	 43.8 ± 5.2 36.7 ± 6.1 28.3 ± 4.5 24.3 ± 5.8 34.7 ± 4.2 30.9 ± 4.6 24.4 ± 3.9 22.7 ± 3.0	*% <12* Summer: Men: 18% Women by dress style: Western: 31% Hijab[a]: 55% Niqab[b]: 83% Winter: Men: 46% Women by dress style: Western: 75% Hijab[a]: 77% Niqab[b]: 82%	Dress style Winter	Convenience sampling

Table 3 continued

Author	Year	Country–city	Latitude	*N*	Gender	Age (years) Mean ± SD or range	25(OH)D Mean ± SD (ng/ml)	25(OH)D Cut-off values (ng/ml)	Predictors	Comments
Mirsaeid	2004	Iran–Tehran	35°N	1172	682 men 490 women	3–69	Men: 35 ± 26 Women: 21 ± 22	*% <20* Men: 35% Women: 9.6	Season	Cluster random sample
Atli	2005	Turkey–Ankara	40°N	420	Elderly: 111 men 309 women	NA	NA	*% <15* Women in old-age home: 54% Women in own home: 18% Men old-age home: 18% Men own home: 4%	Age, UV[c] light index	Cross-sectional
Hashemipour	2006	Iran–Tehran	35°N	1210	495 men 715 men	20–69	All: 13 ± 16.5	*% <5* All: 9% *% between 5–10* All: 56%	Gender Season	Randomized clustered sampling from the Tehran population
Saadi	2006	UAE–Al Ain	24°N	259	Women	20–85	All: 10.1 ± 4.3	*% <8* Premenopausal: 39%	Season (low in summer due to avoidance of heat)	Subjects recruited through advertisements
Arabi	2006	Lebanon–Beirut	33°N	443	157 men 286 men	65–85	*Median* 11.3 Men: Women: 9.6	*% <10–12* Men: 37% Women: 56% *% between 10 and 20* Men: 57% Women: 39%	Gender	Randomly recruited based on geographical maps
Hosseinpanah	2008	Iran–Tehran	35°N	245	Postmenopausal women	40–80	All: 29.2 ± 24.9	*% <10–12* All: 5% *% between 10 and 20* All: 38%	Menopause	Cross-sectional, random sampling

[a] Hijab: Covering dress sparing face and hands

[b] Niqab: Totally covering dress

[c] UV: Ultraviolet

NA Data not available

whereas 42% of girls and 46% of boys had levels between 10 and 20 ng/ml at the end of winter, with lower proportions at the end of summer [58]. The corresponding numbers for adolescents from the NHANES III study were 1–5% [63].

Diarrhea and maternal vitamin D status were risk factors for low vitamin D levels in infants [49, 64]. Gender, physical activity, clothing style, season, and socioeconomic status were independent risk factors for low 25(OH)D levels in older children (Table 2) [56–58, 61, 62]. Several of these risk factors were also predictors for vitamin D and calcium intake [65]. Indeed, although mean estimated calcium intake varied between studies, the mean intake was below the RDA recommendation for age in most studies when assessed.

Adults

In adults, comparable results were observed (Table 3). One of the first studies conducted on apparently healthy adults from the region evaluated a small sample of university students and elderly from Saudi Arabia, and revealed a mean 25(OH)D level ranging between 4 and 12 ng/ml [66]. In a study of 316 Lebanese adult volunteers, mean 25(OH)D (SD) level was 10(7) ng/ml, levels below 12 ng/ml were noted in 72% of the group, and the proportions were 84% in women and 48% in men [67]. In a sample of 465 adult Lebanese women of reproductive age, with conservative dress style, the mean 25(OH)D level in the summer was 11 ng/ml, and 65% had a level below 10 ng/ml, 35% had levels between 10–20 ng/ml [68]; the mean vitamin D level was almost identical in a sample of 321 mostly in premenopausal Saudi women [69]. The proportions for the same cut-off values in age-matched American women from the NHANES study were 12% and 82%, respectively [70]. In a study of 126 young adult Jordanians, 60% had 25(OH)D levels below 12 ng/ml, the proportions being 72% in the winter and 50% in the summer [71]. In a sample of 245 postmenopausal Iranian women, mean age 57 years, 5% had 25(OH)D levels below 10 ng/ml and 37% had between 10 and 20 ng/ml [72]. However, the proportions were much higher in a random sample of 1200 Iranian men and women, 8% had 25(OH)D levels below 5 ng/ml and 60% had levels below 10 ng/ml [73]. The mean 25(OH)D level was 10 ng/ml in 259 Emirati women, vitamin D levels were lowest, and PTH levels highest in the middle of summer, due to avoidance of going outdoors during the very hot summer season [74]. In a sample of 453 elderly Lebanese, age 73 years, mean 25(OH)D level was 10 ng/ml, 37% of men and 56% of women had levels below 10 ng/ml; the proportions from a sample of similarly aged subjects from Turkey with a mean 25(OH)D below 15 ng/ml were between 28–54% for women and 4–18% for men, depending on their living environment (old age home versus own home) (Table) [75, 76]. Similarly, it has been reported that up to 35% of elderly people in Israel have vitamin D deficiency or insufficiency, another subgroup of the population identified to be at higher risk were Ultra-Orthodox Jewish women, due to their conservative dress code [77].

The mean 25(OH)D level was low averaging 10 ng/ml in studies conducted in Lebanese, Saudi, Emirati, and Iranian women [67–69, 74], with a similar mean in elderly Lebanese [75]. The proportion of subjects with vitamin D levels below specific cut-offs varied between 60 and 65% for a vitamin D level of <10 ng/ml in Lebanon, Jordan, and Iran [68, 71, 72]. In the elderly Lebanese, 37% of men and 56% of women had vitamin D levels below 10 ng/ml [75]; the corresponding proportions were 8% for men and 14% for elderly subjects participating in the Longitudinal Aging Study Amsterdam [78]. Inadequate vitamin D intake, urban dwelling, female gender, conservative clothing style with a cover, season, age, and high parity were independent predictors of low vitamin D levels (Table 3) [67, 71, 73, 74, 79–81]. Other high risk subgroups are patients with specific diseases. In an international epidemiological investigation of women with osteoporosis, the highest proportion of hypovitaminosis D was noted in the Middle East [82]. Of 360 consecutive Qatari patients, mostly women, attending an outpatient rheumatology clinic, 56% had a mean 25(OH)D level below 20 ng/ml [83]. In a survey of 338 elderly admitted to a geriatric hospital in Tel Aviv Israel, with a mean 25(OH)D level of 13 ng/ml, 35% had a level below 10 ng/ml [84], compared to 22% for the same cut-off in a group of 290 elderly patients admitted to a medical ward in Boston [85]. Finally, 80% of elderly with hip fractures in Israel had hypovitaminosis D [77].

Immigrants from Middle East

Immigrants from Asian countries carry a high risk for severe vitamin D deficiency [86, 87]. Serum 25(OH)D was reported to be below 10 ng/ml in 40% of non-western immigrants and to exceed 80% in pregnant women originating from Turkey and Morocco in the Netherlands [88, 89]. In a cross-sectional population-based study of 1000 immigrants living in Oslo, natives of Turkey, Sri Lanka, Iran, Pakistan, and Vietnam, the median levels in Iranian women were 10.8 ng/ml, and 45% had levels below 8 ng/ml; with comparable numbers in women from Turkey [90].

Impact of Hypovitaminosis D on Musculoskeletal Outcomes

Although the two studies relating maternal or neonatal 25(OH)D levels to anthropometric measures of the neonates in the Middle East have yielded conflicting results, several studies worldwide suggest that neonate size, or bone mass may be affected by maternal vitamin D status [14, 91].

The deleterious impact of hypovitaminosis D on musculoskeletal health is unequivocal. It is illustrated in the inverse relationship between levels of 25(OH)D and parathyroid hormone, direct correlations between vitamin D and bone mass as well as muscle mass, and the efficacy of vitamin D in reducing falls and fractures [14, 44, 92]. Limited studies from the region yielded comparable results. The negative impact of low vitamin D on mineral metabolism is illustrated in the inverse relation between 25(OH)D and PTH levels noted in Lebanese adolescents, adults, and elderly, reminiscent of similar findings in other populations ($R = -0.19$ to -0.22) [58, 67, 75, 93]. A similar negative relationship was noted in Saudi women ($R = -0.28$) [69], Emirati women ($R = -0.22$) [74], and Iranian women ($R = -0.25$ with Ln PTH) [72]. While no relationship between 25(OH)D level and BMD was detected in Saudi women, a positive relationship between 25(OH)D and spine, but not hip BMD *Z*-score was noted in postmenopausal Iranian women [94]. Similarly, a correlation was also noted between 25(OH)D level and spine, hip, and forearm BMD in elderly Lebanese ($R = 0.13$–0.3), but disappeared in analyses adjusting for age, height, lean mass, and PTH levels [75]; consistent with findings in Iranian women [72]. Vitamin D supplementation for 1 year increased lean mass, bone area, and bone mass in a randomized controlled trial in Lebanese adolescent girls [59]. In that trial, girls with the lowest levels had the highest increments in bone mass; and the effect was modulated by vitamin D receptor polymorphisms.

Recommendations for Treatment

Whereas there is little photosynthesis above and below latitudes of 40° North and South during winter months, the latitudes of the Middle East allow the production of vitamin D throughout the year [3]. Barriers to sun exposure including fear of skin cancer and skin damage, cultural lifestyles including a conservative concealed clothing style, low outdoor activity and low intake of vitamin D enriched foods, and the lack of governmental regulation for food fortification with vitamin D in several countries in the region, render supplementation of the most efficacious mean to achieve desirable levels. A desirable 25(OH)D level of 30 ng/ml is recommended to optimize musculoskeletal health in adults [3, 44, 92], and a similar target was suggested for the pediatric age group [14, 46]. Such a level was also demonstrated to optimize calcium transfer into the milk of a breast feeding mother to satisfy her infant's needs [44]. Doses of vitamin D needed to reach the above desirable level are anticipated to exceed the recommended doses in subjects from western counties, due to the significantly lower baseline vitamin D levels in subjects from the Middle East. In a recent review of strategies to prevent and treat vitamin D deficiency, it was underscored that vitamin D_2 may be less effective than vitamin D_3 in maintaining serum 25(OH)D levels [44], and thus when available the use of D_3 would be preferable. Summarized below are results from interventional studies conducted in the Middle East. The type of vitamin D used in the various studies discussed is specified when reported. The evidence provided herein, and from other studies conducted worldwide, is used to derive treatment recommendations.

Rickets

Prevention of Rickets

In a Cochrane review of interventions to prevent nutritional rickets in terms of infants, four studies qualified for inclusion, rickets did not occur in patients or controls in two of those studies, and only one study was conducted in the Middle East [8]. In the controlled trial from Turkey, 676 children aged 3–36 months, recruited from a rural community setting, received placebo or 400 IU of vitamin D daily over a period of 12 months. The RR for developing rickets in the treated group was 0.04 [0–0.71] compared to the controls. In the second randomized study conducted in urban China, oral vitamin D_3 of 300 IU/day during the first 12 months administered with oral calcium supplementation from age 5 till 24 months, resulted in a RR for developing rickets of 0.76 [0.61–0.95]. The authors concluded that preventive measures using calcium and vitamin D in high risk patients were indicated. The high risk group specified included infants and toddlers living in Africa, Asia, and the Middle East [8].

Treatment of Rickets

Various regimens have been used to treat rickets in the Middle East, mostly conducted in non-randomized, non-blinded, and interventional studies. In a study of 200 cases of rickets from Iran, subjects mostly below 3 years of age, classical rickets usually responded within 2–3 weeks of having received one injection of vitamin D at a dose of 600,000 IU [33]. Similarly, treatment of 47 Jordanian infants with nutritional rickets with one injection of 600,000 IU of vitamin D resulted in a substantial improvement in X-ray abnormalities, normalization of serum calcium and phosphate levels, and a significant decrement in alkaline phosphatase within 3 weeks of therapy [18]. In a dose ranging study of 52 Turkish infants with nutritional rickets and a mean age of 10 months, subjects were randomized to receive one oral dose of vitamin D of 50,000 IU, 300,000 IU, or 600,000 IU, and all received oral calcium for 1 week. On the 30th day there was no difference in the improvement between the three groups, and all patients had improved by the 60th day post-therapy, however, eight infants developed hypercalcemia, six of which were allocated to the high dose group [38]. Treatment of 50 Iraqi infants with rickets and growth failure with a daily injection of 5,000 IU of vitamin D resulted in clinical and radiological improvement within 6 weeks of therapy (cumulative dose 210,000 IU) [23]. Treatment of 102 Saudi infants with daily vitamin D at doses of 2,500 IU/day for a month (75,000 IU total dose) followed by 400 IU/day of vitamin D resulted in normalization of the serum alkaline phosphatase from over 1,000 IU/l to below 500 IU/l in 90% of subjects 1 month post-therapy [25]. The efficacy of one intramuscular (IM) injection of 600,000 IU of vitamin D was compared with that of 2,000 IU of oral vitamin D daily for 4 weeks in Kuwaiti infants with rickets, and both groups subsequently received 400 IU of vitamin D daily for 6 months [11]. Whereas a prompt response was noted in the group receiving IM therapy, no or a minimal response was noted in 40% of subjects assigned to the oral group. Conversely, comparison of a single oral dose of vitamin D_3 of 600,000 IU to an oral daily dose of 20,000 IU for 30 days in 20 Turkish infants with nutritional rickets resulted in comparable decrements in serum alkaline phosphatase, and similar increments in serum calcium, phosphorus, and in bone mineral density [95]. In an interventional study conducted in 19 Emirati young children, with stunted growth and mean age 17 $\pm$ 6 months, treatment with ergocalciferol (2,000–5,000 IU/day) daily for 3 months followed by 400 IU/day for variable periods resulted in a mean increment in height *Z*-score of 0.86 $\pm$ 0.95 [31]. Similarly, treatment of 46 Qatari infants with rickets, decreased height, and growth velocity standard deviation scores, with one injection of vitamin D_3 of 300,000 IU resulted in significant increments in these variables, but not in normalization of stature [96]. A randomized trial compared calcium, vitamin D, and a combination of both in 42 Turkish infants with rickets randomized to calcium lactate 3 g/day, vitamin D 300,000 IU IM once, or both [97]. Whereas all groups experienced increments in serum calcium and a decrease in serum alkaline phosphatase by the 4th week of therapy, the most substantial increment was in the combination group. Treatment of 34 Saudi adolescents with 1200 mg calcium and 4,000–5,000 IU of vitamin D_3/day or with α-calcidol 0.05–0.08 μg/kg resulted in normalization of serum alkaline phosphatase at a mean duration of 19 months (range 6–38 months) [27].

In summary, treatment of rickets with intramuscular injections of vitamin D at doses of 150,000–600,000 IU/dose, with repeated dosing as needed, resulted in clinical, biochemical, and radiological improvement within weeks and may improve the compliance. Conversely, daily oral supplementation with doses of 2,000–5,000 IU/day for several weeks may be as efficacious. Children with rickets from Egypt, Saudi Arabia, and the United Arab Emirates had a low calcium intake. Therefore, assessment of calcium nutrition and concomitant therapy with calcium is indicated and would expedite clinical recovery. Prevention of rickets in neonates and infants with vitamin D at a dose of 400 IU/day is justified based on evidence the provided above.

Hypovitaminosis D

Pregnant/Lactating Mothers

The only interventional study in this age group from the region randomized 90 lactating and 88 nulliparous women to receive 2,000 IU D_2/day or 60,000 IU D_2/month over 3 months. The mean 25(OH)D levels in lactating women increased from 9.2–10.8 ng/ml to 15.2–16.8 ng/ml at 3 months, and the increments did not differ between the two regimens. The mean 25(OH)D levels in nulliparous women increased from 7.6 ng/ml to 15.6–16.8 ng/ml. The above doses were able to raise 25(OH)D levels to above 20 ng/ml only in one-third of the subjects [98]. Although vitamin D nutrition during pregnancy and lactation seems to be important for offspring's skeletal health, and may contribute to genetic programing of the offspring for the development of chronic diseases in later life, trial based evidence testing the safety and efficacy of vitamin D supplementation during these demanding reproductive years is currently lacking [14, 91]. It is nevertheless suggested that women should be replaced with vitamin D with monitoring of serum 25(OH)D levels to a target of 30 ng/ml [44].

Infants/Children/Adolescents

Data pertaining to vitamin D nutrition during infancy and pre-pubertal years is also scarce. The most recent recommendations from the American Academy of Pediatrics recommend 400 IU/day of vitamin D in infants, children, and adolescents [99]. However, although such recommendations may be adequate for subjects with mild degrees of hypovitaminosis D, they would be suboptimal for subjects with more severe deficiencies as described for subjects from the Middle East, and at periods of peak bone mass accrual [14, 46]. A randomized double-blind placebo controlled trial conducted in Lebanese adolescent girls demonstrated the safety and efficacy of weekly vitamin D_3 administration at doses equivalent to 400 IU/day and 2,000 IU/day of vitamin D_3, in increasing bone mass, bone area, and muscle mass [59, 100]. Only the higher dose resulted in mean increments in 25(OH)D levels from the mid-teens (in ng/ml) to the mid-thirties, whereas the mean increment with the 400 IU/day dose was 4 ng/ml, with a mean level remaining below 20 ng/ml [59]. There was a trend for further increments in musculoskeletal outcomes at the higher dose and in prepubertal girls [59, 100].

Elderly

In a recent review of the evidence from several randomized controlled trial for the beneficial effect of vitamin D on musculoskeletal outcomes in the elderly, it was concluded that levels above 26 ng/ml would optimize bone health, reducing bone loss and fractures, and levels above 30 ng/ml would optimize muscle health, improving muscle performance, and reducing fractures [92]. It has become increasingly recognized from data available in western countries that adequate intake for vitamin D of 600 IU/day for the elderly may be insufficient, and that 800 IU/day may be more adequate [44]. However, this may not apply to elderly individuals from the Middle East, who have lower baseline 25(OH)D levels [75–77, 101]. A study comparing the efficacy of 3,000 IU/day of vitamin D_2 for 12 weeks, 25 μg/day of 25(OH)D_3 for 1 week, and 0.5 μg/day of one α-OHD_3 for 8 weeks, in 30 elderly subjects from Beer Shiva Israel with a mean baseline 25(OH)D level of 15 ng/ml, demonstrated that supplementation with the D_3 and not the D_2 preparation significantly raised mean serum 25(OH)D levels [102]. More recently, a short term randomized trial allocated 48 subjects with hip fractures from Haifa, mean age 81 years, mean 25(OH)D of 15 ng/ml, to vitamin D_3 1,5000 IU daily, or 10,500 IU weekly, or 45,000 IU once monthly. Such doses resulted in achieving a 25(OH)D level above 20 ng/ml in only half of the subjects [101]. Furthermore, although comparable mean 25(OH)D levels, varying between 29 and 37 ng/ml, were reached with the three dosing regimens, the monthly once dose may be particularly attractive because it may improve the patient adherence. Furthermore, only the monthly dosing regimen substantially reduced circulating PTH levels [101], an independent predictor of bone loss in the elderly [103].

Conclusion

Vitamin D levels are quite low across all age groups in the Middle East. The persistence of rickets, and its sequela on morbidity and mortality in general, on growth and musculoskeletal outcomes in particular, is alarming. Whereas consistent predictors of rickets in infants were low maternal vitamin D levels, and exclusive, and prolonged breast feeding; family crowding, lower socioeconomic status, lower parental educational level, and low calcium intake were additional risk factors in some studies. The skeletal manifestations of rickets were variable, and a common presentation was that of acute respiratory tract diseases and gastroenteritis, underscoring the importance of vitamin D as a potent immunomodulator. Various high dose vitamin D regimens, along with calcium supplementation resulted in the healing of clinical and radiographic features of rickets within weeks, but only partially corrected the growth retardation. Prevention of rickets with vitamin D, at a dose of 400 IU/day, is justified in neonates, infants, and toddlers.

Skin color is darker in some countries in the Gulf area, and obesity is a major public health problem in the Middle East across age groups, and both conditions are known predictors of low vitamin D levels. Risk factors for hypovitaminosis D included female gender, multi-parity, season, conservative clothing style, low socioeconomic status, and urban living. Overt clinical manifestations of insufficient vitamin D levels were almost non-existent. However, the negative impact of low vitamin D levels on indices of mineral bone metabolism and the positive effect of vitamin D replacement on musculoskeletal outcomes support recommendations to optimize vitamin D status across all life stages. Whether vitamin D supplementation will also have a positive impact on chronic diseases associated with hypovitaminosis D, including the metabolic syndrome and type II diabetes, prevalent conditions in the Middle East, needs to be established.

Current recommendations for daily intake of vitamin D are likely to be suboptimal for subjects from Middle East. The extensive body of evidence regarding the prevalence of hypovitaminosis D in the Middle East, information regarding the safety and efficacy of vitamin D at relatively high doses, and data from randomized dose-ranging studies in adolescents and elderly, justify the following suggested doses. Daily vitamin D, at doses of 1,000–2,000 IU in infants and adolescents, and 2,000–4,000 IU in elderly, with periodic monitoring and coupled with adequate calcium nutrition are recommended. Intermittent dosing, using a cumulative amount of vitamin D proportionate to the daily dose (for e.g., 7,000–14,000 IU/week instead of 1,000–2,000 IU/day), may enhance compliance. Further research is needed to conclusively define optimal vitamin D levels, and determine the doses and regimens of vitamin D for pregnant and lactating women, infants and adolescents, and elderly subjects from the Middle East.

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