Is There an Epidemic Vitamin D Deficiency in German Orthopaedic Patients?

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Abstract

Background Vitamin D plays an essential role in bone health and muscle function. Some studies have shown a widespread rate of vitamin D deficiency in the general population, but few have reported on the vitamin D status of orthopaedic patients.

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All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request. Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Questions/purposes We investigated (1) the extent of hypovitaminosis D in orthopaedic patients, (2) seasonal variations in vitamin D levels, and (3) possible risk factors for insufficient vitamin D levels.

Methods Vitamin D levels in 1119 patients consecutively admitted to an orthopaedic surgery department in 2011 were measured. To investigate the correlation between climate factors and vitamin D levels, the sunshine hours for each month in 2011 were collected by Deutscher Wetterdienst (the German weather service) in the region where most tested patients lived. The prevalence of normal (> 30 ng/mL), insufficient (20–30 ng/mL), and deficient (< 20 ng/mL) 25-hydroxyvitamin D levels was determined. Univariate and multivariate analyses were used to assess risk factors for insufficient vitamin D levels.

Results Overall, 84% of patients had insufficient levels of vitamin D and 60% were vitamin D deficient. Only 15% were in the target range of 30 to 60 ng/mL. The prevalence of low vitamin D levels was greater during winter and months with fewer sunshine hours. Vitamin D levels did not vary according to age, sex, and disease. Individuals with obesity, hypertension, and osteoporosis were more likely to have low vitamin D levels compared with their healthy counterparts.

Conclusions There is an alarmingly high rate of hypovitaminosis D and vitamin D deficiency among orthopaedic patients in this region of Germany, whose latitude (50° N) is approximately the same as those of Vancouver (49°, 15' N) and Paris (48°, 51' N). Given the well-known effects on bone metabolism and muscle health, low vitamin D levels may negatively affect patients. Screening and treating hypovitaminosis D appears to be important in this patient population.

Level of Evidence Level II, prognostic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Hypovitaminosis D has been described in several studies in numerous segments of the global population [29, 36]. It is estimated to affect more than 1 billion people of all races, age groups, and ethnic backgrounds [19]. High rates of vitamin D deficiency have been described among the elderly [17, 30, 31]. A British study revealed a lower vitamin D level in people older than 65 years than in the general public [17]. In postmenopausal American women taking antiosteoporotic medicine, more than 50% had inadequately low vitamin D levels [11]. Even young and healthy cohorts are at risk of hypovitaminosis D. In an American study from 2004, 52% of Boston-based adolescents with Hispanic or black origins showed hypovitaminosis D [12]. Vitamin D deficiency has reached global proportions, with studies showing low vitamin D levels in Irish adolescents [15] and in the Chinese population [9].

Data on vitamin D status among the German population have revealed low vitamin D levels [34]. In 14,000 individuals aged between 1 and 79 years, 62% of adolescent boys, 64% of adolescent girls, 57% of men, and 58% of women had vitamin D levels less than 20 ng/mL [16]. A 2012 study of 1578 patients in an elderly care rehabilitation facility in Germany showed severe vitamin D deficiency with values less than 10 ng/mL in 68% of patients [37]. Only 4% of the patients had levels in the target range of 30 to 60 ng/mL [37].

Vitamin D plays a pivotal role in bone mineralization, with vitamin D deficiency resulting in decreased bone mineralization and secondary hyperparathyroidism and increased cortical bone loss. In certain cases, severe vitamin D deficiency can lead to osteomalacia. An autopsy study of deceased individuals with clinically healthy bones found histopathologic signs of osteomalacia with vitamin D levels less than 30 ng/mL in 25% of all bone samples taken [33]. With vitamin D levels greater than 30 ng/mL, there was no sign of any bone disorder [33]. Furthermore, hypovitaminosis D has been linked to the pathogenesis of osteoporosis and hip fractures [26, 35].

The major source of vitamin D for most people is casual exposure of the skin to sunlight [5]. Owing to Germany's geographic location, sufficient intradermal vitamin D production from sunlight is achieved only during the summer months; in autumn and winter, little vitamin D synthesis from sunlight exposure occurs [18, 37]. A limited number of foods naturally contain vitamin D (fish, egg yolk, organ meats such as liver). Dietary intake is low in many countries, therefore, the use of supplements is important and should be recommended for vulnerable groups such as infants and inactive elderly subjects [23]. Despite reports showing a widespread rate of vitamin D deficiency in the

general population [12, 29, 36, 37], there has been only one study to our knowledge reporting on the vitamin D status of orthopaedic patients [3]. An adequate level of vitamin D is critical for musculoskeletal health and function and may improve postoperative settings. Data revealing the prevalence of vitamin D insufficiency and deficiency may be of value for the treating orthopaedic surgeons to prevent potential negative consequences in the operative and postoperative settings. To examine the vitamin D status of orthopaedic patients in Germany, the vitamin D levels of patients scheduled to undergo orthopaedic surgery in a German university hospital were tested after admission. We asked the following questions: (1) What is the prevalence of vitamin D insufficiency and deficiency? (2) Is there a seasonal variation of vitamin D deficiency and insufficiency in German orthopaedic patients? (3) What risk factors are associated with vitamin D insufficiency?

Patients and Methods

Between January 1, 2011 and December 31, 2011, the serum 25-OH-D levels of all patients admitted to the orthopaedic department of our institution (1119 patients) were measured on admission. Blood generally was taken on the day of admission. The mean age of the patients was 58 years (± 17.9 years) (Table 1). For the purpose of our analysis, age was categorized into four groups (younger than 30 years, 31–50 years, 51–69 years, 70 years and older) to account for the different dietary and lifestyle habits of patients in these age groups and to investigate their potential effects on serum 25-OH-D levels.

Measurement of serum 25-OH-D was standardized; the hospital laboratory used the ARCHITECT® 25-OH Vitamin D assay (Abbott GmbH & Co KG, Wiesbaden-Delkenheim, Germany). The ARCHITECT® 25-OH Vitamin D assay is a delayed one-step immunoassay including a sample pretreatment for quantitative determination of vitamin D in human serum and plasma using chemiluminescent microparticle immunoassay technology with flexible assay protocols.

Patient demographic variables and background data were collected by chart review and were evaluated for potential relationship with 25-OH-D levels. Noted variables included age, sex, primary musculoskeletal diagnosis, BMI, comorbidities (Table 1), and any vitamin D supplements taken before admission.

As yet there is no universally accepted classification of vitamin D levels. Vitamin D status was categorized primarily according to cut-off points used by Hollis [20] and Grant and Holick [13]. We defined sufficient vitamin D status as a serum 25-OH-D level greater than 30 ng/mL.

Table 1. Patient characteristics

Characteristics	Tested patients
Number of patients	1119 (100%)
Men	482 (43%)
Women	637 (57%)
Age (years)	58 (+/-17.9)
Age groups	
Younger than 30 years	105 (9.3%)
30–50 years	214 (19%)
51–70 years	436 (39%)
Older than 70 years	365 (33%)
Alcoholism	28 (2.5%)
Nicotine abuse	101 (9%)
Obesity (BMI > 30 kg/m ²)	244 (22%)
Carcinoma	174 (16%)
Psychiatric diseases (depression, schizophrenia, borderline psychosis)	183 (16%)
Osteoporosis	162 (15%)
Hypertension	449 (40%)
Cardiovascular disease (chronic/congestive heart failure, myocardial infarction)	
Thyroid abnormality (hypothyroidism/hyperthyroidism)	137 (12%)
Pulmonary disease (chronic obstructive pulmonary disease, asthma)	81 (7.2%)
Renal failure	92 (8.2%)
Infectious diseases (HIV; hepatitis A, B, C; tuberculosis)	22 (2%)
Diabetes	147 (13%)
Oral vitamin D supplement	130 (12%)

Vitamin D inadequacy was defined as a serum 25-OH-D level less than 30 ng/mL and was further divided into vitamin D insufficiency (20–30 ng/mL) and vitamin D deficiency (< 20 ng/mL). The distribution of 25-OH-D and the percentages of patients with insufficient (20–30 ng/mL) and deficient (< 20 ng/mL) 25-OH-D levels were determined.

To investigate the correlation between climate factors and vitamin D levels, the sunshine hours for every month in 2011 were collected by Deutscher Wetterdienst (the German weather center) in the region around Mainz, Germany. Weather data were taken for a radius of 50 km around the city center, corresponding to the living area of most tested patients. For each month we correlated the mean sunshine hours with the mean vitamin D levels measured in the same month to evaluate any significant correlation.

We used univariate analyses to assess the independent relative risk for vitamin D inadequacy or deficiency associated with potential risk factors (age, sex, nicotine abuse,

obesity (defined as a BMI greater than 30 kg/m²), carcinoma, psychiatric diseases, osteoporosis, hypertension, diabetes, cardiovascular diseases, alcoholism, hyperthyroidism/hypothyroidism, pulmonary diseases, renal failure, infectious diseases). All analyses were performed with use of two-tailed tests. The level of significance was set at *p* value of 0.05 or less. Ninety-five percent CI and *p* value were estimated for each risk factor.

To determine what factors are predictors and what factors are confounders of hypovitaminosis, D multivariate linear regression analysis using the vitamin D level as a continuous variable was performed. All collected potential risk factors (age, sex, nicotine abuse, obesity [defined as a BMI greater than 30 kg/m²], carcinoma, psychiatric diseases, osteoporosis, hypertension, diabetes, cardiovascular diseases, alcoholism, hyperthyroidism/hypothyroidism, pulmonary diseases, renal failure, infectious diseases) were included. The level of significance was set at a *p* value of 0.05 or less. With use of a stepwise-forward method, variables were considered to be of significance if they had a final *p* value of 0.05 or less after adjusting for all other variables in our model.

Results

Overall, 84% of patients were vitamin D insufficient and 60% were vitamin D deficient. Of the 1119 vitamin D serum levels measured in this study, only 15% were in the target range of 30 to 60 ng/mL and 1.5% had vitamin D levels higher than 60 ng/mL. The serum 25-OH-D levels for all 1119 patients were normally distributed, with a mean of 17.3 ng/mL, and minimum and maximum values less than 8 ng/mL and 78.5 ng/mL, respectively.

Variations in vitamin D levels between the darker and brighter halves of the year were seen in our patients. During the summer months, the mean 25-OH-D level was 18.75 ng/mL, and during the darker 6 months of the year, the mean level was 16.1 ng/mL. The lowest 25-OH-D concentrations occurred in November (13.7 ng/mL) and peak concentrations occurred in July (22.35 ng/mL) (Fig. 1). The mean sunshine hours per month showed a strong correlation (*p* = 0.005, Pearson's correlation 0.083) with mean 25-OH-D levels (Fig. 2), with higher mean vitamin D serum levels during months with more sunshine hours.

Univariate analyses showed that obesity (*p* = 0.003; odds ratio, 3.06), hypertension (*p* = 0.013; odds ratio, 2.07), osteoporosis (*p* = 0.002; odds ratio, 6.78), diabetes (*p* = 0.001; odds ratio, 4.5), and renal failure (*p* = 0.016, odds ratio 4.79) were associated with hypovitaminosis D. Remarkably, patients with oral vitamin D supplementation before admission had a significantly higher vitamin

Fig. 1 A graph shows the mean 25-OH-D level per month during 2011. During the summer months, the mean 25-OH-D level was 18.75 ng/mL, and during the darker 6 months of the year, the mean level was 16.1 ng/mL. The lowest 25-OH-D concentration occurred in November (13.7 ng/mL) and peak concentration occurred in July (22.35 ng/mL).

Fig. 2 A graph shows the correlation between mean sunshine hours per month and the mean 25-OH-D level, with higher 25-OH-D levels correlating with higher sunshine hours per month.

D level ($p = 0.012$) than patients without any vitamin D supplements. Age ($p = 0.612$) and gender ($p = 0.325$) were not associated with differences in 25-OH-D levels in our univariate analysis. The following variables also were not associated with hypovitaminosis D: nicotine abuse ($p = 0.953$), carcinoma ($p = 0.495$), psychiatric diseases ($p = 0.32$), cardiovascular diseases ($p = 0.715$), alcoholism ($p = 0.075$), hyperthyroidism/hypothyroidism ($p = 0.551$), pulmonary diseases ($p = 0.394$), and infectious diseases ($p = 0.372$) (Table 2).

Multivariate linear regression analysis was performed to evaluate possible predictors for hypovitaminosis D. Variables were considered to be clinically relevant risk factors or predictors if the final p value was less than 0.05.

As in the univariate analysis, osteoporosis was found to be significantly associated with low vitamin D levels ($p = 0.004$), as was hypertension ($p = 0.031$) and diabetes ($p = 0.031$) after adjustment for possible confounders in the

multivariate linear regression analysis. All other factors found to be significantly associated with low vitamin D levels in the univariate analysis showed no significant relationship and were dropped from the model (obesity ($p = 0.056$), and renal failure ($p = 0.319$) (Table 3).

Discussion

Vitamin D plays an essential role in bone health and muscle function. Studies have shown a widespread rate of vitamin D deficiency in the general population [30, 36], but only one to our knowledge has reported on the vitamin D status of orthopaedic patients [3]. The protective and therapeutic effects of vitamin D on bone and calcium metabolism are well known [33]. Extremely low vitamin D levels have been associated with osteomalacia and impaired muscle function [24]. Epidemiologic evidence suggests a possible positive effect of higher vitamin D levels on immune status [25, 40], carcinoma [42], multiple sclerosis [1], cardiovascular diseases [32], and others [19]. We therefore investigated (1) the extent of hypovitaminosis D in orthopaedic patients, (2) seasonal variations in vitamin D levels, and (3) possible risk factors for insufficient vitamin D levels.

There are several limitations to our study. First, the majority of the tested patients in this study were of Euro-caucasian heritage with white skin tones. Given the predisposition of darker skin-toned individuals toward lower 25-OH-D levels, hypovitaminosis D among darker skin-toned orthopaedic patients may be underrepresented in this study [3]. Second, effects of vitamin D supplementation may be underrepresented in this study. Owing to the availability of vitamin D supplements from supermarkets, pharmacies, drug stores, and online stores, the collected data on vitamin D supplementation is very prone to errors and provides very little information [37]. Third, the actual daily sunlight exposure of our patients is only

Table 2. Univariate analyses of potential risk factors for vitamin D insufficiency and deficiency

Variable	Mean vitamin D level (ng/mL)	Significance (p)	95% CI
Age group (n = 1119)			
< 30 years (n = 105)	19 (+/-17.5)	0.699	
31–50 years (n = 214)	18.8 (+/-18)	0.612	
51–70 years (n = 436)	18 (+/-9.4)	0.693	
> 70 years (n = 365)	16.7 (+/-11.2)	0.72	
Sex (n = 1119)			
Male (n = 482)	19.8 (+/-14.9)	0.325	–0.84 to 2.53
Female (n = 637)	20.6 (+/-12.1)	0.325	–0.84 to 2.53
Alcoholism (n = 28)	15.9 (+/-6.4)	0.075	–9.27 to 0.44
Nicotine abuse (n = 101)	20.3 (+/-12.8)	0.953	–2.6 to 2.77
Obesity (BMI > 30 kg/m ²) (n = 244)	17.6 (+/-9.3)	0.003	–5.4 to –1.67
Carcinoma (n = 174)	19.6 (+/-19.9)	0.495	–2.91 to 1.41
Psychiatric diseases (n = 183)	19.4 (+/-12.1)	0.32	–3.18 to 1.04
Osteoporosis (n = 162)	16.9 (+/-12.9)	0.002	3.3 to 7.81
Hypertension (n = 449)	19.1 (+/-11.3)	0.013	–3.78 to –0.45
Cardiovascular disease (n = 243)	20.6 (+/- 19.4)	0.715	–2.1 to 3.04
Thyroid abnormality (n = 137)	20.7 (+/-13.5)	0.551	–3.62 to 6.78
Pulmonary disease (n = 81)	18.5 (+/- 12.5)	0.394	–5.71 to 2.25
Renal failure (n = 92)	17.8 (+/-10)	0.016	–4.91 to –0.51
Infectious diseases (n = 22)	17.8 (+/-7.2)	0.372	–8.23 to 3.09
Diabetes (n = 147)	17 (1/-9.8)	0.001	–6.16 to –1.46
Vitamin D supplement (n = 130)	24.7 (+/-14.2)	0.012	2.42 to 7.68

Table 3. Multivariate linear regression analyses of potential risk factors for hypovitaminosis D

Risk factor	Standard error	Regression coefficient	Beta coefficient	p value
Osteoporosis	1.669	4.81	0.134	0.004
Hypertension	1.006	–2.17	–0.08	0.031
Diabetes	1.301	–2.79	–0.74	0.031

approximated, not truly known. Fourth, elderly patients are more likely to be indoors regardless of time of year compared with younger, active patients. In this context, it is difficult to separate age from sunlight exposure as a risk factor for hypovitaminosis D. Furthermore, the activity level of our patients is unknown.

Fifth, we did not gather any information on the use of sunscreen in our patients. Owing to Germany's geographic position, the use of sunscreen as a part of everyday life is not as common as in some countries. Few data have been published regarding the effect of sunscreen on circulating vitamin D levels, but the results indicate that sunscreen interferes with cutaneous vitamin D production [28].

We found a high prevalence of low serum levels of vitamin D in the orthopaedic patient population. These results are consistent with those of a similar study investigating the prevalence of vitamin D deficiency [3]. Schilling reported that 89% of tested patients in an elderly

care rehabilitation facility had a vitamin D deficiency (defined as a level less than 20 ng/mL) [37]. Bogunovic et al. reported a 43% rate of vitamin D insufficiency in all 723 patients; among those, 40% were vitamin D deficient [3]. A possible explanation of this low rate of vitamin D deficiency in comparison to our results may be the exclusion of patients with comorbid medical conditions that precluded surgery.

In addition, we also showed the extent of seasonal variation in 25-OH-D levels [38]. To our knowledge, no studies to date have described the association between mean sunshine hours and mean 25-OH-D serum levels in central Europe or comparable latitudes (eg, Vancouver, 49°, 17' N). Brustad et al. reported seasonal variations in vitamin D in northern regions (69° N) comparable to our results, but owing to a generally high dietary intake of vitamin D in the tested subjects, the mean vitamin D levels were sufficient (> 30 ng/mL) during all tested seasons [4]. We were able to

show a correlation between sunshine hours per month and patient serum vitamin D levels, with higher mean vitamin D serum levels during months with more sunshine hours. However, even in the months with the most sunshine, the mean 25-OH-D level was not sufficient. In May, the sunniest month in the region around Mainz, we measured a mean 25-OH-D level of 18.75 ng/mL. These data suggest increasing vitamin D production from sunlight is not a realistic option for most orthopaedic patients living in latitudes comparable to that of Mainz (50° N; eg, Vancouver [49°, 17° N], Paris [48°, 51° N], or Kiev [50°, 17° N]).

As in other studies, the mean level of 25-OH-D varied by obesity, diabetes mellitus, renal failure, hypertension, and osteoporosis [6, 27, 41]. In contrast to other studies [3, 22], we were not able to show a variation in 25-OH-D level by age. This finding is contradictory; it may be a habit of older orthopaedic patients being less active and spending less time outdoors than younger persons. The correlation between physical activity, time spent outdoors, and 25-OH-D level has been described [10]. This is likely to be an explanation for the low serum vitamin D levels in our patients with musculoskeletal diseases. We did not identify any sex-related prevalence of vitamin D deficiency. The reported association between sex and vitamin D varies, with some studies describing higher rates in men [3, 14] and others in women [8, 21]. Bogunovic et al. [3], in a prevalence study, and Guardia et al. [14], reported male sex as a risk factor for vitamin D deficiency.

We observed a higher rate of vitamin D deficiency among patients with an established diagnosis of osteoporosis. This finding is not surprising as a couple studies have established the association between vitamin D deficiency and osteoporosis [11, 14]. However, if patients with an established diagnosis of osteoporosis were treated following the national guidelines, we should find a lower prevalence of vitamin D deficiency [3]. The 2009 guidelines of Germany's osteology organization (Dachverband Osteologie) recommend a daily 800 to 2000 IU vitamin D supplement for patients with osteoporosis and a serum 25-OH-D level of 20 ng/mL [7]. Two studies evaluated the positive effects on bone metabolism and potential decrease in the risk of falls and fractures resulting from a sufficient vitamin D supply [2, 39]. In contrast to other developed countries, the diet in Germany is not fortified with vitamin D. In addition, the cutaneous production of vitamin D is reduced during low winter sun exposure caused by the geographic location.

We found a high frequency of vitamin D deficiency among orthopaedic patients in central Germany. More than 80% of the patients in our orthopaedic department were vitamin D insufficient, with values measured below the target of 30 to 60 ng/mL. Adequate vitamin D levels are required for effective bone metabolism, especially among patients with musculoskeletal diseases, but also for many

paracrine effects. Screening and treating hypovitaminosis D is difficult, but it appears to be important in this patient population.

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