



## PREVALENCE OF ABNORMAL BONE MINERAL DENSITY IN HIV-POSITIVE PATIENTS IN IBADAN, NIGERIA

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### Abstract

#### Background:

There have been reports of high rate of abnormal bone mineral densities (BMD) among people living with HIV. Following the introduction of combination antiretroviral therapy (CART) into Nigeria, the country is now experiencing an increasing population of HIV positive patients. There is paucity of data about osteoporosis/osteopaenia and abnormal bone mineral density in this population.

#### Aim and Objectives:

The aim of the study was to determine the prevalence and determinants of osteopaenia/osteoporosis in a cohort of HIV-positive patients in Nigeria.

#### Patients and Methods:

The BMD of a group of patients attending the outpatient clinic of the University of Ibadan, Nigeria was assessed using a DXA machine. The relationship of bone mineral density to body weight, CART status, protease inhibitor use, and gender was investigated. Their CD4 counts and viral load were also estimated.

#### Results:

A total of 1005 patients participated with a mean age of  $41.3 \pm 10$  years. There were 724 females (72.0%), 29.7% were single. The median length of diagnosis was 2 years (Range 1-18 years). The Median CD4 count was 371 cells/ml and Median viral load was 200 copies/ml. Of this sample, 785 (78.1%) were on CART with 95 (12.6%) on protease inhibitor. The mean body mass index (BMI) was  $23.7 \pm 4.7$  with 9.2% underweight and 12.6% obese. The prevalence of osteopaenia and osteoporosis were 46.6% and 31.9% respectively, while 19.6% had normal bone mineral density (BMD). Osteoporosis was significantly higher in those aged above 40 years ( $p=0.00001$ ), the females ( $p=0.022$ ), the single ( $p=0.028$ ) and the underweight ( $p=0.0001$ ). There was no significant difference in BMD of those with or without protease inhibitor containing medications as well as treatment patients.

Prevalence, Nigeria

## Introduction

Bone is a metabolically active organ that supports and gives form to the body in addition to performing many other functions<sup>1</sup>. The shape of bone is maintained by remodeling which results from the activities of osteoclasts and osteoblasts. After skeletal maturity, there follows a period of skeletal consolidation but peak bone mass is attained at about the age of thirty-five years. Subsequently, there is a steady decline in bone mass irrespective of race or sex with 0.5 to 1 percent of the total bone mass lost annually<sup>2</sup>.

In osteoporosis, there is skeletal failure as opposed to skeletal loss and the disease can be clinically defined as having a lower bone mass than might be expected for age and sex and characterized by potential increase in fracture occurrence<sup>1</sup>. Osteoporosis poses a special clinical dilemma because it does not have pathognomonic symptoms and affected persons only seek medical attention when sentinel events like fractures, low back pain and symptomatic vertebral collapse occur. It is estimated that over 200 million women suffer from this disease<sup>3</sup>.

Bone mineral density (BMD) measurement is used for the diagnosis of osteoporosis as it accounts for about 80% of bone strength and correlates strongly with fracture risk and load-bearing capacity of the spine and hip<sup>4</sup>. Dual-energy x-ray absorptiometry (DXA) scan is the gold-standard in measuring BMD and this technique estimates the absorption of radiation by the skeleton and the values obtained are expressed in terms of T-scores and Z-scores<sup>2,5</sup>. The World Health Organization outlines three classes of bone mineral densities (normal, osteopenia and osteoporosis) based on the T-scores as calculated by the number of standard deviations below the mean values for healthy young adults (25-35 years) with sex and ethnicity matched reference population; the Z-score compares the BMD to an age-matched reference of the same gender and is used for patients less than 50 years old<sup>1,6,8</sup>.

The effectiveness of Combination Antiretroviral Therapy (CART) deployed in combating HIV infections has resulted in longevity of the survivors<sup>7</sup>. However, this has not come without a price. Numerous studies from developed countries have shown a high prevalence of abnormal bone densities as well as osteoporotic fractures among HIV-positive patients, especially those on CART<sup>2,8-13</sup>. In the meta-analysis by Brown and Qaqish<sup>14</sup>, the prevalence of osteoporosis in HIV-positive patients was three times higher than in HIV-negative controls<sup>14</sup>. The prevalence of abnormal Bone Mineral Density (BMD) varies in different populations, but even less is known about the character of bone mass among HIV-positive patients in Sub-Saharan Africa. Nigeria is home to 3 million people living with HIV at the end of 2012<sup>12</sup>. Fifty percent of these people are women aged 15 years and above. With the introduction of CART in Nigeria, the country is now home to an increasing number of HIV-positive patients on life-long medications and there is paucity of data on osteoporosis and abnormal bone mineral density among people living with HIV whether or not on medication. This information is vitally important for developing appropriate management protocols, mapping out preventive strategies against fragility fractures and for planning health service needs. This study thus sets out to determine the prevalence of abnormal bone mineral density in a sample of HIV-positive patients in Ibadan, Nigeria and assess the associated risk factors.

## Patients and Methods

Between 1<sup>st</sup> September and 31<sup>st</sup> December, 2010, patients with HIV infection attending the Presidential Emergency Plan for AIDS Relief/AIDS Prevention Initiative in Nigeria (PEPFAR/APIN) clinic at the College of Medicine, University of Ibadan had their bone mineral density (BMD) evaluated after informed consent was obtained. Ethical clearance was obtained from the Ethics Review Committee. Information acquired included age, sex, demographics, weights, heights, duration of diagnosis and duration of HIV therapy.

### Bone Mineral Density Evaluation.

All data obtained were entered into a proforma and processed with the Statistical Package for the Social Sciences version 16 (SPSS Inc., Chicago, Illinois). Descriptive statistics were obtained and  $\chi^2$  test calculated for categorical data while Mann Whitney U tests were carried out for continuous data. A multivariate logistic regression analysis was carried out using factors found to be significant on initial bivariate analysis. Statistical significance was considered at a level of  $p \leq 0.05$ .

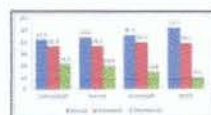
## Results

A total of 1005 patients participated in the study. The mean age of the respondents was  $41.3 \pm 10.0$  years with 52.1% aged below 40 years whilst 481 (47.9%) were aged over 40 years. There were 724 (72.0%) females and 281 (28.0%) males. None of the patients had deformity of the left hand and wrist. The median length since diagnosis of HIV was 2 years (Range 1- 18 years) and 70.3% were married at the time of the study. The mean CD4 count was 371 cells/ $\mu$ L ( $>200$  cells/ $\mu$ L in 84.7% and  $\leq 200$  cells/ $\mu$ L in 15.3%) and the median viral load was 200 copies/ml ( $>400$  copies/ml in 49.1% and  $\leq 400$  copies/ml in 50.9%) at the time of the study as shown in [Table 1](#). Of the respondents, 785 (78.1%) were on Combination Anti-Retroviral Therapy (CART) and of this number 99 (12.6%) were on protease inhibitors (PI) ([Table 1](#)). The mean Body Mass Index (BMI) was 23.9. 9.2% were underweight, 57.7% had normal BMI, 2.1% were overweight whilst 10.0% were obese ([Table](#)

[Table 1](#)

**Characteristics of the study patients, including BMI, CD4 counts and viral load**

The Bone Mineral Density (BMD) values revealed osteopenia in 468 (46.6%) of the respondents, osteoporosis in 321 (31.9%) subjects and normal BMD values in 197 (19.6%). Bivariate analyses revealed that the prevalence of osteoporosis in these patients was higher in those aged above 40 years ( $p=0.00001$ ), higher among the female gender ( $p = 0.022$ ), higher in 'single' respondents ( $p = 0.028$ ) and highest in underweight respondents. The relative protective effect of obesity is shown in [Figure 1](#). Although the prevalence of osteoporosis was observed to be higher among those on protease inhibitors (38.4%) compared to those on other forms of antiretroviral therapy (33.4%), this finding was not statistically significant ( $p = 0.242$ ). Also, although the prevalence of osteoporosis was higher amongst those on CART (33.4%) compared to those on no treatment (26.8%), it did not reach statistical significance ( $p = 0.065$ ).



[Figure 1:](#)

**The effect of BMI on bone mineral density in HIV infection**

Using multivariate logistic regression, the odds of having osteoporosis was 6 folds higher among the underweight, 4 folds higher among the normal weight individuals and 2 folds higher among the overweight compared to obese respectively. Other significant factors were female sex (OR 1.96; 95% CI 1.39-2.77) and age  $> 40$  years (OR 2.03; 95% CI 1.51- 2.27).

## Discussion

In this study, the prevalence of osteopenia and osteoporosis were 46.6% and 31.9% respectively, giving an overall prevalence of abnormal bone mineral density (BMD) of 80% in the study population. This high level of abnormal BMD has not been noted in other studies<sup>11,12,16-20</sup>. The causes of low bone mass in individuals with HIV infection are multifactorial and include the viraemia arising from the HIV infection, CART related factors and traditional osteoporosis risk factors<sup>2,8-10</sup>. HIV proteins have been shown to cause an increase in osteoclastic activity as well as promote osteoblastic apoptosis both of which lead to reduction in bone mass. The role of treatment

BMI, time on protease inhibitors, time on tenofovir and current use of protease inhibitors (PI) were associated with demineralization.

Although T scores are often reserved for patients above 50 years and the Z-score reserved for those young, in this study, the T-scores were utilized for all the patients since there are no records of population based BMD values in our environment. As in other studies, lower BMD values are associated with increased female sex and underweight. The association of osteoporosis in this study with single status (never married or divorced) is observed and would need further studies.

There are some limitations to this study. The DXA scan machine that was deployed for this study measured BMD at the distal radius. Other studies measured BMD at the lumbar spine, the proximal femur and total hip. Also, other risk factors for low BMD like Vitamin D levels and gonadal hormone levels as well as bone metabolism were not evaluated.

Though the relationship of BMD and fracture is not linear, increasing rates of fractures are being reported amongst patients with HIV infection<sup>13,24,25</sup>. Thus the need to emphasize this problem in our environment. Whilst our findings are similar to the reports from other environments<sup>9,17,19</sup>, the results of our study have potential to impact the treatment modalities of these patients in Nigeria. This has become necessary because the PEPFAR/APIN program in Nigeria is undergoing re-organization with increasing transfer of ownership and management to Nigerian Institutions and secondary as well as primary care facilities. In addition, the number of orthopaedic surgeons are far too few to cope with the consequences of this large number of Nigerians with potential risk of fracture and other disabilities. As late presentations for most diseases (including HIV infection) amongst Nigerians are rampant, the treatment protocols may be skewed when compared to similar cases in developed countries. It has been proposed in the US that a DXA scan should be carried out in HIV-infected subjects  $\geq 50$  years of age with additional risks for osteopenia/osteoporosis, and pharmacologic treatment initiated in post-menopausal women and men aged  $\geq 50$  years with a T-score of  $\leq -2.5$  in the hip, femoral neck and spine or those with history of fragility fracture<sup>26,27</sup>. With the peculiarity of our environment and since the patients surveyed in this study had bone demineralization, it may probably not be out of place to recommend the DXA scan for all People living with HIV (PLHIV) attending treatment clinics in Nigeria at the commencement of bisphosphonates along with nutritional support for those with low BMI as appropriate for their BMD.

## Conclusion

A high prevalence of abnormal bone mineral density was found in HIV positive patients in Nigeria. Patients above 40 years and a body mass index class of underweight were significant associated factors. Routine bone mineral density assessment is recommended as an adjunct in the evaluation of HIV positive patients in Nigeria.

## Footnotes

**Competing Interests:** The authors have declared that no competing interests exist.

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