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BONE NOURISHMENT IN HIV INFECTED ON HAART PATIENTS- EXPERIENCE IN TERTIARY CARE HOSPITAL

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ABSTRACT

Increased life-expectancy and the need for long-term antiretroviral therapy have brought new challenges to the clinical management of HIV-infected individuals. While the prevalence of osteoporosis and fractures is probably increased in HIV-infected patients, optimal strategies for risk assessment and treatment in this relatively young population are yet to be defined. Prevention of bone loss is likely to become an important component of HIV care as the HIV-infected patient population grows older. In this article, we present an overview of the prevalence of bone nourishment in individuals with HIV.

KEYWORDS: HIV, ARVs, HAART, Osteonecrosis, NRTIs, NNRTI's

INTRODUCTION

As the HIV/AIDS pandemic continues to expand, the moral imperative to provide safe and efficacious treatment options becomes of paramount interest to the international health-care communities. The use of antiretroviral therapy (ART) has become the cornerstone of the clinical armamentarium available to prevent transmission and slow progression of the infection in people living with HIV/AIDS (PLHA) worldwide1. Efforts have begun for a significant scaling up of the use of antiretroviral drugs (ARVs) in settings such as sub-Saharan Africa where the epidemic has had its most devastating impact. However, questions have been raised about the use of ART against a background of health problems not often seen in the developed world2.Bone mineral metabolism is one in which many of the patients range of bone-related conditions from osteonecrosis to osteopenia and osteoporosis has been reported in HIV-infected adults and children (*1*,*2*,*3*). In addition to the traditional risk factors for these bone-related conditions (i.e., age, gender, weight), the relative contribution of HIV and/or treatments has emerged as an additional risk factor (*3*,*4*). Evidence indicates that HIV per se causes problems with bone mineralization (*2*,*4*,*5*). What is less clear is the relative contribution of ART to these problems (*6*). This lack of clarity is in part due to the complexity of bone mineralization processes and the nature and the range in quality of the studies that examined these relationships in HIV-positive people. In addition, the effect of ART on bone may vary between classes of drugs as well as among drugs within the same class (*7*). Consequently, a disparity exists within the literature examining the bone–ART relationship; some investigators have reported no effect (compared with HIV-positive drug-naïve subjects [*8*]), a negative effect (*9*) and a beneficial effect (*10*) of ARV therapies. Several studies of bone turnover in HIV-positive patients suggest low rates of bone formation with high levels of bone resorption, an uncoupling of turnover and formation that may be deleterious(*10*). Some studies have compared HIV-infected men and women with and without lipodystrophy and have reported an association between bone loss and visceral fat or lipodystrophy (*11*, *12*).

Huang et al. (*13*) in a further evaluation of these relationships in women identified hormonal status

(specifically androgen deficiency) as a distinguishing concomitant of bone loss. Carr et al. (*14*) reported that osteopenia in their cohort of 221 HIV-positive men (32 drug naïve, 42 receiving NRTIs and 147 receiving NRTIs and PIs) was associated with lower weight before initiation of therapy and NRTI-associated lacticacidemia but not lipodystrophy. Aside from the already established risk factors for decreased bone mineralization and related conditions in individuals without HIV infection (e.g., poor calcium and vitamin D status, age, gender), specific nutritional factors have been examined in relation to the potential adverse effects of HIV and ART on bone health. In an in vitro study aimed at exploring the effects of PIs on vitamin Dmetabolism, indinavir and ritonavir reduced the rate of conversion of 25-hydroxyvitamin D to the active form 1,25-dihydroxyvitamin D3 in a dose-dependent manner (*15*). eichmann et al. (*5*) evaluated these relationships specifically as they exist in HIV-positive women. They measured bone mineral density and related bone variables including vitamin D in 50HIV-positive women who were not receiving ART during the study. Compared with age-matched healthy HIV-negative control women, the HIV-positive women had significantly lower bone density measures and circulating concentrations of 1,25-dihydroxyvitamin D3. They also reported a significant positive correlation between CD4+ counts and vitamin D levels. Dolan et al. (*18*) reported lower bone density in HIV-positive women compared with control subjects matched for age and body mass index. Decreased levels of 1, 25-dihydroxyvitamin D3 were also seen but did not correlate with bone density. It is unclear whether bone problems are due to metabolic derangement resulting primarily from HIV infection, use of ART or a combination of both. Nonetheless, bone loss is a potentially serious problem that affects the long-term health and quality of life of PLWHA, and assessment of bone health should become part of the clinical care of PLWHA. As discussed below, of particular concern are the implications for perinatally infected children who experience years of exposure to both HIV and ART. To prevent these complications and to ensure an enhanced quality of life, strategies will be needed for the incorporation of assessment of not only bone health but also risk factors that can be controlled—including diet—into clinical care. Availability and applicability of procedures and technologies for the assessment of bone status and factors that may contribute to bone health will be contingent on the setting and the clinical capacity of the caregivers. The present study aims to Clinical study of Bone nourishment in HIV infected on HAART patients

METHODS

The secondary data of prospective and cross sectional study was obtained from the ART centres of Bangalore city. Total 250 patients secondary data were collected from ART records of both ARV book and ART white card. The HAART details like duration, onset of therapy, type of therapy, regimen details (NRTI and NNRTI's were extracted from the relevant sources of ARV record. Adverse drug reaction and serious adverse drug reaction on HAART regimen were documented and correlate with last HAART have been taken by the PLHIV's. Demographic profile, age, gender match and lost to follow-up and duration of lost to follow-up details were included in the study. Laboratory parameters like bone mineral density (done in private set up) and nutritional status of the patients with respect to duration of HAART therapy were documented from the care givers. Complications of bone were correlated with body mass index and fat composition. Collected data was analysed by using the SAS -6.50 Version. Univariate analysis was performed to draw the significant inference.

RESULTS

Table 1

SL	Associated Variables	No (%)	ODD Ratio	P-Value
1	**Gender** **Male** **Female**	 175(70.0%) 75(30.0%)	 0.81-0.93 0.26-0.33	 **0.00**** **0.00****
2	**Age (Yrs)**	43.16±1.48	0.74-0.78	**0.02** ^{ns}
3	**Education** **Illiterate** **Literate**	 212(85.0%) 38(15.0%)	 0.91-0.98 0.12-0.14	 **0.01**** **0.22** ^{ns}
4	**Economic status** **BPL** **APL**	 180(72.0%) 70(28.00%)	 0.89-0.93 0.36-0.42	 **0.00**** **0.11** ^{ns}
5	**Occupational status** **Employed** **Unemployed**	 81(32.40%) 169(67.60%)	 0.52-0.63 0.82-0.89	 **0.36** ^{ns} **0.00****
6	**HAART Details** **NRTI's** **NNRTI's** **PI's**	 142(56.80%) 72(28.0%) 36(14.44%)	 0.76-0.81 0.62-0.70 0.21-0.32	 **0.00**** **0.42** ^{ns} **0.56** ^{ns}
7	**Duration of HAART**	288±13.16	0.94-0.98	**0.00****
8	**WHO-IVStage**	214(85.60%)	0.82-0.89	**0.00****
9	**Malnourishment** **SVM**	36(14.40%)	0.11-0.13	**0.362** ^{ns}
10	**Adverse drug reaction** **Serious adverse drug reaction**	105(42.0%)	0.88-0.91	**0.00****
12	**Bone nourishment on NRTI's** **Bone nourishment on NNRTI's**	15(6.0%) 08(3.20%	0.63-0.72 0.42-0.54	**0.00**** **0.00****

**, Significant @1% level, ns-Non significant

The mean age of the patients was 43.16±1.48. Male comprises 70% and female was 30% respectively. 85.0% of the patients belong to illiterate and 72.0% apparently had below poverty line. The mean duration of HAART treatment received was 288±13.16 weeks. 85.0% of the patients WHO IV clinical staging and 14.40% had Sever malnourished .Nearly 42.0% patients had challenging with adverse drug reaction. More number of PLHIV received NRTI's 56.80%, NNRTI's 28.0% ; and Protease inhibitor was 14.44%. The bone nourishment was positively associated with NRTI's and NNRTI's regimen .Prolonged taking treatment can affect the bone density in PLHIV's.

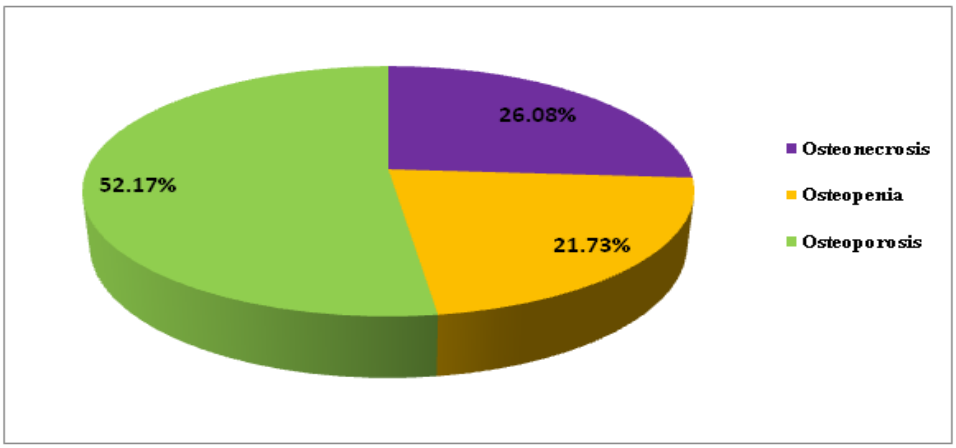

Figure 1: Bone Nourishment in PLHIV's who Received NRTI's and NNRTI's Regimens are Osteonecrosis

Use of corticosteroid drugs is considered a major risk factor for osteonecrosis These drugs are often used long-term for treatment of inflammation caused by diseases like rheumatoid arthritis or lupus, and short-term in the treatment of infections like *Pneumocystis carinii* pneumonia or PCP; long-term use is definitely a risk factor; whether short-term use might also increase the likelihood of developing osteonecrosis is unclear. Alcohol abuse, bone injury, bone infections, and scuba diving are additional risk factors because each of these can contribute to decreased blood supply to the bone. Some HIV+ people develop Addison's disease, an adrenal gland condition that results in reduced production of the steroid hormone called cortisol. It is usually treated with low doses of hydrocortisone (30 mg or so daily), a dosage level that is not usually thought to cause avascular necrosis but might contribute1. The hip is usually the first place that osteonecrosis of bone shows up, but it may also develop in the shoulder, knee, or hand. Common early symptoms include pain in the hip joint or groin area which may radiate down the leg to the knee, and may in some cases be quite excruciating. Some people will develop stiffness in the hip area (often particularly noticeable upon awakening), occasional aching (especially after long periods of walking or standing), and/or a decreased range of motion. For osteopenia and osteoporosis, those things well-known to help prevent or reverse osteoporosis in general may certainly help. Included would be weight-bearing exercise, a nutrient-rich diet in order to ensure the presence of all the nutrients needed by bone to grow, and additional supplementation with calcium, magnesium, and vitamin D. If osteonecrosis is detected early on, small holes can sometimes be drilled in the bone to increase blood flow and allow new blood vessels to grow (a process called core decompression surgery), thus helping to slow worsening and reduce pain. However, there are no known curative measures that will permanently prevent a downhill slide toward bone death.

Osteopenia

In osteopenia and the more severe osteoporosis, there is a gradual loss of bone tissue that occurs when the body's normal constant loss of bone cells (bone resorption) is not equaled by constant replacement (bone formation), resulting in gradually thinning and weaker bones that may become brittle and break easily. It is possible that HIV infection itself contributes to this. HIV+ people are known to have abnormally high levels of pro-inflammatory cytokines (cell-produced chemicals that cause inflammation) as well as vitamin D deficiency, both of which could contribute to disturbed bone metabolism. In one significant study, researchers compared levels of osteocalcin, a blood serum marker for bone formation, to levels of C-telopeptide, a serum marker for bone resorption, and found that HIV+ people with advanced disease and high viral loads had increased levels of C-telopeptide (indicating more than usual bone loss), markedly depressed osteocalcin levels (indicating less than usual bone formation), and higher levels of pro-inflammatory cytokines. Interestingly, there was no correlation between osteocalcin and C-telopeptide levels. In the HIV-negative, these are normally in balance with each other, an indication that bone loss and growth are matched. After 24 months of HAART treatment, there was a decrease in the inflammatory cytokines and a marked rise in serum osteocalcin levels, with the result that osteocalcin and C-telopeptide levels were once again appropriately correlated. So it appears that in these people HAART had the beneficial effect of normalizing bone growth and loss processes[13].

Osteoporosis

A more advanced bone problem in which bone mass is decreased and there is an increased risk fracture. In osteopenia and the more severe osteoporosis, there is a gradual loss of bone tissue that occurs when the body's normal constant loss of bone cells (bone resorption) is not equaled by constant replacement (bone formation), resulting in gradually thinning and weaker bones that may become brittle and break easily. **It is possible that HIV infection itself**

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DISCUSSIONS

In a larger cohort study, Madeddu et al. (*109*) evaluated the association between ART and bone health in 172 HIV-positive patients (112 men and 60 women). Of these patients 92 were receiving HAART with PIs, 60 were receiving NNRTIs or triple combination NRTIs but no PIs and20 were drug naïve. There were 64 HIV-uninfected control subjects. Bone mineral density and 1, 25-dihydroxyvitamin D3 were measured. Circulating 1, 25-dihydroxyvitamin D3 levels were lower in all three HIV-positive groups than in HIV-uninfected control patients, but were lowest in the HIV-infected individuals receiving PI-containing therapy, and levels were positively correlated with bone mineral density in all HIV-positive groups. The incidence of osteopenia was greater than 30% in all HIV positivegroups (higher in ART groups than the naïve group). Osteoporosis was documented only in the group receiving PIs. Although 25-hydroxyvitamin D was not assessed, these investing at orsconcluded that ART has a negative effect on vitamin metabolism that contributes to bone problems in HIV-positive patients.

In addition to the possible contributions of HIV and protease inhibitors, many people may have additional risk factors for the development of osteoporosis14. Lowered sex hormone levels, common in both men and women with HIV disease, may increase risk, making hormone testing and appropriate replacement a must 11. Nutritional deficiencies resulting from malabsorption and other problems may contribute to the bone problems, Long-term consumption of an acid-forming diet could contribute, certain drug treatments that many people with more advanced HIV disease may have been given—especially corticosteroid drugs such as those used in the treatment of PCP—are also tied to an increased risk of osteoporosis. Many people may also have one or more of the additional risk factors that affect the general population—smoking, extended immobilization of the body (due to injury or other illness) or anything else that results in lack of weight-bearing exercise, alcoholism, failure to achieve an optimal bone mass by age 30, thyroid problems, adrenal gland abnormalities, and others9. Last but not least, research has shown that people who are co infected with HIV and either hepatitis B virus (HBV) or hepatitis C virus (HCV) may be at even greater risk for bone disorders12. For osteopenia and osteoporosis- both men and women, checking levels of the hormone DHEA would be important since this hormone is important for bone health15. The use of natural anti-inflammatory agents like omega-3 fatty acids and ginger might also be useful. If osteonecrosis is detected early on, small holes can sometimes be drilled in the bone to increase blood flow and allow new blood vessels to grow. Bone nutrients. Supplementing with calcium (1,000 mg daily for men, and 1,000-1500 mg for women), magnesium (500-600 mg; excess magnesium can cause loose stools so watch for this), and vitamin D (800 IU daily) may be important for the prevention of osteopenia and osteoporosis. As discussed above, deficiencies of these nutrients have been reported in HIV+ people, and long-term supplementation may be crucial for helping to prevent problems. Other nutrients involved in the production of bone tissue include boron, manganese, zinc, copper and silicon. A potent multiple vitamin/mineral supplements will usually contains. Supplementation with sulfur-containing substances can provide necessary building blocks for bone and connective tissue. Included are MSM (methylsulfonylmethane; doses of 2,000 mg daily might be appropriate), chondroitin sulphate and glucosamine sulfate (a combo formula containing both could be used in doses of one capsule, two or three times daily).

CONCLUSIONS

Nutritional supplements, regular exercise, fresh fruits and vegetables can able to reduce the bone nourishment. Early intervened treatment is more essential for osteoporosis and necrosis complications.

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