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Original article

Vitamin D status in young HIV infected women of various ethnic origins: Incidence of vitamin D deficiency and possible impact on bone density

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SUMMARY

Background: Decreased bone mineral density (BMD) was reported in HIV infected patients. Mechanisms leading to this decrease are poorly understood.
Aims: To assess factors relating to BMD in young HIV infected Israeli women of Ethiopian and Caucasian origin.
Patients and methods: 75 young HIV infected women aged 34.5 ± 8.5 followed up at the Institute of Allergy, Clinical Immunology & AIDS filled a questionnaire about sun exposure, daily calcium intake and dress habits. Data about HIV status and treatment regimens were collected from the patients' charts. Serum hydroxyvitamin D [25(OH)D] levels, bone turnover markers and bone densitometry were evaluated.
Results: 28 (65%) of Ethiopians and 2 (6.25%) of Caucasians had 25(OH)D serum levels <10 ng/ml (vitamin D deficiency), $p = 0.001$. 21 (67.7%) Ethiopians and 16 (39%) Caucasians avoided sun exposure, $p = 0.019$. Mean daily calcium intake was 491 ± 268.6 mg and 279 ± 252.6 mg, respectively, $p = 0.001$. *Z* scores < −1 found at Lumbar spine in 26 (89.7%), at Femoral neck in 20 (69%) at Total hip in 17 (58.6%) of vitamin D deficient patients compared to 20 (48.8%), 17 (41.5%), 9 (22%), in patients with 25(OH)D > 10 ng/ml, $p < 0.01$, <0.03, <0.001, respectively.
Significantly more Ethiopian than Caucasian women covered their face (32.3% and 9.5%, $p = 0.003$) and hands (58.1% and 30.9%, $p = 0.03$). There was no difference in bone turnover markers levels.
Conclusion: Poorer vitamin D status was observed in Ethiopian women might be one of the important factors related to lower BMD in this group.

1. Introduction

Several studies have reported a high prevalence of bone demineralization in HIV-infected patients. A recent meta-analytic review has shown a prevalence of osteoporosis in 15% of HIV-infected individuals, 3.7 times greater than in HIV-uninfected controls.[1]

Different mechanisms influencing BMD in HIV infected patients have been postulated. Some of them consider a direct effect of HIV upon osteogenic cells, persistent activation of proinflammatory cytokines, up-regulation of TNF alpha that induced apoptosis in the osteoblast model,[1] other- influence of the GH-IGF-1-IGFBPs system[2] and estrogen deficiency.[3–6]

Several studies postulated an association between protease inhibitor (PI) treatment and reduced bone density,[7–15] but others failed to demonstrate this association.[16,17] Interference of PI with vitamin D metabolism was also observed.[18] Other ART drugs have also been suggested as etiological factors.[19] Association between decrease in BMD and older age, homosexual transmission group, low body mass index, low HIV plasma viral load and low CD4 lymphocyte count nadir was also reported.[20] A high frequency of vitamin D deficiency has been found in HIV infected patients with reduced BMD,[8,21] and also in general adult HIV-infected

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population.[22] Another study suggested that the burden of metabolic bone disease in HIV positive patients with Highly Active Anti-Retroviral Therapy (HAART) associated lipodystrophy may be greater in whites than in African–Americans,[23] while another found the opposite.[24]

Aims of our study were to assess factors that might be related to BMD status in young HIV infected Israeli women of Ethiopian (ET) and Caucasian (CA) origin: present and past HIV status, antiretroviral treatment, vitamin D status, daily calcium intake, sun exposure, clothing habits.

2. Subjects and methods

2.1. Patents

Young HIV infected women o Ethiopic (ET) and Caucasian (CA) origin with regular menses, living in Israel for at least ten years, who were followed up at the Institute of Allergy, Clinical Immunology & AIDS at Rambam Health Care Campus.

The study was conducted during the summer 2009. Patients with chronic diseases and medications that could interfere with bone metabolism, except antiretroviral therapy, were excluded from the study.

The study was approved by the local ethics committee. All patients gave a written informed consent.

2.2. Data collection

Data about the HIV status (CD4 count and viral load), details of past and present antiretroviral treatment were retrieved from the patients' charts. Sun exposure, and dress habits were assessed by questionnaire. Daily calcium intake was calculated from a short version Food Frequency Questionnaire focused on calcium content of food sources. Similar content food products were grouped together as generic sources – for example milk and dairy products, high calcium content vegetables etc. In this manner the most prevalent calcium rich products were surveyed. Portion size was determined according to average size for the target population. Data on calcium content was then calculated according to the Ministry of Health "Zameret" computer program data base.

A detailed medical history was obtained from all patients.

Special attention was paid to the presence of lipodystrophy, hyperlipidemia and diabetes. We also assessed the patients' performance status according to the WHO criteria. Weight and height were measured and BMI was calculated.

2.3. Laboratory evaluation

Serum calcium, inorganic phosphate, creatinine, albumin, and liver enzymes were assessed, using standard laboratory techniques (Hitachi 747, Roche).

Hydroxyvitamin D 25(OH)D was assessed by ^{125}I-radioimmunoassay (DiaSorin, Stillwater, Minnesota, USA), PTH (Intact) And bone turnover markers serum C-terminal telopeptide of type 1 collagen (CTX) and procollagen type 1 nitrogenous propeptide (P1NP) by CobasE411 Roche Diagnostics GmbH, Mannheim.

Reliability information: for 25(OH)D intra- and interassay coefficients of variation (CV) were between 6.7 and 8.63%; for CTX intra- and interassay coefficients of variation (CV) were between 1.61 and 1.26%; for P1NP intra- and interassay coefficients of variation (CV) were between 2.08 and 2.85%; for PTH intra- and interassay coefficients of variation (CV) were between 0.69 and 1.88%.

HIV plasma RNA was measured by real-time PCR using the Cobas AmpliPrep HIV-1 Test (Roche Molecular system, Branchburg, New Jersey, USA), and CD4 cell counts were measured using flow cytometry.

Vitamin D status was defined as follows: serum levels of 25(OH) D $<$ 10 ng/ml – vitamin D deficiency; 10 $<$ 25(OH)D $<$ 20 ng/ml – vitamin D insufficiency, 20 $<$ 25(OH)D $<$ 30 ng/ml- as vitamin D inadequacy. Serum levels of 25(OH)D $>$ 30 ng/ml defined as vitamin D adequacy.

2.4. BMD measurements

BMD measurements of the lumbar spine (L2-L4), femoral neck and total hip were performed using dual energy X-ray absorptiometry (Lunar DPX scanner, Madison, WI, USA). BMD results were expressed in comparison to young adults (*T*-scores) and in standard deviation scores compared to age matching controls (*Z*-scores).

2.5. Statistical methods

The data were evaluated by SPSS software, version 15 (SPSS Inc. Chicago, IL, USA). Fisher's Exact Test and Pearson chi-square tests were used for detection the differences in the prevalence of all the categorical and dichotomy variables between the two groups, (Ethiopian vs. Caucasian). Parametric *T*-test and Non Parametric *t*–test (Mann–Whitney *U* test) were applied- to compare differences in age, and laboratory exams between the two groups.

Multivariate analysis by the logistic regression was employed to study the parameters associated with low vitamin D ($<$15 ng/ml) or higher vitamin D $\geq$ 15 ng/ml.

$P < 0.05$ was considered significant.

3. Results

Seventy five HIV infected women aged 34.5 $\pm$ 8.5participated in the study; 43 (57.3%) ET and 32 (42.7%) – CA. All the women had regular menses and no one was on birth control pills, no one reported previous fractures.

The demographic data of the study population are summarized in the Table 1. There were no differences between the two study groups, in age, BMI, the duration of HIV since diagnosis, mean nadir, and the current CD4 cell count, percentage of patients with detectable viral load and percentage of patients receiving HAART or with previous HAART (Table 1). The highest viral load ever reported

Table 1
Characteristics of young ET and CA HIV infected women, their HIV status and antiretroviral treatment in the study population.

	Ethiopian	Caucasian	*P* value
Number	43	32	
Age mean $\pm$ SD	35.9 $\pm$ 8.2	34.8 $\pm$ 8.7	NS
BMI mean $\pm$ SD	23.5 $\pm$ 4.2	25.1 $\pm$ 4.9	NS
Waist/hip ratio mean $\pm$ SD	0.9 $\pm$ 0.9	0.9 $\pm$ 0.1	NS
HIV status			
Duration HIV (months since diagnosis) $\pm$ SD	67.7 $\pm$ 34.6	56.3 $\pm$ 32.5	NS
Actual CD4 cell count cells/μl mean $\pm$ SD	233 cell/mm $\pm$ 136	264 cell/mm $\pm$ 210	NS
Nadir CD4 count cells/μl mean	143 cell/mm $\pm$ 167	185 cell/mm $\pm$ 92	NS
Patients with Viral Load $>$ 50 copies/mL *N* (%)	2 (5)	1 (4)	NS
Highest viral load ($\log_{10}$copies/mL) (mean)	138,000 copies/ml	435164 copies/ml	$P < 0.03$
Antiretroviral treatment (ART)			
Current or prior HAART *N* %	35 (82)	20 (64)	NS
Duration HAART month	43	48	NS
[a]PI therapy *n*/month $\pm$ SD	20/91 $\pm$ 33.8	21/85 $\pm$ 42.9	NS

[a] Protease Inhibitors used were: Lopinavir/ritonavir, invirase/ritonavir, indinavir.