

Highly prevalent vitamin D deficiency and insufficiency among an urban cohort of HIV-infected men under care

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Background

Recent reports document vitamin D deficiency, low bone mineral density and increased fracture rate among HIV-infected adults receiving combination antiretroviral therapy (cART) [1,2,3,4]. However, in the general adult population, inadequate serum vitamin D levels have also been associated with diminished lower-extremity muscle strength or sarcopenia manifesting as a propensity to fall among the elderly, hypertension, insulin resistance, colon cancer and inefficient innate immune response [5,6,7,8,9,10,11]. These nonskeletal pathologies are also experienced by those with HIV infection and in some cases may also be associated with or worsened by poor vitamin D nutriture. Threshold serum vitamin D concentrations for achievement of skeletal and nonskeletal effects may differ. This has led to the designation of values greater than those associated with prevention of overt osteopathy but less than those associated with optimal nonskeletal effect, as insufficient [10]. We hypothesized that vitamin D insufficiency, as well as deficiency, would be prevalent in our urban cohort of HIV-infected men.

Objective

Investigation of Vitamin D adequacy in HIV-infected men receiving ambulatory care.

Methods

Prospective period prevalence study conducted in urban private Infectious Disease practice at latitude N 40, 46 minutes; Queens, New York, United States of America. From November 20, 2008 to January 22, 2009, HIV-infected men presenting for routine care, without clinically apparent disease, were evaluated. Exclusion criteria were current receipt of medications known to interfere with vitamin D metabolism, e.g., antimycobacterials, rifampin, anticonvulsants, corticosteroids, active infectious process, cirrhosis, known kidney or bone disease or malignancy. Patients age, ethnicity, risk factor, year of diagnosis HIV infection, year of receipt of first cART, tobacco, vitamin and mineral supplement use, current weight loss or history of wasting, regularly scheduled aerobic and resistance exercise, height, weight, waist, hip, wrist and mid-upper arm circumferences were determined. cART was defined as any regimen containing three or more antiretrovirals. Current medications were verified by the treating physician and adherence confirmed by the patient prior to examination. Hepatitis C or B virus coinfection, screened for by routine serology at entry into care, were not exclusion criteria.

Body mass index (BMI) was calculated as weight in kg/height in m². Frame size was defined by height (cm)-to-wrist circumference (cm) ratio: small frame > 10.4, medium 10.4 to 9.6 and large < 9.6. Wrist circumference was measured immediately distal to the styloid process. Waist circumference was measured at the level of the umbilicus. Mid-upper arm circumference (MUAC) was measured at midpoint between the acromial and olecranon processes of the scapula and ulna, respectively. MUAC circumference percentiles are from the National Health and Nutrition Survey II.

Serum total 25-[OH] vitamin D was determined by immunoassay (RIA) at Quest Diagnostics, Teterboro, NJ or Labcorp, Raritan N.J. Serum albumin, total calcium, CD4 absolute, percentage, CD4-to-8 ratio and viral load (VL) were determined at the same clinical laboratories or the New York Hospital Queens clinical laboratory.

Vitamin D deficiency was defined as total serum 25-[OH] vitamin D < 50 nmol/L, severe deficiency ≤ 25 nmol/L, insufficiency as > 50 nmol/L but < 75 nmol/L and sufficiency as ≥ 75 nmol/L [11].

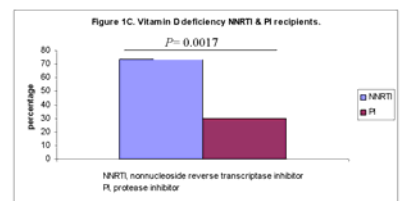
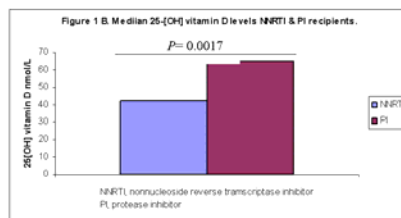
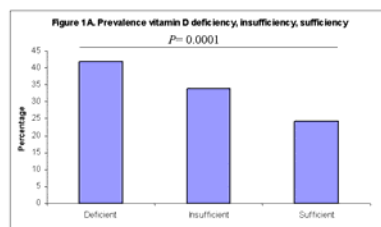
Chi-squared and Fishers exact tests of statistical significance were performed for categorical variables and median two-sample test (nonparametric method) for continuous variables using SAS version 9.1 software (SAS Institute Inc, Cary, North Carolina, USA).

Results

62 men were evaluated during their routine office visits. Median age 48, ethnicity: 46.8% Hispanic, 33.9% white and 16.1% black. Median duration known HIV infection 12 years, risk factor 77.4% men who have sex with men, 91.9% receiving cART, 85.5% VL < 200 copies/ml and median CD4 542 (25th)0.63. NNRTI and PI receipt, 30.7% and 59.7%, respectively. 84.2% of patients receiving cART were undetectable (i.e., VL of < 48 copies/ml). Median: BMI 26.4, MUAC 317 mm (25th percentile), and waist circumference 95 cm. 50% medium frame, 40.3% large frame and 9.7% small frame. Median albumin 42g/L. 17.7% of patients reported current tobacco use. 40.3% of patients reported having experienced wasting or severe weight loss in the past, usually at diagnosis. Only 2 patients (3.2%) reported current weight loss.

The prevalence of vitamin D deficiency was 41.9% (11.3% were severely deficient), 33.9% were vitamin D insufficient and only 24.2% sufficient, $P = < 0.0001$ (Figure 1A.). Median vitamin D: 42.4 nmol/L versus 64.9 nmol/L for NNRTI and PI recipients, respectively, $P = 0.0017$ (Figure 1B.). 73.7% (14/19) of NNRTI recipients versus 29.7% (11/37) of PI recipients were vitamin D deficient, $P = 0.0017$ OR 6.62 (95% CI 1.91-22.89) (Figure 1C.). Tobacco use correlated with severe deficiency, $P = 0.032$. Ethnicity, current CD4, history of wasting or current nutritional parameters did not correlate with vitamin D deficiency or insufficiency. There were no clinically significant differences in median age or duration of known HIV infection among patients who were vitamin D sufficient, insufficient or deficient. Median age: 48, 46, and 50 years, duration known HIV infection: 11, 10 and 14 years, deficiency, insufficiency and sufficiency, respectively.

Hispanic patients were the most frequent ethnicity, 46.8% (29/62), in the cohort. 37.9% (11/29) were vitamin D deficient and 41.4% (12/29) insufficient, similar to overall results



Discussion

Our investigation demonstrated that vitamin D insufficiency, as well as deficiency, is highly prevalent among HIV-infected men under care. Three in four patients (75.8%) had inadequate serum vitamin D levels, 41.9% deficient and 33.9% insufficient. Inadequate serum 25-[OH] vitamin D levels occurred in these men in spite of stable viral suppression. Our cohort, largely employed and under private care, were unlikely to be experiencing effects of socioeconomic marginality or food insecurity. Median BMI, waist and mid-upper arm circumferences, and albumin levels were not suggestive of prevalent chronic undernutrition or obesity. Measurement of serum 25-[OH] vitamin D occurred prior to the months of February and March when nadir vitamin D levels would be expected among subjects residing in the northeastern United States [12]. To date, our study is the only HIV specific report of vitamin D nutriture limited to winter months. Our findings are consistent with those of earlier investigators who demonstrated, using an *in vitro* system, that received solar UVB radiation in the northeastern United States from November through February is not sufficient for cutaneous vitamin D synthesis [12]. HIV-infected men residing in the same communities would likely also experience "vitamin D winter" due to seasonal quantitative and qualitative change in received solar radiation. Sedentary or indoor urban lifestyle and/or regular use of sunscreen may be contributory behavioral factors.

There were highly significant differences between the PI and NNRTI recipients' median serum 25-[OH] vitamin D levels and rates of deficiency. NNRTI recipients were greater than 6 fold more likely to demonstrate deficiency. An earlier cross-sectional survey investigation and two case reports also document an association of NNRTI receipt with vitamin D deficiency [3,13,14]. However, the effect in the cross-sectional survey was less pronounced than that seen in our cohort [3]. Our findings, the association of NNRTI receipt with lower median serum 25-[OH] vitamin D and deficiency, are consistent with NNRTI effect on vitamin D metabolism.

Our findings suggest that periodic screening of serum vitamin D, and supplementation as needed, should be considered in the routine care of HIV-infected men.

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