The Dependency of Vitamin D Status on Anthropometric Data

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Abstract

Background: Hypovitaminosis D appears to parallel several cardiovascular and pulmonary diseases. However, previous findings cannot be considered conclusive, since the association may have been confounded by different anthropometric variables that were not accounted for. The present cross-sectional study was conducted to investigate the association between important explanatory variables and circulation levels of vitamin D.

Methods: A total of 553 individuals attending the metabolic and medical lifestyle management clinic of the Burdwan district of India were selected from 1289 people by simple random sampling, and information regarding relevant variables and their blood was obtained. Serum 25-hydroxyvitamin (OH) D level and forced expiratory volume in 1 second were measured. Associations between different explanatory variables and circulatory 25(OH) D were analysed in linear regression models.

Results: Of the population studied, 53% had insufficient vitamin D levels, while approximately 9% were vitamin D deficient. Variables that significantly associated with lower 25(OH)D levels were obesity, current smoking, forced expiratory volume 1 and depression.

Conclusion: Lower serum levels of vitamin D were associated with different variables that should be explored in several diseases before a conclusion of hypovitaminosis D is drawn.

Keywords: vitamin D, confounding variables, vitamin D deficiency, obesity, 25(OH)D

Introduction

The role of vitamin D in calcium and bone homeostasis is well described. In recent years, it has been recognised that, in addition to this classical function, vitamin D modulates a variety of processes and regulatory systems, including host defence, inflammation, immunity, and repair (1). A low level of vitamin D in blood is common, and represents a major health problem. Early in life, vitamin D deficiency causes growth retardation and rickets, while it is well known to accelerate osteopenia and osteoporosis in adults. Accumulating evidence also links a low vitamin D nutritional status to highly prevalent chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, cardiovascular diseases (2–4) and chronic obstructive pulmonary disease (COPD) (5). However, there is a need to examine the causal relationship between levels of vitamin D and different contributory variables. These facts prompted us to study the relationship between important variables, such as age > 50 years, female gender, obesity and underweight, seasonal variation, forced expiratory volume $(FEV)_1$ or depression and levels of vitamin D. As 25-hydroxyvitamin (OH) D is the principal circulating vitamin D metabolite, and is recognised as the optimum short-term biomarker of total exposure to vitamin D (6), we measured this metabolite to detect vitamin D status.

Materials and Methods

Study area

The present study was conducted in the Department of Biochemistry of Burdwan Medical College, Burdwan, West Bengal, India, with the collaboration of a metabolic and medical lifestyle management clinic. All participants were recruited from the same geographical area of the northern and southern areas of the Burdwan district.

Selection of participants

A total of 553 individuals were selected, from 1 289 healthy people residing in the study area, by simple random sampling between February 2011 and May 2013, after informed consent

had been received. Information regarding age, gender, smoking habits and history of depression were gathered. All participants who had been diagnosed with autoimmune diseases, COPD or cancer in the last 5 years were excluded.

Anthropometric measurements

Weight and height measurements were obtained using standardised techniques (7). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m²). The participants were categorised as underweight (BMI < 18.5), normal (BMI 18.5–24.99), overweight (BMI 25.0–29.99) or obese (BMI 30.0 or more), according to the current World Health Organization classification.

Pulmonary function tests

Pulmonary function was measured by trained staff, both pre-and post-inhalation of 0.4 mg salbutamol, using a spirometer (HELIOS 401). As FEV_1 is the most reproducible lung function test parameter, it is the most suitable for the assessment of a large group of people. Spirometric values were post-bronchodilator measurements, and absolute values were expressed as percentage predicted of reference values (8).

Measurement of depression symptomatology

Depressive symptomatology was measured using the Centre for Epidemiologic Studies Depression Scale (CES-D), whereby a positive score of 16 or more defined depression (9).

Collection of samples

Peripheral venous blood was drawn and allowed to coagulate at room temperature for 30–45 min, and was then centrifuged at 2500x g for 15 min. All serum samples were stored at −70 °C until chemical analysis was performed.

Parameters assay

Serum 25(OH) D was estimated by enhanced chemiluminescent assay (ECI) using instrument VITROS ECi (Johnson & Johnson) and a dedicated reagent (10).

Statistical analysis

We performed standard statistical analysis on the data for biochemical analysis using the Statistical Package for Social Sciences (SPSS) 11.5 software for Windows. Serum concentrations of 25(OH)D were normally distributed. Differences in mean 25(OH)D by univariate predictors were examined with parametric tests. We analysed the relationship between study category and levels of 25(OH)D, by both linear and logistic regression, after adjusting for possible confounders, such as season, gender, age, BMI, smoking, and comorbidities. A cut off level for vitamin D deficiency was defined as 20 ng/mL for the logistic model. When building the regression models for the levels of vitamin D among the study population, we used a backward stepwise method for both the linear and logistic models. The following variables were included from the beginning; age, gender, BMI, food habits, FEV_1, comorbidity, and CES-D score. Variables remained in the model if their significance level was less than 0.10. After the first run, all excluded variables were reintroduced one at a time.

Results

The characteristics of the study population

Personal profile and clinical details of the study population are shown in table 1. Data are expressed as numbers (group percentages in parentheses) for categorical variables and mean values standard deviation (SD) for continuous variables. When variables were not normally distributed, median values (Q1–Q3 IQR in parentheses) are given instead (indicated by †); IQR means interquartile range. Pack-years were expressed as the numbers of packs of cigarette smoked per day x the number of years the person has or had smoked. Quit-years were the number of years since a patient had stopped smoking.

Distribution of concentration of serum 25(OH)D among study population

The median serum 25(OH) D level of the study population was 26 ng/mL. On the basis of changes in parathyroid hormone levels and intestinal calcium transport that have been noted, values of 20–30 ng/mL are considered to be vitamin D relatively insufficient (4), while deficient serum levels are < 20 ng/mL (11) and desirable (or sufficient) circulating vitamin D levels are at least 30–40 ng/mL (4,12,13). However, there are suggestions that levels above 40 ng/mL may be necessary for optimal immune functioning and overall health (14–16). In the present study, almost 53% of the population had vitamin D levels in the insufficient range, and approximately 9% were vitamin D deficient (< 20 ng/mL), as shown in figure 1.

Factors associated with 25(OH)D in the study population - univariate analysis

Concentrations of 25(OH)D for different explanatory variables among the study population

are shown in table 2. Age > 50 years, female gender, obesity and underweight, seasonal variation or depression were all associated with significantly lower levels of serum 25(OH)D. Seasonal variation of serum 25(OH)D3 was defined as the difference between winter and summer values (17).

Factors associated with 25(OH)D in the study population – multivariate analysis

To demonstrate the role of lung function, obesity, smoking and season in reduction of serum vitamin D, multiple and logistic regression analysis was performed. We found that mean

Table 1: Personal profile and clinical details of the study population

Demographic profiles	Number (%) (n = 552)	
Age (44 ± 7.14)		
< 50 years (32 ± 7.83)	282	(51)
> 50 years (57 ± 6.31)	270	(49)
Gender		
Male	319	(58)
Female	233	(42)
BMI (kg/m²) (23.56 ± 5.83)		
< 18.5	22	(4)
18.5−24.9	315	(57)
25−30	160	(29)
> 30	55	(10)
Smoking habits		
Never	121	(22)
Ex-smoker	188	(34)
Current smoker	243	(44)
Pack-years†	39	(30−52)
Quit-years	1	(0−8)
Depression, CES-D score ≥ 16		
Yes	28	(5)
Season#		
Winter	88	(16)
Spring	116	(21)
Summer	304	(55)
Autumn	44	(8)
Food habits		
Vegetarian	265	(48)
Non-vegetarian	287	(52)

#Season was defined as winter (December-March), spring (April-May), summer (June-September) and autumn (October−November).
*FEV₁: Forced expiratory volume in 1 second that is expressed in % of VC.
Abbreviations: BMI = body mass index; CES-D = Centre for Epidemiologic Studies Depression Scale.

Table 2: Serum concentration of 25(OH)D in ng/mL, for different confounding variables

Contributory variables	25(OH)D in ng/mL	P value
Age (year)		
< 50	32.25 ± 7.56	0.001
> 50	22.48 ± 5.38	
Gender		
Male	30.37 ± 10.1	0.015
Female	24.7 ± 9.6	
BMI (kg/m²)		
< 18.5	20.7 ± 9.8	0.042
18.5−24.9	31.87 ± 7.93	
25−30	33.93 ± 6.31	
> 30	26.21 ± 8.75	
Smoking habits		
Never	34.56 ± 9.28	0.031
Current smoker	22.23 ± 9.56	
Ex-smoker	26.73 ± 10.26	
Depression		
Yes	25.97 ± 9.96	0.002
No	29.32 ± 7.32	
Season		
Winter	28.61 ± 9.25	0.916
Spring	27.36 ± 5.37	
Summer	30.37 ± 6.26	
Autumn	26.62 ± 8.47	
Food habits		
Vegetarian	23.83 ± 5.82	0.179
Non-vegetarian	30.72 ± 4.28	

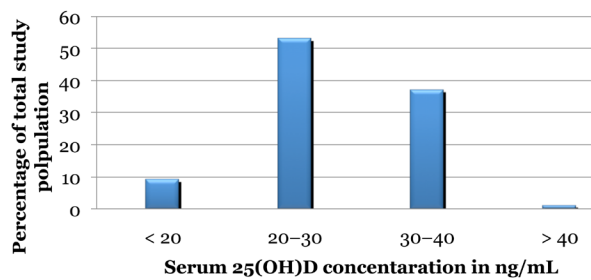Abbreviation: BMI = body mass index.

Figure 1: Bar chart of serum 25(OH)D concentration in the study population.

levels of 25(OH)D remained reduced in serum, even after adjustment, as shown in tables 3 and 4.

Discussion

Vitamin D deficiency causes the development of imbalanced calcium- and phosphate-homeostasis, as well as the bone diseases osteopenia, osteoporosis, rickets, and osteomalacia, with a subsequently increased fracture risk (18). In order to identify the different important predicting variables of circulating

Table 3: Multiple linear regression analysis showing the relationship between baseline predictors and serum levels of 25(OH)D

Explanatory variables	25(OH)D		
	Coefficient	**95% CI**	**_P_ value**
BMI (kg/m²)	−0.38		
< 18.5	−2.78	−0.57 to −0.18	< 0.001
18.5–24.9	0	−6.56 to 1.09	0.12
25–30	−1.56	−3.75 to 0.68	0.15
> 30	−6.65	−9.65 to −3.65	< 0.001
Season			
Winter		0	
Spring	3.23	−0.05 to 6.12	0.051
Summer	7.03	4.32 to 9.45	< 0.001
Autumn	2.74	−1.75 to 7.12	0.22
Depression (CES-D score ≥ 16			
Yes	−3.26	−5.79 to −0.81	0.006
No	0		
Smoking			
Ex	0	−6.15 to −1.93	< 0.001
Current	−4.09		
Comorbidity			
< 2	0		
≥ 2	0.148	0.139 to 0.157	< 0.001
Dietary habits			
Non-vegetarian	0		
Vegetarian	−3.94	−4.89 to −3.12	0.002
Body complexion			
Clear	0		
Fair	2.95	−0.45 to 5.56	0.28
Black	−0.158	−0.96 to −0.194	< 0.001

Abbreviations: BMI = body mass index; CES-D = Centre for Epidemiologic Studies Depression Scale; CI = confidence interval; _P_ value is statistically significant (_P_ < 0.05).

vitamin D, we analysed the association of these variables with 25(OH) D levels. Age is an important predictor of circulating vitamin D levels; we found that aged individuals possessed a lower amount of this vitamin. Vitamin D synthesis occurs in the skin in response to light, but this decreases in efficiency with increasing age (19).

Since the levels of several hormones, including sex hormones, can be modified by vitamin D (20,21) it is not surprising that women had lower levels of vitamin D in serum than did men in the present study. On average, men have 10–15% less fat content than women with the same BMI (22). Therefore, less vitamin D will be stored in fat tissue after cutaneous synthesis and more will stay in the blood in men (23).Vitamin D is also eliminated faster from the blood than it is from fat (24), and the amount of 25(OH)D in fat tissue may not be sufficient to maintain more stable serum 25(OH)D levels throughout the year. In addition, women have a larger amount of subcutaneous fat, which may store more vitamin D (4,23). It has recently been hypothesised that vitamin D-binding protein (DBP) may also play a role in gender differences in vitamin D status (25). Interestingly, the correlations between DBP and adiposity (percentage body fat) were negative

Table 4: Multiple logistic regression analysis showing the relationship between baseline predictors and serum levels of 25(OH)D

Explanatory variables	25(OH)D < 20 ng/mL		
	OR	95% CI	*P* value
BMI (kg/m²)	1.03	1.04 to 1.18	0.007
< 18.5	1.36	0.57 to 3.89	0.42
18.5-24.9	1		
25-30	1.04	0.56 to 1.99	0.7
> 30	4.18	1.94 to 9.03	< 0.001
Season			
Winter	1		
Spring	0.74	0.35 to 1.53	0.41
Summer	0.24	0.12 to 0.45	< 0.001
Autumn	0.58	0.21 to 1.65	0.28
Depression (CES-D score ≥ 16			
Yes	1.72	0.89 to 3.27	0.078
No	1		
Smoking			
Ex	1	1.78 to 5.37	< 0.001
Current	3.18		
Comorbidity			
< 2	1		
≥ 2	5.32	1.67 to 9.75	< 0.001
Dietary habits			
Non-vegetarian	1		
Vegetarian	2.98	1.12 to 3.47	< 0.001
Body complexion			
Clear	1		
Fair	0.43	0.22 to 0.69	0.12
Black	4.92	2.87 to 6.23	< 0.001

Abbreviations: BMI = body mass index; CES-D = Centre for Epidemiologic Studies Depression Scale.

in men and positive in women (25). In women, DBP was significantly higher than in men, and correlated positively with total 25(OH)D (17).

Adiposity and BMI in non-morbidly obese individuals are also inversely correlated with vitamin D status. A previous study found that the association between adiposity and serum 25(OH)D is greater than that between body weight and BMI (26). This may be because BMI and body weight do not necessarily reflect the percentage of body fat. Athletes and other well-trained people may have a relatively high BMI, and may be considered overweight, or even obese, but they have quite a low total fat mass (27). Outdoor activity may reduce the risk of hypovitaminosis D by 50%, but severely obese people may be outdoors less often, because they have limited mobility (28,29). A possible explanation for obesity-associated vitamin D insufficiency is a decreased bioavailability of 25(OH)D3, as body fat may act as a reservoir for storage of the fat-soluble vitamin D, reducing its bioavailability (23). A negative correlation between serum 25(OH)D levels and magnitude of weight loss in patients after surgical treatment for morbid obesity confirms this theory (24,30). A contributory factor to the low vitamin D status among obese people might be a lower than average exposure to the sun of large body areas. It is assumed that secondary hyperparathyroidism, observed frequently in overweight and obese populations (31), may be the result of low serum 25(OH)D levels.

Season was not a strong predictor of 25(OH)D levels in our study. Vitamin D is a fat-soluble vitamin, so it can be stored in the body and might be minimally affected by seasonal variation. Cigarette smoking is also a potential explanatory variable of vitamin D concentration; we found that concentration was significantly reduced in smokers. Current smokers primarily exhibit increased skin aging induced by smoking (32) and this leads to a reduced capacity for synthesis vitamin D in aging skin (1). Nevertheless, the study could not excluded the racial effect on vitamin D level and further study is needed to confirm the fact.

In accordance with several previous studies, we found an increased prevalence of vitamin D deficiency in participants with depression (29,33) or depressive symptoms (34). This is most likely due to patients with depression typically spending less time outdoors, being careless regarding their food intake and having less physical activity.

After adjustment, it was clearly demonstrated that all the individual variables were separately responsible for a low level of vitamin D level in

the serum of the participants.

Conclusion

Several confounding variables (such as age, gender, food habits, nutritional status, mental status of individual, smoking habits, and lung function) affect circulating levels of vitamin D, and these have strong individual causal relationships with regard to reducing these levels in blood in the normal population. Therefore, the lower serum level of vitamin D that is associated with different variables should be explored before drawing a conclusion of hypovitaminosis D in several diseases.

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Conflict of Interests

None.

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Authors' Contributions

Conception and design: SD
Analysis and interpretation of the data and final approval of the article: MP
Critical revision of the article for the important intellectual content: SD, MP, AD

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