Published in final edited form as:

Clin Endocrinol (Oxf). 2008 September ; 69(3): 374–381. doi:10.1111/j.1365-2265.2008.03216.x.

Vitamin D and bone health in adults with cystic fibrosis

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Summary

Background—Cystic fibrosis (CF) patients have chronic pancreatic insufficiency leading to malabsorption of fat-soluble vitamins, including vitamin D which can contribute to poor skeletal health and respiratory function.

Objective—This study evaluated the prevalence of vitamin D insufficiency and its impact on bone and respiratory health in adults with CF.

Design and measurements—This was a retrospective study in which data were collected from medical records over a 2-year period. Data included patient demographics, lung function, biochemical data, bone mineral densities, X-rays and ascertainment of use of vitamin supplements. Data were collected from medical records at a single accredited CF Center. Serum 25-hydroxyvitamin D [25(OH)D] levels and bone mineral density studies were also collected.

Patients—A total of 185 adults with CF were identified with a mean age of 29 ± 9 years.

Results—The prevalence of vitamin D insufficiency [25(OH)D < 75 nmol/l] was 76%. Mean serum 25(OH)D concentrations were 58.8 ± 30 nmol/l. Use of specific vitamin D supplementation was protective against vitamin D insufficiency whereas use of multivitamins was not. There was a small, but significant, positive association between serum 25(OH)D and FEV₁ per cent predicted after controlling for age, gender, BMI and race ($R^2 = 0.30$, $P < 0.001$). A high prevalence (27%) of vertebral fractures was detected on lateral chest X-ray.

Conclusions—The prevalence of vitamin D insufficiency and poor skeletal health is high in the US CF population. Vitamin D status appears to be positively associated with lung function. Prospective studies to examine the impact of correction of vitamin D insufficiency on skeletal and lung health in adult CF are warranted.

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Introduction

Cystic fibrosis (CF) is one of the most common fatal genetic disease in non-Hispanic whites in the United States. CF is characterized by chronic respiratory failure (the most common cause of death), recurrent infections and pancreatic insufficiency, leading to decreased life expectancy.¹ Over the past several decades, improvements in respiratory and nutritional care and the development of specialized CF care centres have increased the life expectancy for CF significantly.² However, this improvement in median survival, now at 36.5 years³ has come at the expense of early development of adult-onset diseases, including osteoporosis.

The cause of low bone density in adults with CF is due to many factors, including genetics,⁴ glucocorticoid use, poor nutrition, hypogonadism, physical inactivity and malabsorption of vitamin D due to fat malabsorption from pancreatic insufficiency.⁵ The exact pathogenesis of poor skeletal health in CF patients is unclear; however, nutritional factors likely play a major role.⁶

One of the major nutritional factors that results in poor skeletal health in CF patients is vitamin D insufficiency. Serum 25-hydroxyvitamin D [25(OH)D] levels in CF patients start to decline in adolescence.⁷ This phenomenon is thought to be secondary to fat malabsorption as well as decreased exposure to sunlight.⁸ Lark *et al.* demonstrated that adult CF patients absorb 50% less vitamin D than matched healthy controls.⁹ The prevalence of vitamin D insufficiency [defined as a serum 25(OH)D level < 75 nmol/l] was reported to be as high as 81% in one specialized CF centre.¹⁰ Vitamin D insufficiency increases the risk for osteoporosis and subsequently vertebral fractures. The prevalence of occult vertebral fractures has been reported to be as high as 51% in the adult CF population.¹¹ Vertebral fractures result in chronic pain and kyphosis, which further result in worsening respiratory health.¹²

In addition to preserving skeletal health, vitamin D may have other health benefits, including improving both respiratory muscle and skeletal muscle function.^{13,14} In healthy adults studied in the Third National Health and Nutrition Examination Survey (NHANES III), there was a positive association between vitamin D status and lung function (measured by forced expiratory volume in the first second or FEV₁).¹⁴ Also, several trials have demonstrated that vitamin D administration may improve muscle function by preventing falls in the elderly.¹⁵ Furthermore, vitamin D may play a beneficial role in improving the innate immune system against chronic respiratory infections by up-regulating specific antimicrobial peptides.¹⁶

In the present study, we sought to determine the prevalence of vitamin D insufficiency and vertebral fractures and to examine other bone health parameters in our population of adults with CF. We also sought to determine what factors were associated with vitamin D insufficiency. Finally, we sought to determine whether there was an association between vitamin D status and FEV₁ as previously reported in non-CF populations.¹⁴

Methods

Study design

The study was approved by the Emory University Institutional Review Board (IRB). We conducted a retrospective chart review examining records of patients seen at the Emory University Cystic Fibrosis Center in 2004 and 2005.

Subjects

All men and women of 18 years and older were included for the analysis. The diagnosis of CF was made by either a positive sweat test and/or genetic testing, together with the appropriate clinical signs and symptoms.

Study protocol

Using medical records, we collected basic demographic information including each subject's age, race and gender. Lung function was measured using the FEV₁, a marker of severity of lung disease in CF. The best and worst forced expiratory volumes in one second (FEV₁) were measured by spirometry and expressed as a percentage of the predicted value, corrected for height, age, race and gender. We chose to analyse both best and worst FEV₁ as markers of clinical stability. We collected each subject's documented use and quantity of multi-vitamins, vitamin D supplements, calcium supplements and pancreatic enzymes.

We collected information related to bone health including serum 25(OH)D, intact PTH, total calcium, alkaline phosphatase, and albumin concentrations in blood. Serum calcium, alkaline phosphatase, and albumin were measured by a colorimetric assay (Beckman analyser). Intact PTH and 25(OH)D levels were determined by chemiluminescent immunoassay (ARUP, Salt Lake City, UT) during this study period. When subjects had multiple tests for vitamin D status, we used the first 25(OH)D concentration collected.

The calcium level reported was corrected for albumin {corrected calcium = serum calcium + $[0.8 \times (4 - \text{serum albumin})]$ }. Those values of calcium or albumin that did not have the other corresponding value were not included. In all comparisons the laboratory values used were those from the same or closest to the same date when the 25(OH)D level for that year was drawn. When reporting seasonal variation of vitamin D level, all 25(OH)D levels documented for each patient were used. The seasons were arranged accordingly: Winter: December, January, February; Spring: March, April, May; Summer: June, July, August and Fall: September, October, November. Subjects were considered to have vitamin D insufficiency if the 25(OH)D level was < 75 nmol/l and vitamin D deficiency if the 25(OH)D level was < 37.5 nmol/l.

Bone mineral density (BMD) measurements

We collected BMD (g/cm²) measured in the lumbar spine (L1–L4) using a GE Lunar Prodigy scanner (software version 7.53). We collected the absolute BMD values (g/cm²), Z-score and T-score. We also calculated how many subjects had T-score < -2.5 and T-scores > -1 and < -2.5.

Radiographic analysis

A single radiologist reviewed lateral chest radiographs from subjects who had radiographic films available for thoracic vertebral deformities. The presence of vertebral fractures was defined by a 25% or greater decrease in vertebral body height; those fractures were graded using the Genant classification method.¹⁷

Statistical analysis

Data analysis was performed on GRAPHPAD INSTAT version 3.00 (San Diego, CA) and SAS 9.1 (SAS Institute, Cary, NC). Descriptive statistics were used to determine the means and SD of the subjects' demographics. The 25(OH)D levels were normally distributed. Both independent samples *t*-test and paired *t*-tests were used to compare means depending on the situation. Fisher's exact test was used to compare categorical data if counts were < 5; otherwise, Pearson's χ^2 was used. The 25(OH)D levels were correlated to covariates (gender, age, BMI and race) using Pearson's *r* correlation. We used multiple linear regression using PROC REG to examine the association between FEV₁ and 25(OH)D and stepwise regression using PROC LOGISTIC to calculate odds ratios. Factors examined included multivitamin use, pancreatic enzyme use, race, vitamin D supplement use, BMI, age, gender and season of blood draw. We considered each 25(OH)D measure to be unique even though some subjects had multiple 25

(OH)D levels to ensure that we accounted for the appropriate season of blood draw. We used Proc GLM with a repeated statement to compare means of these samples. One way analysis of variance (ANOVA) was used to assess seasonal variation of 25(OH)D levels. A $P < 0.05$ was considered statistically significant.

Results

Subjects

We identified 185 adult subjects with CF attending the Emory University Cystic Fibrosis Center during 2004 and 2005. Demographic data are displayed in Table 1. The population was comprised of 98 (53%) males and 87 (47%) females; and 172 (93%) non-Hispanic whites and 13 (7%) non-Hispanic blacks. Baseline characteristics of the population revealed a mean age of 29 ± 9 years and a mean BMI of 21.2 ± 3.3 . The best mean FEV₁ per cent predicted was 64.2 ± 24.7 and the worst FEV₁ per cent predicted was 49.9 ± 22.9 , respectively.

Seventy per cent of subjects reported use of daily multivitamins during 2004–05 (Table 1). Less than half of the subjects (47.6%) reported the use of vitamin D supplementation (typically in the form of an ADEK vitamin or combined with calcium supplements, in the range of 200–1200 IU daily). Two subjects received replacement doses (50 000 IU weekly and 50 000 IU every 3 weeks, respectively). Only 37% (68 subjects) were taking both multivitamin and vitamin D supplements during the 2-year period. Forty-three per cent of subjects took calcium supplements and 88% were receiving replacement pancreatic enzymes.

Markers of bone health

Vitamin D Status—Serum 25(OH)D concentrations were determined in 156 patients over the 2-year period indicating that 14.8% of patients did not have 25(OH)D levels checked during that time period (Table 2). Using the first 25(OH)D measure, the mean 25(OH)D levels were in the insufficient range at 58.8 ± 30 nmol/l. As 44.8% of subjects had follow-up measures for 25(OH)D, we conducted sensitivity analyses in those with repeat measures. The mean 25(OH)D using the average of all 25(OH)D collected for an individual patient was 55 ± 30 nmol/l which was not statistically different from the mean 25(OH)D using just the first measure. Vitamin D insufficiency [25(OH)D level < 75 nmol/l] was present 76% subjects while 23.0% of subjects had evidence of vitamin D deficiency [25(OH)D < 37.5 nmol/l]. The mean corrected serum calcium (mg/dl) was 9.3 ± 0.4 while the mean serum albumin level was 3.6 ± 0.4 g/dl. The mean alkaline phosphatase was 120 ± 88 unit/dl. There were no differences in corrected serum calcium or alkaline phosphatase when comparing vitamin D insufficient and sufficient subjects.

Bone mineral density—Eighty-four subjects (45%) had BMD testing over the 2-year period. During the study period, 34 of the 84 subjects (52%) with BMD measurements had a T-score < -1.0 and 8 (10%) had a T-score < -2.5 at the lumbar spine (Table 2).

Factors associated with vitamin D insufficiency

We pooled 2004 and 2005 data to determine factors associated with vitamin D insufficiency. The prevalence of vitamin D insufficiency was higher in men than in women (84% in men vs. 70% in women, $P = 0.02$) (Table 3). Black subjects had lower 25(OH)D than white subjects (Table 4) and not one black patient was sufficient while only 25% of white subjects were sufficient (Table 3). As expected there was also seasonal variability with the greatest deficiency occurring in the winter (Tables 3 and 4, RFig. 2). Those who used a vitamin D supplement had significantly less vitamin D insufficiency and had higher 25(OH)D levels compared to those who did not use a supplement (Tables 3 and 4) Each of these factors, except gender, was significant after stepwise logistic regression (Table 5). Those who failed to use vitamin D

supplements had a greater risk of insufficiency ($O = 2.5$, 95% CI = 1.44–4.21) and as did blacks ($OR = 10.6$, 95% CI = 4.04–27.72). Having blood a 25(OH)D measure drawn in the fall was inversely associated with vitamin D insufficiency ($OR = 0.52$, 95% CI = 0.41, 0.66) when compared with those having a measure in the winter.

We examined the linear associations of 25(OH)D with race, vitamin D supplement use, season, age and BMI (modelled as continuous variables), pancreatic enzyme use and gender. Stepwise regression revealed that race, vitamin D use and season were significant (Table 6). Black race was associated with an average 25(OH)D decrease of 31.0 nmol/l. Those using vitamin D supplements had higher average 25(OH)D levels than those who did not use supplements (15.4 nmol/l, $P = 0.003$).

There was a positive association between vitamin D status and lowest annual per cent predicted FEV_1 ($\beta = 0.25$, $P = 0.05$, Fig. 1). This model ($R^2 = 0.30$, P of model < 0.0001) controls for age, gender, BMI and race which were all significant confounders of this association. There was also a positive but weak association between best annual FEV_1 per cent predicted and 25(OH)D ($\beta = 0.24$, $P = 0.07$), although this did not reach significance.

Vertebral deformities

One hundred and forty-three subjects (77%) had lateral chest radiographs during the study period. Thirty-nine subjects (27%) had at least one vertebral fracture over the 2-year period. Sixteen subjects (11%) had two vertebral fractures and 8 (6%) had three or greater. Out of a total of 71 vertebral fractures, most fractures (86%) were grade 1 according to Genant's method;¹³ 11% were grade 2 and only one was a grade 3 fracture. A discrepancy between the 2 years was seen in 12 subjects; 7 had new fractures in 2005 and 6 had fractures in 2004 that were not reported on X-rays from the comparison year.

Of those subjects with vertebral fractures, only 30 (77%) had vitamin D levels documented. The mean vitamin D level in those with vertebral fractures was 60 ± 30 nmol/l, which was not statistically significantly different from subjects without fracture. Twenty-four subjects (80%) had vitamin D insufficiency [25(OH)D < 75 nmol/l] and five (17%) had vitamin D deficiency [25(OH)D < 37.5 nmol/l]. Subjects who had evidence of a vertebral fracture had lower FEV_1 compared to subjects without a vertebral fracture ($P < 0.001$). There were no differences in age, BMI, vitamin D supplement or multivitamin supplement use comparing those with vertebral fractures and those without vertebral fractures.

Discussion

The major finding from our study was that the majority of our CF adult population had vitamin D insufficiency, and approximately one quarter of those had vitamin D deficiency with blood 25(OH)D levels < 37.5 nmol/l. We also discovered that vitamin D status was infrequently checked in our CF Centre population. Less than two-thirds of the subjects in our study had an annual 25(OH)D determination over a 2-year period. Recommendations by the CF Consensus Conference advise checking vitamin D status at least yearly.¹⁸

Similar to other studies, we also found a strong seasonal variation in 25(OH)D levels. This reinforces the need for vitamin D screening prior to and during the winter months.¹⁹ In some CF patients who have low normal vitamin D status (i.e. 75–100 nmol/l) prior to and/or during the winter, it may be appropriate to treat with pharmacological doses of vitamin D in the winter months to prevent insufficiency.

The prevalence of vitamin D insufficiency in our study may be higher than previously reported studies as we employed the newly established cut-off of 75 nmol/l as proposed by the Cystic

Fibrosis Foundation.^{5,10,19,20} Our results are most consistent with Boyle *et al.* who found that 81% of 134 adult patients with CF were vitamin D insufficient [25(OH)D < 75 nmol/l].¹⁰ Optimal levels of 25(OH) have been proposed to be at least 80 nmol/l²¹ to best prevent fractures and to maximize intestinal calcium absorption.²²

Another important finding from our study is the significant positive association between 25 (OH)D and lung function, as expressed by FEV₁ per cent predicted. This finding is consistent with the recent NHANES III cross-sectional study.¹⁴ A positive relationship was seen in a similar cross-sectional study in CF subjects by Stephenson *et al.* who found a trend towards higher FEV₁ associated with higher 25(OH)D.¹⁹ The underlying causal relationship between vitamin D level and respiratory status is currently not well understood. Vitamin D improves muscle strength in the elderly to prevent falls;¹⁵ however, the effect of vitamin D on respiratory muscles has not been studied. It is also plausible that patients with more severe disease, and therefore lower FEV₁ per cent predicted, have decreased physical activity and less sun exposure resulting in decreased vitamin D production in the skin. Low bone density resulting from chronic pulmonary disease is associated with risk for kyphosis and vertebral fractures which can further decrease FEV₁.^{23,24} An interventional study with vitamin D to improve respiratory status has not been published to date.

Another key finding from our study was that the majority of subjects who underwent BMD testing had low bone density. There was a trend of lower BMD with lower 25(OH)D; however, this did not reach statistical significance. Further, there was a high prevalence of thoracic vertebral fractures in our population which was associated with lower FEV₁. This is similar to what has been previously reported.^{25,26} Aris *et al.* reported the presence of occult fractures in 51% of their CF population by lateral chest X-ray.²⁷ Lateral chest X-rays often do not adequately evaluate the spine and are even more difficult in CF patients who frequently have parenchymal abnormalities which obscure vertebral bodies. Therefore, the high prevalence of vertebral fractures in our patient population is likely an underestimation of the total number who with vertebral fractures.²⁸ The rates of occult vertebral fractures found in our CF population are higher than the prevalence than seen in middle-aged men and women (14%).²⁹ The presence of a vertebral fracture increases the risk for subsequent vertebral and hip fractures; thus, it is important that these patients are identified and appropriately evaluated for osteoporosis therapy.³⁰

Use of a multivitamin containing 400 IU of vitamin D alone was not protective against vitamin D insufficiency. However, use of a separate vitamin D supplement was positively associated with a reduced risk of vitamin D insufficiency, though it did not absolutely prevent vitamin D insufficiency. This finding is consistent with published literature that this level of vitamin D supplementation is not sufficient to prevent vitamin D insufficiency in most individuals with CF.^{10,19}

Correction of vitamin D insufficiency can be challenging in the CF population. Boyle *et al.* found that 61 out of 66 CF subjects with vitamin D insufficiency failed to raise 25(OH)D above 75 nmol/l with ergocalciferol 50 000 twice a week for 8 weeks.¹⁰ An additional 33 subjects completed a second course of ergocalciferol 50 000 IU twice a week for 8 weeks and none of the subjects achieved 25(OH)D levels above 75 nmol/l. Ergocalciferol (vitamin D₂) has been reported to be less effective than cholecalciferol (vitamin D₃) in non-CF populations in raising 25(OH)D levels.³¹ Stephenson *et al.* conducted a retrospective study in 249 adult subjects with CF to examine whether cholecalciferol corrected vitamin D insufficiency. When CF subjects with vitamin D insufficiency were counselled by dieticians to take additional cholecalciferol averaging 500–700 IU daily for > 3 months, only 17% reached the optimal 25(OH)D level of > 75 nmol/l. The CF consensus conference guidelines for bone health recommend considering phototherapy in CF patients who continue to be vitamin D insufficient.⁵ There are limited

published protocols on how to improve vitamin D status by using UVB radiation. Chandra *et al.* demonstrated in a small pilot study that a portable desktop device used commercially for tanning could raise 25(OH)D levels in adult CF subjects after 8 weeks; however, levels still remained in the insufficient range.⁸ Gronowitz *et al.* demonstrated in 30 adolescent and adult CF subjects that UVB radiation by an indoor lamp three times a week for 6 months could effectively increase 25(OH)D levels from a mean of 55–110 nmol/l.³² There still remains a significant need to develop a standard protocol to improve vitamin D status in adolescent and adult CF patients. Vitamin D is likely needed in much higher doses than the current guidelines.

There are limitations to this study. Our data were cross-sectional and as such, we cannot demonstrate a definite causal relationship of vitamin D insufficiency on fractures or FEV₁. Our study included only adults, and as such, the findings may not be applicable to other age groups, such as adolescents or children with CF. Further, the vast majority of our patients were white, and again the findings may not apply to other patients of different races. However, the distribution of races in our study is reflective of the United States CF population as a whole. Another limitation of our study is that we did not adjust our results for socioeconomic status. There are some data that socioeconomic status influences health outcomes in CF.³³

In summary, our study revealed a high prevalence of vitamin D insufficiency in adults with CF and inadequate screening for vitamin D status. We also found a high prevalence of unrecognized vertebral fractures by lateral chest X-ray and that higher vitamin D status was associated with better lung function. Improved screening and treatment of vitamin D insufficiency is urgently needed in this population. Clinical studies should examine what is the optimal level for 25(OH)D in CF patients for skeletal health and the role of vitamin D for other nonskeletal functions including respiratory health and immune function against chronic respiratory infections.

Acknowledgments

The authors would like to acknowledge the assistance from the staff of the Emory University Cystic Fibrosis Center, Dr Arlene Stecenko and Dr Michael Schechter. This work was supported by grants from Proctor & Gamble Pharmaceuticals, NIH Grant #K23AR054334 and Cystic Fibrosis Foundation Center Grant, #C029-07, University Research Committee (URC) of Emory University and the UV Foundation.

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Fig. 1.

Lowest annual FEV₁% compared to blood 25-hydroxyvitamin D concentrations in adult subjects with cystic fibrosis. The lowest annual FEV₁% predicted annually for each subject was plotted vs. 25-hydroxyvitamin D (nmol/l) over a two year period (2004–05). There is a positive correlation between FEV₁% predicted and 25-hydroxyvitamin D ($\beta = 0.25$, $P = 0.05$) when controlling for gender, race, age and BMI.

Fig. 2. Seasonal variation of 25-hydroxyvitamin D [25(OH)D] in adult subjects with cystic fibrosis. The mean 25(OH)D levels (nmol/l) of adult CF subjects from each season over the 2-year period were compared using one-way ANOVA. Winter months had the lowest levels (44 ± 24) compared to the spring (59 ± 29), summer (67 ± 27) and fall (71 ± 33) ($P < 0.0001$).

Table 1

Demographics of study population

	2004–2005
Total	185
Age (years)	29 ± 9
Race	
White	172 (93%)
Black	13 (7%)
Sex	
Male	98 (53%)
Female	87 (47%)
BMI (kg/m ²)	21.2 ± 3.3
FEV ₁ % Predicted	
Best	64.2 ± 24.7
Worst	49.9 ± 22.9
Reported MVI use (%)	129 (69.7%)
Reported vitamin D supplement use (%)	88 (47.6%)
Reported calcium supplement use (%)	80 (43.3%)
Reported pancreatic enzyme use (%)	145 (88.4%)

Data are presented as mean ± SD.

Table 2

Markers of bone health in adult (age 19–67 years) cystic fibrosis subjects seeking treatment at the Emory Cystic Fibrosis Centre (Atlanta, GA) from 2004 to 2005

	<i>N</i> = 183
Frequency of 25(OH)D testing	85.2%
Mean 25(OH)D concentration (nmol/l)	58.8 ± 30
Prevalence of vitamin D insufficiency (< 75 nmol/l)	76.3%
Prevalence vitamin D deficiency (< 37.5 nmol/l)	23.0%
Per cent of subjects with 25(OH)D levels tested in both 2004 and 2005	25.7%
Corrected calcium level (mg/dl) [†]	9.3 ± 0.4★
Albumin (g/dl) [†]	3.6 ± 0.4
Alkaline phosphatase (unit/dl) [†]	120 ± 87.9
Spine L1–L4	<i>N</i> = 84
Bone mineral density (g/cm ²)	1.1 ± 0.2
Z-score	−0.42 ± 1.46
Subjects with T-score > −2.5 and T-score < −1.0★	34/84 (52.4%)
Subjects with T-score < −2.5★	8/84 (9.5%)

All mean ± SD.

★ Six subjects had measures done in both 2004 and 2005, only 2005 measure was used.

[†] Some subjects had multiple blood draws, only first measure was used.

Table 3

Covariates associated with vitamin D insufficiency [25(OH)D < 75 nmol/l]

Prevalence of vitamin D insufficiency in subgroups			
	Prevalence of vitamin D insufficiency		P
Gender			
Men	88/105	84%	
Women	81/115	70%	0.019★
Race			
White	151/202	75%	
Black	18/18	100%	0.015★
Use of vitamin D supplement			
Yes	56/85	66%	
No	76/91	84%	0.007★
Use of multivitamin			
Yes	88/118	75%	
No	45/59	76%	0.81★
Season			
Winter	49/59	88%	
Spring	40/48	82%	
Summer	20/31	79%	
Fall	22/27	65%	0.02★

Mean covariates according to vitamin D status					
	Vitamin D insufficiency			Those sufficient in vitamin D	
	N	Mean	SE	N	Mean
BMI	156	21.4	0.30	49	20.5
Age	169	29.7	0.67	51	29.6
Worst FEV ₁	132	48.8	2.02	42	51.9
Best FEV ₁	152	65.0	2.01	29	64.4

★ Pearson's χ^2 -test.

[†]Independent sample's *t*-test.

Table 4

Covariates associated with 25(OH)D in cystic fibrosis subjects seeking treatment at the Emory Cystic Fibrosis Centre (Atlanta, GA) from 2004 to 2005

Factors correlated with 25(OH)D				
	BMI	Age	Worst FEV ₁	Best FEV ₁
Pearson's <i>r</i>	-0.09	-0.02	0.16	0.10
<i>P</i> value	0.21	0.72	0.04	0.17

Mean 25(OH)D (nmol/l) for categorical variables				
Mean 25(OH)D	Mean	SE	<i>P</i>	
Gender				
Men	56.8	2.8	0.42★	
Women	62.3	2.9		
Race				
White	61.8	2.1	0.012★	
Black	35.8	4.1		
Use of vitamin D supplement				
Yes	68.5	3.7	0.041★	
No	53.5	2.8		
Use of multivitamin				
Yes	61.3	2.9	0.90★	
No	59.5	4.0		
Season				
Winter	44.2	3.2	0.02†	
Spring	58.9	4.2		
Summer	68.7	5.1		
Fall	70.1	4.3		

★Independent samples *t*-test.

†ANOVA.

Table 5

Factors associated with vitamin D insufficiency using logistic regression in cystic fibrosis subjects seeking treatment at the Emory Cystic Fibrosis Centre (Atlanta, GA) from 2004 to 2005

	Full model		★ Reduced model	
	Odds ratio	95% CI	Odds ratio	95% CI
Use of vitamin D supplement	2.23	(1.16, 4.27)	2.47	(1.44, 4.21)
Race	14.95	(4.15, 53.85)	10.6	(4.04, 27.72)
Gender	0.55	(0.28, 1.08)	0.67	(0.40, 1.14)
Season	0.45	(0.33, 0.60)	0.52	(0.41, 0.66)
Age	1.02	(0.98, 1.06)		
BMI	0.99	(0.89, 1.09)		
Multivitamin use	1.31	(0.65, 2.59)		
Pancreatic enzyme use	0.98	(0.21, 4.50)		
	Wald's- χ^2	$P < 0.0001$	Wald's- χ^2	$P < 0.0001$
	47.9		53.6	

★ Reduced model derived using stepwise regression in SAS using PROC Logistic.

Factors associated with vitamin D insufficiency using linear regression in cystic fibrosis subjects seeking treatment at the Emory Cystic Fibrosis Centre (Atlanta, GA) from 2004 to 2005

Table 6

Variable	Full Model			Reduced Model		
	Regression coefficient	SE	P	Regression coefficient	SE	P
Race★	-34.1	9.7	0.0006	-31.0	7.1	< 0.0001
Vitamin D use†	-14.5	5.2	0.0071	-15.4	4.2	0.0003
Season‡	11.9	2.2	< 0.0001	9.8	1.8	< 0.0001
Age	-0.38	0.31	0.24			
BMI	0.08	0.81	0.92			
Pancreatic enzyme use§	0.76	12.4	0.95			
Gender¶	6.85	5.54	0.22			
R²	F value	P		R²	F value	P
0.33	7.80	< 0.0001		0.26	20.08	< 0.0001

★ Negative value indicates that Blacks had a lower 25(OH)D level than Whites.

† Negative value indicates that those not using vitamin D supplements had lower 25(OH)D level than those using supplements.

‡ Season compares those with a winter/spring level to those with a summer/fall level, positive number indicates that those with a fall/summer level had higher 25(OH)D levels.

§ Positive value indicates that pancreatic enzyme supplement users had higher 25(OH)D level than non-users.

¶ Positive value indicates that females had higher 25(OH)D levels than males.