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Vitamin D Levels in an HIV-Infected and Uninfected Cohort in New York City

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Abstract

Background: Vitamin D deficiency is a pervasive problem. We were interested in comparing vitamin D levels and associated characteristics of 2 different patient populations from the same immediate urban environment, one HIV-infected and the other uninfected.

Methods: Charts were retrospectively reviewed and data abstracted for HIV-infected patients from a hospital-based HIV clinic and HIV-negative patients from a nearby private practice. Vitamin D deficiency was defined as 25 (OH) D < 30 ng/ml.

Results: Ninety percent of the 133 HIV-infected patients and 56% of the 104 HIV-uninfected patients were vitamin D deficient (p<0.0001). Vitamin D deficiency was not associated with age, gender or BMI in either group. In the HIV cohort vitamin D deficiency was associated with Efavirenz use (p=0.015) but not with other antiretrovirals, Race/Ethnicity, viral suppression or CD4 count.

Conclusion: In light of the prevalence of vitamin D deficiency, routine testing of vitamin D levels should be considered for all patients and particularly for those who are HIV-infected.

Keywords

Vitamin D; HIV; Body Mass Index (BMI)

Introduction

The importance of vitamin D and the myriad of potential consequences related to vitamin D deficiency (VDD) have gotten much attention in both medical and lay media recently. Many conditions have been associated with VDD: bone disorders, cardiovascular disease, cancer, autoimmune diseases, falls, pain, impaired cognitive function [1], immunologic dysfunction [2], depression [3] and even baldness [4]. The thought is that supplementing and correcting VDD, when detected, can improve and possibly prevent many of these ailments. Some studies even show improved mortality [5,6] but to date, data is most convincing regarding bone health [7]. It is estimated that up to 1 billion people worldwide have inadequate vitamin D levels [8]. Certain groups show a higher prevalence and appear to be at increased risk of VDD. Obese people, the elderly and those with dark skin are at particular risk [1]. The literature also demonstrates high rates of VDD in those infected with HIV [9-14]. We sought to compare and contrast the vitamin D levels and associated characteristics, in 2 groups from the same urban geographic area, one HIV-infected and the other not.

Methods

This was a retrospective, cross-sectional, correlational study. Charts were reviewed and data abstracted from two sites with distinct patient populations in Greenwich Village, New York City between June 1st and August 1st 2011. Both sites were within the same postal zip code. Site one was a private practitioner's office where charts of current HIV-uninfected patients seen in the prior two years were reviewed. Site two was a hospital-based HIV clinic where a practitioner reviewed consecutive patients' charts. At both sites the following data were abstracted: serum 25-hydroxyvitamin D level, birth date, gender, Race/Ethnicity, height and weight [if both were available, body mass index (BMI) was calculated], medications (used currently and within the prior 3 months) and CD4 cell count and HIV viral load for HIV-infected patients. For HIV-infected patients, antiretroviral medications were analyzed individually as well as by the total number of agents taken concurrently. Norvir, though used only for boosting, was considered a unique medication. Historical data were lacking to assess the effect of cumulative exposure to antiretrovirals. HIV-infected patients were stratified by viral load as either suppressed (< 400 copies/ml) or not; CD4 counts were analyzed in 2 ways, using mean counts and also based on categories (< 200, 200 – 350, > 350 cells/mm3). All patients with recorded vitamin D levels were included; at site one, anyone with documented HIV infection was excluded. No patient received prior vitamin D supplementation. Each patient was placed in one of four categories relating to their vitamin D level (in ng/ml): sufficient (>30), mild deficiency (20-29.9), moderate deficiency (10-19.9), or severe deficiency (0-9.9).

Continuous variables are described using their means (standard deviations) and medians (interquartile range); categorical variables are reported as 'n' and percentages for each category of interest. Continuous variables were compared by the one-way analysis of variance as well as the non-parametric Kruskal-Walis test. Categorical variables were compared using the Mantel-Haenszel test to take advantage of the ordinal nature of the 4 vitamin D categories. Linear associations between pairs of variables were measured and tested using the Pearson and Spearman correlation coefficients. A multivariate model, controlling for age and sex, was used to compare vitamin D levels between HIV infected and uninfected patients. No adjustments were made for multiple analyses. A p-value < 0.05 was deemed significant. All analyses were performed using version 9.3 of SAS (SAS Institute Inc., Cary, North Carolina).

Results

One hundred four HIV-uninfected patients' charts were reviewed. Mean age was 46.2 years (range, 18-87). Fifty-one percent were female. Fifty-eight patients (55.8%) were VDD of whom 28 (48.3%) were female. Half of the VDD patients were mildly deficient, 21 (36.2%) were moderately deficient and 8 (13.8%) were severely deficient. Information needed to calculate BMI was available only for 36 patients (34.6%); their mean BMI was 25.9. Race/Ethnicity was

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not recorded in most of the HIV-uninfected patients' charts so data relating to this variable are not included for these patients.

There were 133 HIV-infected patients' charts reviewed. Mean age was 48 years, (range, 24-69). Eighty-five percent were male. The mean CD4 count was 489 cells/mm^3 (4-1551), 64.3% were virologically suppressed and 83% were on antiretroviral therapy (ART). One hundred twenty (90.2%) were vitamin D deficient of whom 101 (84.2%) were male. One patient's vitamin D level was listed only as < 25 so he could not be classified as to level of deficiency. Of the remaining 119 patients, 44 (37%) were mildly deficient, 49 (41.2%) were moderately deficient and 26 (21.8%) were severely deficient. Information needed to calculate BMI was available for 102 (85.7%) of the VDD patients and 12 (92.3%) patients with sufficient vitamin D levels. Their mean BMI was 27.2. Table 1 illustrates the categorical variables in both groups studied and their relationships to vitamin D level. Table 2 summarizes the statistics for continuous variables in both groups and how they relate to vitamin D level.

HIV infection was significantly associated with VDD; 90.2% of the HIV-infected patients vs. 55.8% of the uninfected cohort were VDD (p<0.0001). The mean vitamin D level of the HIV-infected group was 19.3 (9.7) ng/ml and was significantly lower than the uninfected cohort mean level of 27.8 (p<0.001). In a multivariate model controlling for age and sex, the results remained virtually the same.

In the HIV-infected group, 37 (31%) of the deficient patients were taking Efavirenz whereas only 2 (15%) of those not deficient were; Efavirenz use was significantly associated with VDD (p=0.015). Fifteen other antiretroviral agents were analyzed and this effect was not found with any other ART nor with the total number of antiretrovirals patients were taking (Spearman correlation coefficient=0.09, p=0.28). There was no association between VDD and virologic suppression, CD4 count and Race/Ethnicity.

Table 1: Distribution of vitamin D status in subpopulations of patients relative to vitamin D level.

Vitamin D Level:	>30	20-29.9	10-19.9	0-9.9	P[a]
HIV-uninfected (n=104)	n=46	n=29	n=24	n=5	
Female (n=53)	25 (47)	18 (34)	7 (13)	3 (6)	0.13
Male (n=51)	21 (41)	11 (22)	17 (33)	2 (4)	
HIV-infected (n=133)	n=13	n=45	n=49	n=26	
Female (n=20)	1 (5)	5 (25)	9 (45)	5 (25)	0.19
Male (n=113)	12 (11)	40 (35)	40 (35)	21 (19)	
CD4 category					
CD4<200 (n=23)	4 (17)	5 (22)	11 (48)	3 (13)	0.85
CD4 200-350 (n=27)	1 (4)	8 (29)	11 (41)	7 (26)	
CD4 >350 (n=82)	8 (10)	31 (38)	27 (33)	16 (19)	
VL <400 (n=87)	8 (9)	32 (37)	30 (34)	17 (20)	0.72
VL >400 (n=46)	5 (11)	13 (28)	19 (41)	9 (20)	
ART (n=107)	9 (8)	38 (36)	45 (42)	15 (14)	0.45
Efavirenz (n=39)	2 (5)	10 (26)	14 (36)	13 (33)	0.015
Race[b] (n=131)					
African American (n=62)	4 (6)	21 (34)	22 (36)	15 (24)	0.38
Hispanic (n=53)	8 (15)	15 (29)	20 (39)	9 (17)	
Caucasian (n=18)	1 (6)	9 (53)	5 (29)	2 (12)	

[a]P-values generated by Mantel-Haenszel test
VL, viral load; ART, antiretroviral therapy
[b]Eliminating Pacific Islander and Unknown race due to n=1 in each.

Table 2: Summary statistics for Age, BMI and CD4 of HIV-uninfected and infected patients relative to vitamin D Level.

Vitamin D Level:		>30	20-29.9	10-19.9	0-9.9	P[a]
HIV-uninfected (n=104)		n=46	n=29	n=24	n=5	
Age	Mean (standard deviation)	49.6 (19.5)	46.9 (18.2)	38.2 (15.3)	48.9 (13.1)	0.06[b]
	Median (interquartile range)	45.3 (3.3)	42.8 (28.5)	33.8 (19.8)	51.9 (13.2)	0.09
BMI	Mean (standard deviation)	25.8 (4.5)	25.8 (6.1)	24.8 (5.0)	31.3 (4.1)	0.28
	Median (interquartile range)	25.9 (5.2)	26.6 (8.4)	23.3 (7.9)	33.4 (7.4)	0.32
HIV-infected (n=133)		n=13	n=45	n=49	n=26	
Age	Mean (standard deviation)	49.9 (9.9)	50.0 (9.2)	48.1 (9.0)	43.3 (10.2)	0.06[b]
	Median (interquartile range)	49.3 (16.1)	48.9 (10.9)	46.2 (14.5)	46.8 (15.5)	0.10
BMI	Mean (standard deviation)	25.6 (3.0)	27.7 (6.3)	26.5 (5.3)	28.5 (7.5)	0.41
	Median (interquartile range)	25.5 (4.0)	25.5 (6.2)	25.7 (5.4)	27.2 (7.8)	0.75
CD4	Mean (standard deviation)	409 (269)	543 (311)	452 (337)	506 (261)	0.39
	Median (interquartile range)	450 (461)	503 (428)	365 (455)	475 (330)	0.25

[a]P-values comparing means were generated by one way ANOVA and comparing medians by Kruskal-Wallis test.
[b]Due to the lack of interaction between patient group and vitamin D level (p=0.12), a pooled analysis for age was done. The mean age between HIV-infected and uninfected patients was not different (p=0.42) and age did not differ across vitamin D levels (p=0.06).

In both the HIV and non-HIV groups there was no association between VDD and age, gender and BMI.

Discussion

We observed a very high rate of VDD in our HIV-infected group that was significantly greater than that observed in their HIV-negative counterparts. Rates of VDD in HIV-infected cohorts reported in the literature range from 29-89.2% [9-14]. Our rate of 90.2% appears to be the highest to date. Adeyemi et al. also compared vitamin D levels in HIV and non-HIV-infected groups. This was in the setting of the Women's Interagency HIV Study (WIHS), which follows HIV infected and at-risk HIV-uninfected women at 6 sites across the USA. They also found a very high rate of vitamin D insufficiency or deficiency among their HIV-infected group (85%) but interestingly, an even higher rate (92%) among those HIV-uninfected [10]. Dao et al. looked at vitamin D levels in patients from 7 distinct HIV clinics in 4 cities (The SUN cohort) and compared them with the general population by drawing from the National Health and Nutrition Examination Survey (NHNANES) data base. They too found a high rate of vitamin D insufficiency or deficiency, 70.3%, in their HIV patients and again even higher, 79.1%, in the comparator group [11]. It is not clear why we saw a higher rate of VDD in our HIV group while these other 2 studies found the opposite. One way our study differs is that all of our patients were from the same, very localized, geographic area. Climate and latitude effect vitamin D levels and patients from these other studies were spread out across the country. Since Race/Ethnicity data were not available for our controls, it is possible that patients more likely to be VDD (e.g. blacks/Hispanics) were underrepresented in the control group, hence bringing down the rate. However, Race/Ethnicity was not associated with VDD in our patients where that data were available. Lastly, the NHANES data base does not exclude HIV-infected people so Dao's study did compare their HIV group to the general population but not to an exclusively HIV- negative control group. The fact that all of our patients lived in a large metropolitan area also likely contributed to the high rates of VDD we observed. VDD has been associated with urban dwelling when compared to nonurban and rural residence; the speculation is that smog limits sunlight penetration resulting in less vitamin D synthesis [15,16].

In our HIV-infected cohort, as in other studies, Efavirenz use was significantly associated with VDD [11,14,17]. Similar to Dao's study, there was no association with VDD and CD4 cell count or viral load suppression [11]. This is contrary to Adeyemi et al. who found higher vitamin D levels in patients virologically controlled and with higher CD4 cell counts [10]. Others found an association with VDD and lower CD4 cell counts [17] and with being on ART [14,17]. Theodorou et al. specifically observed that duration of ART and the need for second-line regimens was associated with VDD [14].

Contrary to other reports [1], we found no association with VDD and age, gender or BMI in either study group or with Race/ethnicity in our HIV-infected group.

A possible limitation to our study is that not all patients at both sites routinely had vitamin D levels drawn. So, there may have been some selection bias when choosing in which patients to check vitamin D levels. However, this is not likely. Firstly, the private practitioner was also one of the providers at the clinic; presumably his practices remained consistent. Secondly, the demographics of the HIV clinic cohort closely match the demographics of the clinic population overall. The literature strongly demonstrates that season affects vitamin D levels [18,19]. So, another possible limitation is that since the month vitamin D levels were measured was neither standardized nor recorded, seasonal variations in levels could not be accounted for. However, this was equally true for both groups. Also, the vast majority of vitamin D levels in the study were measured by just 2 practitioners and it was their standard practice to measure levels on all patients for at least the 2 years leading up to the study. Levels were measured routinely throughout the year without regard to season. So, it is unlikely that any season would be unduly represented in the data.

Conclusion

VDD is pervasive. We describe a group of HIV- infected patients with an extraordinarily high rate of VDD that was significantly higher than the substantial rate seen in a group of HIV-uninfected patients from the same immediate urban geographic area. Based on our findings, it would seem prudent to routinely test vitamin D levels in all patients and in particular, those HIV-infected.

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