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Epidemiology of vitamin-D-deficiency/insufficiency in different European countries

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St. H. Scharla

Epidemiology of vitamin-D-deficiency/insufficiency in different European countries

Definition of vitamin D deficiency, insufficiency, and hypovitaminosis D

Vitamin D deficiency leads to osteomalacia, a metabolic bone disease characterized by reduced bone formation and decreased mineralization of osteoid. Biochemical abnormalities include decreased serum calcium, increased parathyroid hormone, and increased activity of alkaline phosphatase. Patients with vitamin D deficiency usually exhibit serum concentrations of 25-hydroxyvitamin D (representing the storage form of vitamin D) below 5 ng/ml, and very often 25-hydroxyvitamin D is undetectable.

Growing evidence demonstrates that moderately low levels of vitamin D (vitamin D insufficiency) can already have unfavourable effects on calcium homoeostasis leading to bone loss, even if osteomalacia is not present. A secondary increase in parathyroid hormone is a very early sign of vitamin D insufficiency, with 1,25-dihydroxyvitamin D-levels still being normal [1].

Several investigators found the lower limit of physiological 25-hydroxyvitamin D concentrations at about 12 ng/ml (= 30 nmol/l) [2, 3] or 10 ng/ml (= 25 nmol/l), which is very similar [4].

Using a vitamin D challenge test Bouillon found the lower physiological threshold for 25-hydroxyvitamin D to be 10–15 ng/ml [5], which is in good accordance.

More recent publications report a higher limit for vitamin D insufficiency. Parathyroid hormone was reported to increase already at 25-hydroxyvitamin D concentrations below approx. 30 ng/ml (= 75 nmol/l) [6]. According to a review of the literature this opinion is supported by McKenna [7].

By measuring the decrease of parathyroid hormone following treatment with vitamin D, Malbanan and coworkers found a threshold of 20 ng/ml (= 50 nmol/l) 25-hydroxyvitamin D to define vitamin D insufficiency [8].

In conclusion, 25-hydroxyvitamin D concentrations below 15–20 ng/ml are considered by almost all authors to be insufficient (vitamin D insufficiency), and concentrations between 20 and 40 ng/ml have been termed as "hypovitaminosis D" (7).

Factors influencing vitamin status in Europe

The main sources of vitamin D are skin synthesis under the influence of ultraviolet light (290–315 nm) and dietary intake (especially sea fish, to less extent butter). Therefore, vitamin D supply will be better in populations with regular consumption of sea fish and dairy products, such as Scandinavia or The Netherlands. Supplementation of food with vitamin D is not common in Europe with the exception of some Scandinavian countries. This is in contrast to the U.S.A., where milk is fortified with vitamin D.

Skin synthesis of vitamin D cannot compensate for low nutritional intake, because Europe is located at high latitude reaching from 40° N (Madrid, Spain) to 60° N (Oslo, Norway). Webb and coworkers demonstrated, that photosynthesis of previtamin D is nearly impossible during the winter months at this latitude [9]. From this it is obvious, that vitamin D deficiency may occur even in Southern Europe, but can present a severe problem in Northern Europe.

Populations in Southern Europe usually have more skin pigmentation, which counteracts the larger amount of sunlight in this area.

In elderly people, the ability of skin to produce vitamin D is decreased.

Studies investigating vitamin D status in selected populations

A high prevalence of vitamin D deficiency has been documented in house-bound elderly people of many European countries, such as England [10], Finland [11], Germany [12, 13], and France [14]. A recent study of the author found vitamin D deficiency in all studied residents of a nursing home in Leipzig, Saxonia [15] (Figure 1).

However, vitamin D deficiency/insufficiency is also found in ambulatory elderly people. A Dutch investigation found 25-hydroxyvitamin D concentrations < 8 ng/ml in 16 % of the healthy elderly population [16, 17, 18].

Even in Northern Italy, 38.5 % of all women (mean age 59 yrs,

range 41–80 yrs) had 25(OH)D serum concentrations below 12 ng/ml during winter/spring (December through May), and 12.5 % of the women still had low levels during summer/autumn (June through November) [19].

Vitamin D insufficiency may even occur in adolescents, according to a French study [20], which demonstrated low 25-hydroxyvitamin D concentrations of 6.61 ± 2.04 ng/ml in March. All of the adolescents had vitamin D insufficiency (25(OH)D < 12 ng/ml) and a secondary increase in parathyroid hormone .

McKenna published in 1992 a review dealing with reports on vitamin D status from 1971 to 1990, obtained in 27 regions [4]. In young adults, 25-hydroxyvitamin D values from Europe were significant lower compared to Scandinavia and North America during winter, spring, and fall. Summer values of serum 25(OH)D were not different between the regions. In healthy elderly, trends were similar to those of younger adults but not as marked, with European values being lower compared to Scandinavia or North America in spring and fall. In institutionalized elderly, again the European values were lower than both Scandinavian and North American values, and Scandinavian values were lower than North American values.

In general, the prevalence of vitamin D insufficiency was very low in North America, reached about 4 % to 9% of young adults in Scandinavia, and was > 40 % in young adults in Western/Central Europe during winter. In the healthy elderly population of North America and Scandinavia, nearly 25 % of the subjects had low values in the winter, but less than 5 % had low levels throughout the remainder of the year. In Western/Central Europe, the frequency of vitamin D insufficiency ranged from 8 % to 60 % [4]. It is apparent from this review that vitamin D status is better in Scandinavia as compared to Western/Central Europe.

A high prevalence of vitamin D insufficiency and deficiency is found in immigrants with darker skin pigmentation and/or special dietary habits, such as Indo-Asian immigrants in the United Kingdom [21, 22] or Turkish immigrants in Germany [23]. Among Indo-Asian attendants of a rheumatologic clinic 78 % of the patients had vitamin D deficiency (25-OH-vitamin D < 8 ng/ml) [22].

Figure 1: Vitamin D status in a nursery home in Leipzig, Saxonia, Germany. The concentration of 25-hydroxyvitamin D was significantly lower in the elderly residents of the nursery home compared to a random population sample. Results are presented as box plot diagrams: The crossbar in the box represents the median; 50 % of all values lie within the box; the small vertical bars indicate the range between the 10 % and the 90 % percentile. Data from reference [15].

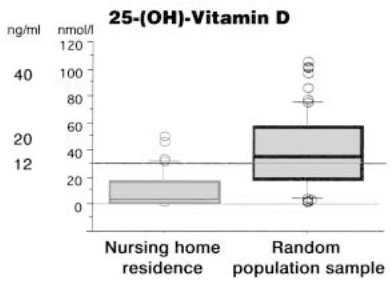
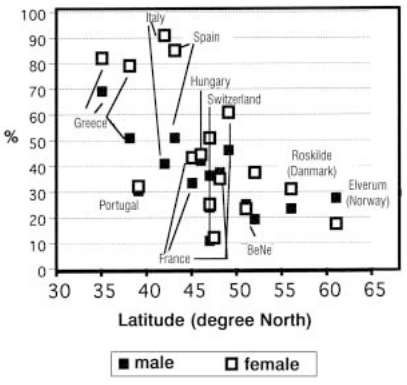


Figure 2: The percentage of the population with vitamin D deficiency (25-hydroxyvitamin D < 12 ng/ml) is plotted against the latitude. Data from reference [24].



Population based studies

The SENECA study was an investigation on the diet and health of elderly people from 19 towns in 11 European countries [24]. Vitamin status was studied during the winter months of January, February, and March. Mean 25(OH)D serum concentrations ranged from 10 ng/ml (Greece) to 24 ng/ml (Switzerland) in men and from 8.4 ng/ml (Greece, Spain) to 19 ng/ml (Norway) in women. Vitamin D insufficiency (defined in this study as 25-hydroxyvitamin D < 12 ng/ml) was much more frequent in mediterranean countries (prevalence up to 83 % in Greek women) than in Northern Europe (18 % in Norway). One factor associated with better vitamin D status was increased fish consumption, other factors were probably fortification of food and a higher percentage of

people taking vitamin D supplements in Scandinavia (Figure 2).

Lifestyle habits such as clothing are probably the reason that vitamin D insufficiency is found to a large amount in mediterranean countries, such as Lebanon. 95 % of the randomly selected women of a village at latitude 33.5° N had vitamin D insufficiency as defined by 25-hydroxyvitamin D < 20 ng/ml (50 nmol/l) [25].

In France, bone turnover was investigated in elderly people selected from a population-based sample within the framework of the EPIDOS INSERM Merck study [26]. The blood samples for determination of 25-hydroxyvitamin D were collected at the end of winter. The mean 25-hydroxyvitamin D concentrations were 17 ± 10 ng/ml, and 39% of the women had vitamin D insufficiency (defined as a concentration < 12 ng/ml). Vitamin D insufficiency was associated with increased parathyroid hormone and increased bone turnover, as assessed by biochemical markers.

Another epidemiologic study compared the vitamin D status in nine geographic regions of France [6]. Blood samples were collected in the winter season (November to April). Latitude and sunshine had significant influence on vitamin D status in this healthy population aged between 35 and 65 years. Vitamin D insufficiency (defined as a 25-hydroxyvitamin D concentration < 12 ng/ml) was present in 14 %, and was even found in the Mediterranean coast region (7 %) (Figure 3).

In Germany, vitamin D status was assessed in more than 415 inhabitants of a small town in southern Germany, who were participating in the European study on vertebral osteoporosis (EVOS) [27]. The subjects (50–80 years) had been recruited using the city register of inhabitants to obtain a population based sample stratified for age and sex. Serum 25-hydroxyvitamin D concentrations were not different in women and men [28], but there was a pronounced seasonal variation [29], figure 4. In late summer, the 25-hydroxyvitamin D concentration was 28 ± 11 ng/ml in men and 27 ± 9 ng/ml in women, whereas in late winter the concentrations were 18 ± 9 ng/ml (men) and 16 ± 9 ng/ml (women). There was a moderate decrease in 25-hydroxyvitamin D concentrations with age, which was more pronounced in females during winter time. 40% of the women and 30 % of the men had vitamin D insufficiency in winter.

The same study demonstrated an association between low vitamin

Figure 3: Vitamin D status (serum concentration of 25-hydroxyvitamin D) in two different French cities located at different latitude, Toulouse in Southern France, and Paris in northern France. Mean and standard devitation are presented. Data from reference [6].

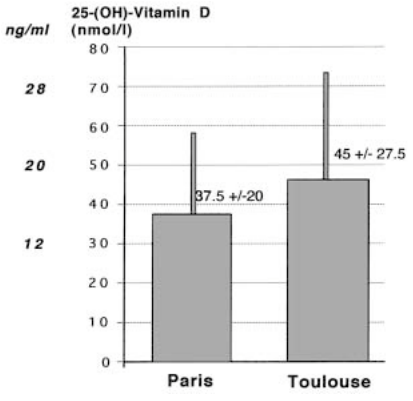
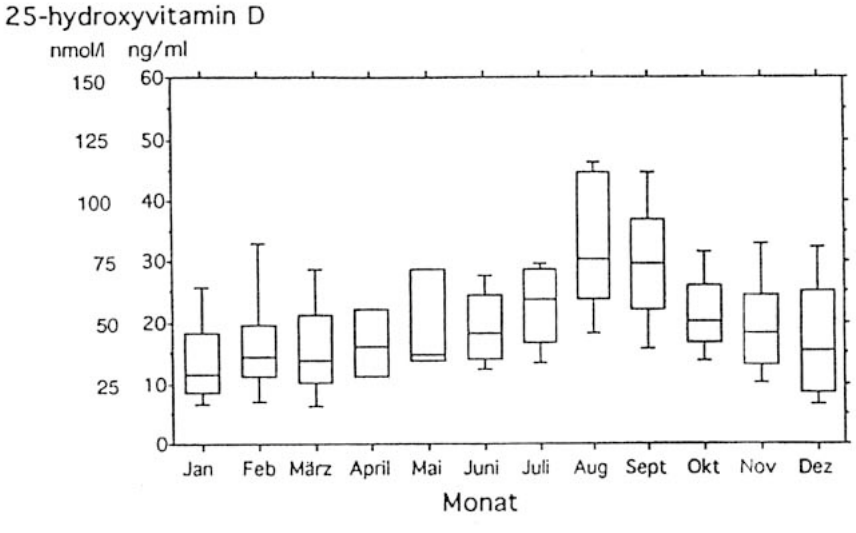


Figure 4: Seasonal variation of 25-hydroxyvitamin D serum concentration in the average German population (age 50–80 years). Results are presented as box plot diagrams: The crossbar in the box represents the median; 50 % of all values lie within the box; the small vertical bars indicate the range between the 10 % and the 90 % percentile. Figure adapted from reference [29].



D status and increased bone resorption in females. Low 25-hydroxyvitamin D concentrations were also associated with lower bone mineral density at the femoral neck in females.

Conclusions

The European population is at high risk for vitamin D insufficiency, because the continent is located at high latitude leading to restricted ultraviolet light exposure. In addition, nutritional supply of vitamin is low in most countries and fortification of food is done only in few countries, mostly in Northern Europe. The intake of vitamin D supplements (which is higher in Northern Europe compared to Southern Europe) seems to have an important impact on vitamin D status. In contrast to prevalent opinions, vitamin D insufficiency is more prevalent in Southern Europe as compared to the North.

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Dr. Scharla is a member of several societies including the International Bone and Mineral Society, the American Society of Bone and Mineral Research and the German Endocrine Society who awarded him the von-Recklinghausen-Award. He has also won a travel award from the International Conference on Calcium Regulating Hormones.

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