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Worldwide vitamin D status

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The aim of the present study is to summarize existing literature on vitamin D levels in adults in different continents and different countries woldwide. The best determinant of vitamin D status is the serum concentration of 25-hydroxyvitamin D (25(OH)D). Most investigators agree that serum 25(OH)D should be higher than 50 nmol/l, but some recommend higher serum levels. Traditional risk groups for vitamin D deficiency include pregnant women, children, older persons, the institutionalized, and non-western immigrants. This chapter shows that serum 25(OH)D levels are not only suboptimal in specific risk groups, but also in adults in many countries. Especially, in the Middle-East and Asia, vitamin D deficiency in adults is highly prevalent.

Introduction

Vitamin D status has been studied in all continents and most countries over the world. Several reviews have been published.[1–8] The best determinant of vitamin D status is the serum concentration of 25-hydroxyvitamin D (25(OH)D).[1] There is no general agreement on the required serum 25(OH)D for an adequate vitamin D status. Most investigators agree that serum 25(OH)D should be higher than 50 nmol/l, but some recommend higher serum levels, e.g. higher than 75 or even 100 nmol/l.[9] The Institute of Medicine has recently recommended that serum 25(OH)D is adequate when it is higher than 50 nmol/l,[10] similar to the recommendation of the Standing Committee of Europe Doctors (www.cpme.eu). Clinical vitamin D deficiency only occurs when serum 25(OH)D is lower than 25 nmol/l. The clinical picture includes muscle weakness, bone pain and fractures, while in children joint swelling and

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deformations prevail. In patients with rickets and osteomalacia serum 25(OH)D usually is lower than 15 nmol/l or even below the detection limit.[11] The variation in serum 25(OH)D measurements is still considerable due to laboratory variation.[12] Different radio-immunoassays yield different results and the variation between laboratories may be as high as 30%. New methods such as liquid chromatography followed by mass spectrometry give better results.[13] Vitamin D status is determined by sunshine exposure, skin pigmentation, clothing style, use of sunscreen, nutrition and supplements. A small part of the serum 25(OH)D comes from dietary intake, especially fatty fish. The dietary intake is more important when sunshine exposure is less. In the next paragraphs vitamin D status is described in different continents and different countries. The emphasis is on vitamin D status in adults. Attention will also be focussed on determinants of vitamin D status and on risk groups for vitamin D deficiency. This chapter will end with a research agenda.

Europe

Vitamin D status in Europe varies according to latitude, season and skin pigmentation. The serum 25(OH)D level as observed in different studies[14–28] is shown in Fig. 1. As visible in this Figure, serum 25(OH)D is higher in Northern Europe than in Southern Europe and higher in Western than in Eastern Europe. The higher levels in Northern Europe were also observed in some multicenter studies in which one laboratory facility was used.[1,6,8,29] The high serum 25(OH)D levels in Norway and Sweden are probably due to a high intake of fatty fish and cod liver oil. The low serum 25(OH)D in Spain and Italy and Greece may be due to more skin pigmentation and sunshine avoiding behavior.

Middle-East

The mean serum 25(OH)D levels in various countries of the Middle-East are shown in Fig. 2. Serum 25(OH)D shows a high variation in these countries.[30–36] In a population study of 1210 men and women

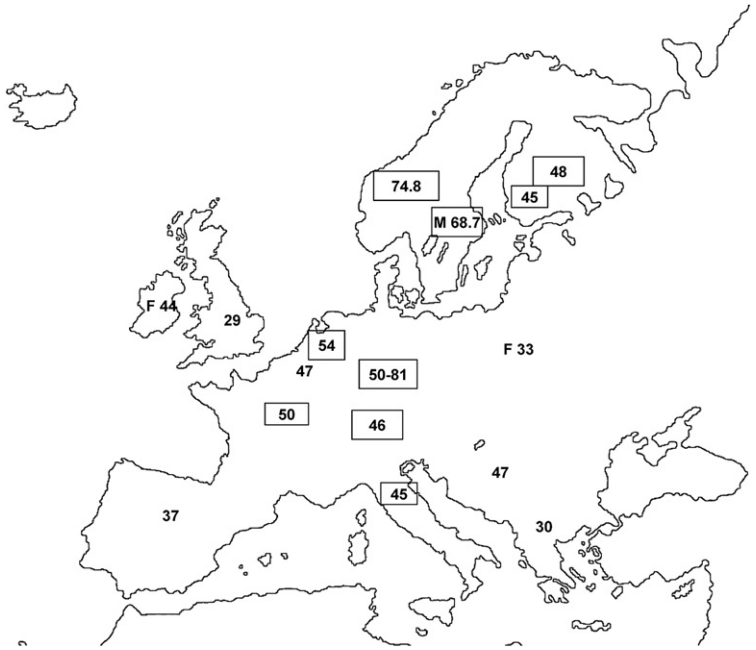

Fig. 1. Mean serum 25(OH)D levels in Europe. The data come from different studies.[14–28] A rectangle around the number indicates that it is a population-based study.

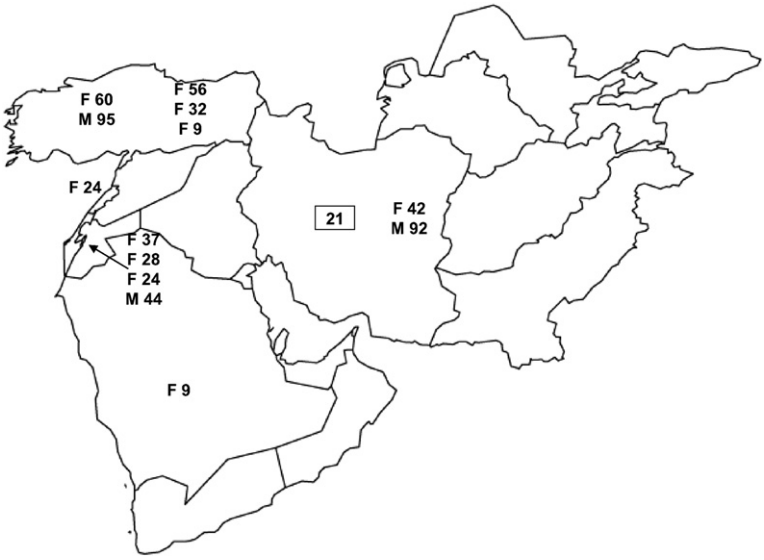

Fig. 2. Mean serum 25(OH)D levels from different studies in the Middle-East.[30–36]

in Iran between 20 and 69 years the mean serum 25(OH)D was 20.6 nmol/l.[35] Vitamin D status was better in girls and boys between 14 and 18 years (mean 42 and 92 nmol/l, respectively).[36] The lowest serum 25(OH)D was seen in a study of older persons in Saudi Arabia with a mean of 9 nmol/l.[34] Studies in Turkey and Jordania in women[30,33] showed a strong relationship with clothing. Serum 25(OH)D decreased from women with western clothing going to traditional women with hijab and completely veiled women with niqab. Men in these countries have higher levels than women.

Africa

Studies from Africa[37–43] show in general adequate or even high mean serum 25(OH)D levels (Fig. 3). Population-based data are not available. The studies from Tanzania and Guinea-Bissau showed a serum 25(OH)D of 87 and 78 respectively in tuberculosis patients.[40,42] In a study in Gambian rural women, serum 25(OH)D was 91 nmol/l.[37] A lower serum 25(OH)D was measured in Tunesia with a mean level of 35 nmol/l in veiled and 43 nmol/l in non-veiled women.[43]

Asia

The mean serum 25(OH)D levels in different studies from Asia are shown in Fig. 4[44–52] A low serum 25(OH)D was observed in hip fracture patients and controls of similar age in a study in Yekaterinburg in Asian Russia.[44] Low serum 25(OH)D levels were also observed in Mongolia with a very low level in rachitic children (7 nmol/l) and pregnant women (26 nmol/l).[45] In a population study in Chinese girls of 12–15 years very low levels were found in winter (12–13 nmol/l).[45] A low serum 25(OH)D was also observed in India especially in women. Vitamin D status was better in Malaysia and Japan.[49–52]

Oceania

The mean serum 25(OH)D levels in different studies from Oceania, i.e. Australia, New Zealand and Pacific Islands, are shown in Fig. 5.[53–59] Although Oceania has a very sunny climate, mean 25(OH)D levels were below 50 nmol/l (39.7 nmol/l in low-level care and 31.4 nmol/l in high-level care) in a large sample of women in residential care in three states of Australia (Western Australia, New South Wales, Victoria).[53] In

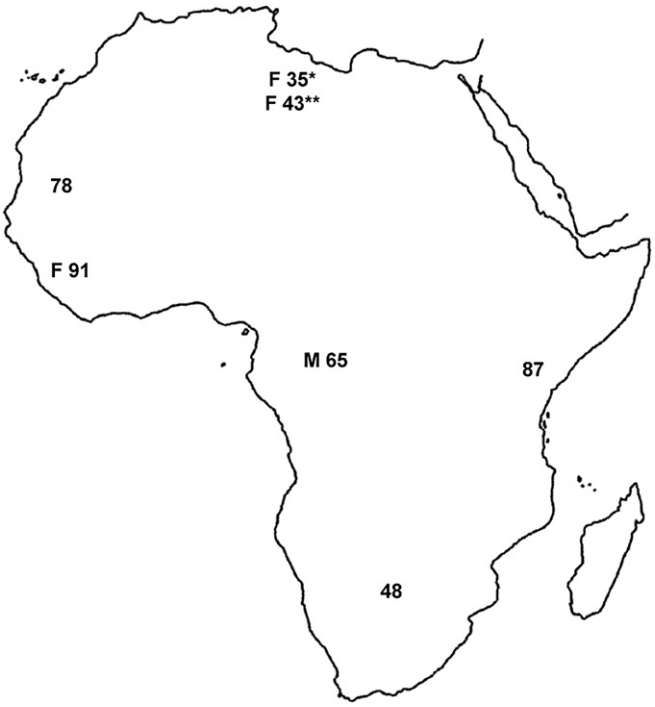

Fig. 3. Mean serum 25(OH)D levels from different studies in Africa.[37–43] *) veiled; **) non-veiled.

individuals aged 60 years and older, mean 25(OH)D levels appear higher in the mainland of Australia than in the island Tasmania.[56] A study in 342 volunteers in Invercargill and Dunedin, New Zealand, showed large seasonal variation with a mean 25(OH)D level of 51 nmol/l in early spring and 79 nmol/l in late summer.[59]

North-America (including Canada and Mexico)

Many studies examining the vitamin D status in North-America were published (Fig. 6,[60–68]), among which several representative samples of the US population. One of the largest representative samples available is The National Health and Nutrition Examination Survey (NHANES). The most recent NHANES data on vitamin D status are from 2005–2006. The mean serum 25(OH)D level in 4495 individuals was 49.8 nmol/l; 50.3 nmol/l in men and 49.5 nmol/l in women.[67] Interestingly, an earlier NHANES study showed a mean 25(OH)D level of 75 nmol/l in 1988–1994 ($n = 18883$) and a mean 25(OH)D level of 60 nmol/l in 2001–2004 ($n = 13369$).[68] Although slightly different age ranges (20 + years in Forrest 2011; 12+ in Ginde 2009), these results indicate a decrease in mean serum 25(OH)D levels in the US population even following adjustment for 25(OH)D assay differences. In a sample of 1606 men aged 65 years and older, the mean 25(OH)D level was 62.8 nmol/l[63]; in a sample of 6307 women aged 65 years and older, the mean 25(OH)D level was 58.0 nmol/l.[64] Very high vitamin D levels were observed in sunny California (mean = 105.0 nmol/l).[65] In a representative sample of the Canadian population, the mean 25(OH)D levels were 65.0, 66.5 and 72.0 nmol/l, respectively, at the ages 20–39, 40–59 and 60–79.[66] Only few studies were published in Mexico. Most of these were in specific risk groups (e.g. children, persons having disease).

South-America

Only few studies on vitamin D status in South-America were published (Fig. 7,[69–72]). Most of these studies were small, and data from several countries are lacking. In a study in Argentina, a clear North-

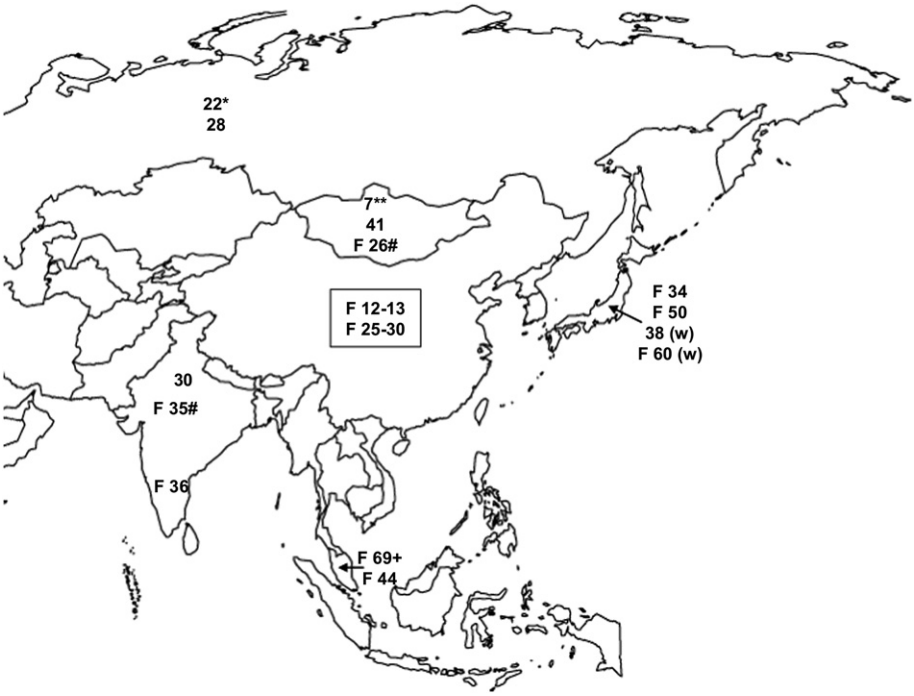

Fig. 4. Mean serum 25(OH)D levels from different studies in Asia.[44–52] *) hip fracture patients; **) rachitic children; #) pregnant women; +) Chinese postmenopausal women; (w) = winter.

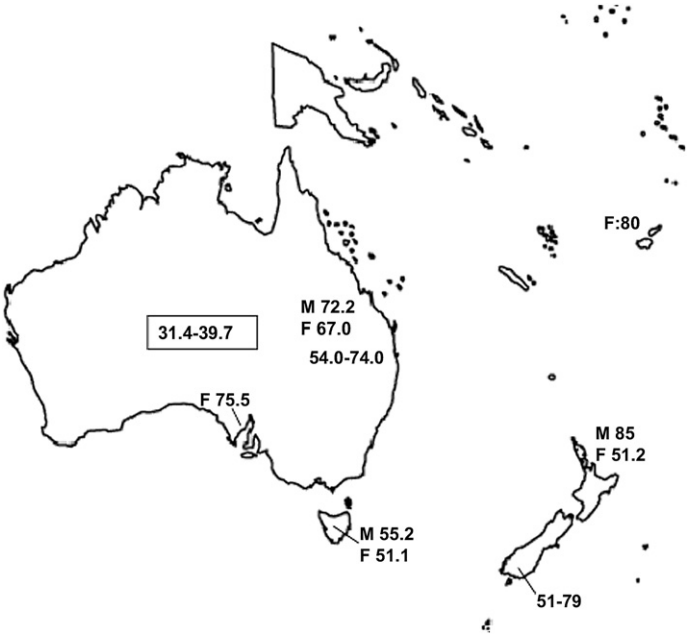

Fig. 5. Mean serum 25(OH)D levels in Oceania.[53–59]

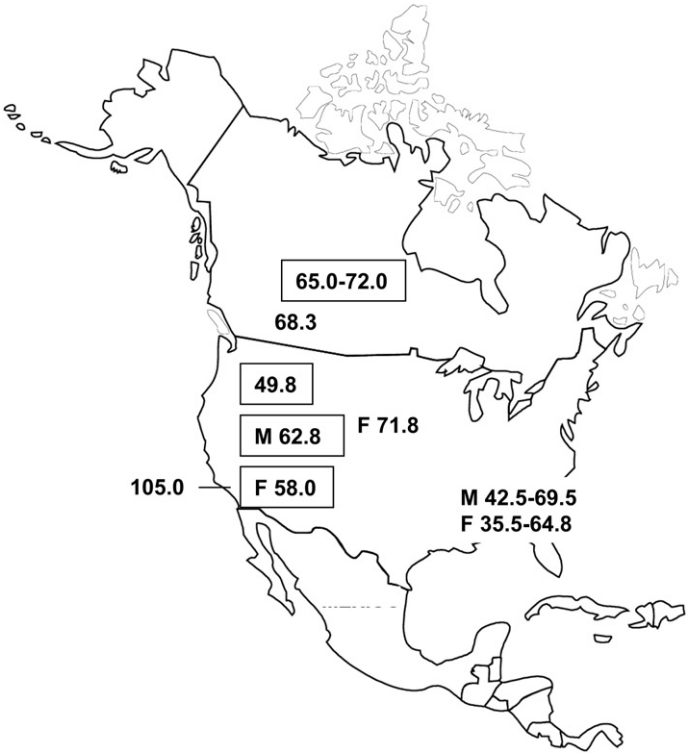

Fig. 6. Mean serum 25(OH)D levels in North-America.[60–68]

South gradient was observed with higher vitamin D levels near the equator.[69] In Chile, lower 25(OH)D levels were observed in postmenopausal as compared with premenopausal women.[71] The observed mean level in postmenopausal women in Chile (48.8 nmol/l) is very similar to the mean 25(OH)D level in independently living elderly in Brazil (49.5 nmol/l).[70]

Risk groups

This chapter shows that serum 25(OH)D levels are suboptimal in adults in many countries. Vitamin D deficiency is even more common in specific risk groups. Vitamin D deficiency is prevalent in pregnant women and their newborns.[46,73–75] The highest risk was observed in black women and their newborns. Low vitamin D levels were also reported in children,[76] esp. obese children,[77] and in adolescents.[5] Low vitamin D status in children and adolescents may be due to reduced intake or synthesis of vitamin D_3 (e.g. being born to a vitamin D deficient mother, dark skin color), abnormal intestinal function or malabsorption (e.g. small-bowel disorders), or reduced synthesis or increased degradation of 25(OH)D or 1,25$(OH)_2$D (e.g. chronic liver or renal disease).[78] Older people have lower dermal synthesis, and especially older people living in homes for the elderly or nursing homes who do not come outside frequently, are at high risk of poor vitamin D status.[53,79–81] Non-Western immigrants migrating to countries at higher latitudes with limited UV-B irradiation are at high risk because of more pigmented skin, the habit to stay out of the sun, the wearing of well-covering clothes, and a diet low in fish and dairy products.[14,82–85] Non-western pregnant women show very low or sometimes undetectable levels.[86] Large ethnic differences in vitamin D levels were reported in the United States, esp. between non-Hispanic white and non-Hispanic black people.[68]

Fig. 7. Mean serum 25(OH)D levels in South-America.[69–72]

Research agenda

Comparisons between countries are more valid when a central laboratory facility has been used. In general, a clear North-South gradient can be observed in global studies using a central laboratory facility.[6] However, unexpectedly an inverse North-South gradient was seen in Europe[6,8] due to a high dietary intake of vitamin D in the Scandinavian countries. Therefore, there is an urgent need for studies comparing countries, using a central laboratory facility. Otherwise, studies should standardize their assays to one gold standard, i.e. liquid chromatography followed by tandem mass spectrometry (LC MS/MS) in order to enhance comparability. In addition, when viewing the Figures in the present study, it becomes clear that there is a need for prevalence studies in the Middle-East, Africa, Asia, Mexico, and South-America. The importance of the dietary intake versus sun exposure should be better defined. The risk groups for vitamin D deficiency have to be described for different countries with respect to age, gender and season. These data are needed to develop supplementation guidelines and programmes.

Conclusion

Vitamin D deficiency has a high prevalence over the world, not only in risk groups. Especially, in the Middle-East and Asia, vitamin D deficiency in adults is highly prevalent. Traditional risk groups include young children, pregnant women, older persons, the institutionalized, and non-western immigrants. Recent studies show that adolescents and young adults are at risk for vitamin D deficiency. Risk factors for vitamin D deficiency include low sun exposure, skin pigmentation, sunscreen use, skin covering clothes and a diet low in fish and dairy products.

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