SHAWA CJW, SITALI JI, BANDA J, MWEEMBA A. Prevalence and determinants of low bone mineral density among people living with HIV on antiretroviral therapy in Lusaka, Zambia: A cross-sectional study. *East Cent Afr J Surg*. 2024;29(1):4-10.
doi:10.4314/ecajs.v29i1.2

Original Research

Prevalence and determinants of low bone mineral density among people living with HIV on antiretroviral therapy in Lusaka, Zambia: A cross-sectional study

Chisomo Joshua Webster SHAWA[1a], Jonathan Ikachana SITALI[2], Justor BANDA[1], Aggrey MWEEMBA[1]

[1] The University of Zambia, [2] Zambia College of Medicine and Surgery

Keywords: bone mineral density, osteoporosis, osteopenia, HIV, AIDS, antiretroviral therapy, Zambia

https://doi.org/10.4314/ecajs.v29i1.2

East and Central African Journal of Surgery

Vol. 29, Issue 1, 2024

Abstract

Background

Reduced bone mineral density (BMD) is a common complication of people living with Human Immunodeficiency Virus (HIV) on antiretroviral therapy (ART). However, there is lack of information on the factors associated with reduced BMD in people living with HIV and on ART. We assessed the prevalence of reduced BMD and its associated determinants in people living with HIV and were on antiretroviral therapy.

Methods

A cross-sectional study on people living with HIV and on ART was conducted at the largest tertiary teaching adult hospital, in Lusaka Zambia from August 1, 2019 December 31, 2020. Included in the study were participants aged between 50 and 69 years of age. A Dual-energy X-ray Absorptiometry scan was employed to assess Bone Mineral Density. Low Bone Mineral Density was defined as both osteoporosis and osteopenia. Logistic regression analysis was employed to establish determinants associated with BMD.

Results

Of the 315 participants, 43.8% were females and the median age was 55.0 years (IQR 60-51). The overall prevalence of reduced bone mineral density was 82.6% and of these, 34.0% had osteopenia and 48.6% osteoporosis. After adjusting for confounders, age 55 years and older (AOR 5.87, 95% CI 3.34-10.30, p=**<0.001**) was independently associated with osteoporosis while CD4 count ≥ 500 cells/mm^3 (AOR 0.21, 95% CI 0.08-0.55, p=**<0.001**) and an increase in Body Mass Index (AOR 0.94, 95% CI 0.90-0.99, p=0.008) were associated with decreased odds of osteoporosis.

Conclusions

Our study highlights a high prevalence of low Bone Mineral Density. Older age was positively associated with osteoporosis while a high CD4 count and high body Mass Index revealed a decreased odds for osteoporosis.

Introduction

Low bone mineral density (BMD) is one of the common complications among people living with Human Immunodeficiency Virus (PLHIV) on antiretroviral therapy (ART).[1] Published studies have reported up to 23.0% rate of osteoporosis and 24.0% to 59.5% of osteopenia in PLHIV compared to 9.0% of low BMD (osteopenia and osteoporosis combined) in the general population.[2-5] Several unmodifiable and modifiable risk factors contribute to the development of low BMD in PLHIV on ART.[6] In the pre-ART era, longer duration of HIV infection, advanced HIV stage, and high levels of viremia were positively linked with greater BMD loss.[7] In the ART era, PLHIV have better quality and increased life and are getting older which predisposes them to increased risk of low BMD.[6]

The effect of low BMD translates to an increased risk of pathological fractures and decreased rate of fracture heal-

a Corresponding author: chisomoshawa@gmail.com

ing.[6] The most common fractures are those of the vertebrae, hip, and wrist.[8] Management of hip fractures almost always requires major surgical intervention and mortality is also increased following vertebral fractures, which results in significant complications including back pain, height loss and kyphosis.[9] So, the early identification and treatment of osteopenia/osteoporosis is critical to prevent fractures in PLHIV.[6]

An understanding of the burden and the associated risk factors for low BMD is needed to warrant a prevention campaign.[6] Currently, there is scanty data on low BMD in sub Saharan Africa to the extent that some scholars have suggested that it is not an important disorder in this setting.[4,10] Several reasons could be given to explain this assertion such as reduced lifespan, under-reporting, or simply the differences in lifestyles.[10] However, recent studies in the sub-Saharan African region have revealed a low prevalence.[11-13]

According to the 2021 Zambia Population-Based HIV/AIDS Impact assessment, the prevalence of HIV amongst older people aged 50 and 54 years old is very high at 29.15 % but it gradually decreases to 7.15% in those above 65 years old.[14] Like many other African countries, Zambia also has paucity of data on low BMD in PLHIV despite the high rate of osteoporotic related fractures (24.3%) observed in the general population.[15] This study investigated prevalence of low BMD and its associated factors in PLHIV at a largest tertiary teaching level hospital, in Lusaka Zambia.

Methods

Study design, setting and population

This was a descriptive cross-sectional study that was conducted from August 1, 2019 to December 31, 2020, at the University Teaching Hospital (UTH), in Lusaka, Zambia. The UTH is the largest teaching tertiary level hospital in Zambia. The Advanced Infectious Disease Center under the Department of Internal medicine is an Adult Centre of excellence that offers advanced HIV care among other services and the center has approximately 13,000 clients on different antiretroviral therapy (ART regimens).

The study included all consented participants who underwent Dual Energy X-ray Absorptiometry (DXA) scanning, between 50 and 69 years of age, and were HIV positive on antiretroviral therapy. Physical activity level was assessed using the International Physical Activity Questionnaire (IPAQ). According to the World Health Organization (WHO) (1994) definition for reduced bone mineral density, the use of t-score applies to adults above 50 years.[16,17] The upper limit recommended for assessment of the International Physical Activity Questionnaire (IPAQ) is 69 years of age.[18] Hence, the age range was adults 50-69 years of age.

Excluded from the study were patients with known risk factors of osteopenia/osteoporosis. These included patients with known diagnosis of hyperthyroidism, hyperparathyroidism, hypogonadism, liver disease, chronic kidney disease, and diabetes mellitus. Patients who previously or were at the time of the study receiving calcium and vitamin D supplements, anticonvulsants, heparin, chemotherapy, oestrogen, and/ or thyroid replacement drugs were also excluded. Patients with a history of immobilization in the past one-month, history of hysterectomy/oophorectomy, and patients with a previous history of spine deformity or spine surgery were also excluded.

Sampling strategy

A systematic random sampling with a sampling interval of 4 was used to select the participants. This was done as follows: the total numbers of clients 50 years and above that were expected to be seen at UTH was 961 (observed in 2019 from records). The expected 961 number of clients were divided by the calculated sample size of 296 number of clients, this gave a sampling interval of 4. Therefore, every 4^{th} person in the order they presented to the facility were recruited in the study. The first client was randomly selected.

Sample size

The sample size was calculated using the Cochran formula as follows:

$$n = \frac{q2p(1-p)}{d^2}$$

Where n is the sample size, q is desired confidence level (95%), p is the estimated proportion of an attribute that is present in the population, p is 26% and d is the desired level of precision 0.05.[5]

$$n = \frac{1.96^2 0.26(1-0.26)}{0.05^2}$$
$$n = 296$$

Participants

A total number of 315 participants were sampled after factoring those that did not meet the inclusion criteria.

Study procedures

Clients were indexed from the Adult Centre of Excellence at UTH, Adult Hospital and Informed consent was obtained. A data collection sheet was used to assess known determinants for low bone mineral density (age, sex, weight, height, previous low-trauma fracture, parent hip fracture, current smoking, alcohol use, current glucocorticoid use, and secondary osteoporosis). Physical activity levels using the validated International Physical Activity Questionnaire (IPAQ) was also assessed.[18]

Clinical examination of all the clients was also done from head to toe to examine for the thyroid gland, Breast, Chest, skin, heart, central nervous and abdomen to assess for any abnormalities.

Baseline blood tests that included full blood count, Erythrocyte sedimentation rate, random blood glucose, and urea and creatinine level were collected. Standard information on HIV infection (CD4 cell count and viral load) was performed. The COBAS 6800 HIV Viral load machine was used to measure the viral load. All blood samples were routinely obtained via venu-puncture in the ante-cubital vein and processed at the main Laboratory at UTH.

BMD was measured using a DXA scan (HOLOGIC device) of the lumbar spine at the first to fourth lumbar vertebrae and the results were given as BMD (g/cm²). DXA Scan was calibrated daily for quality control using the spine phantom and all measurements were done by one qualified technician. All examinations were performed according to the manufacturer's recommendations.

Study outcomes and definitions

The primary outcome of the study was to determine the prevalence of low bone mineral density in PLHIV on ART while the secondary outcomes were the associated factors of osteoporosis.

1. Osteopenia was defined using World Health Organization (WHO) definition as low bone mineral density as a bone density of 1.0 to 2.5 standard deviations less than the mean peak bone mass of a healthy 25-year-old and osteoporosis as Lumbar (L2-L4) density of 2.5 or more standard deviations less than the mean peak bone mass of a healthy 25-year-old (t-score).[8]
2. Low BMD was defined as either osteoporosis or osteopenia or both.[8]

Data collection and statistical analysis

Trained Health personnel obtained data from the participants. The data involved information on age, sex, any history of immobilization passed one month, menstrual and obstetric history in particular age at menarche, years since last menses, and period of pathological amenorrhea before age of 45 years.[8]

With regards to drug history, any drug known to cause reduced bone mineral density past six months was asked, clients on any calcium or Vitamin D supplementation, oestrogen and thyroid replacement drugs were excluded from the study.[8] A passed medical history of Diabetes Mellitus, epilepsy, spine deformity or spine surgery were also excluded from the study as these could comprise DXA scan readings.[8] Background of clients with Hysterectomy or Oophorectomy were also part of the exclusion criteria.[8]

Detailed smoking history if any was obtained to include duration, packs per day, if currently stopped duration since stopping. Alcohol detailed history was also obtained to include duration, frequency, Units per day, if stopped also duration since stoppage.

HIV history which was also matched with the participants' records in their files included duration since diagnosis, total duration on ART, exact type of regimen on and duration. Records of default if any and duration. For any change of regimen, detailed history as above including duration of previous regimen was obtained.[5]

Body weight (Kg) and Height (m) were obtained using a stadiometer. Body mass index for each participant was calculated as weight measured divided by square of height obtained. Clinical assessment of the Thyroid gland, Chest, Breast, and abdomen was done by qualified medical personnel.

Baseline Blood Tests that included full blood count, Erythrocyte sedimentation rate, random blood glucose, and urea and creatinine level were collected. Standard information on HIV infection (CD4 cell count and viral load) were performed. The COBAS 6800 HIV Viral load machine was used to measure the viral load. All blood samples were routinely obtained via venu-puncture in the ante-cubital vein and processed at the main Laboratory at UTH

The International Physical Activity Questionnaire (IPAQ) was used to collect data on Physical activity levels of the participants. The IPAQ comprised questions on frequency, intensity and duration of physical activity that participants do as part of their everyday life in the previous 7 days. The IPAQ was proven to be a valid and reliable tool for measuring Physical Activity among adults aged 18–69 years in diverse settings.[18]

Variable minutes spent on doing physical activity were recorded. The minutes were calculated into metabolic equivalents (METs). METs are defined as multiples of the resting metabolic rate ($1\ MET = 3.5ml\ O_2\ kg^{-1}\ min^{-1}$) and MET-minutes were calculated by multiplying the MET score of an activity (an equivalence of kilocalories for a 60 kg person) by the minutes performed.[18]

Participants were categorized into low, moderate and high Physical Activity levels. Low level Physical Activity comprised participants having the lowest Physical Activity and did not meet the criteria for moderate or high Physical Activity levels. Moderate Physical Activity level comprised participants who did 3 or more days of vigorous Physical Activity for at least 20 minutes per day. Similarly, participants who performed 5 or more days of walking or moderate intensity Physical Activity for at least 30 minutes per day, fell into the moderate Physical Activity level category. High Physical Activity level comprised participants who performed at least 3 days of vigorous intensity Physical activity accumulating at least 1500 MET minutes per week. Similarly, participants who performed 7 or more days of any combination of vigorous Physical Activity, moderate intensity Physical Activity or walking achieving a total of at least 3000 MET minutes per week, fell into the high Physical Activity level category.

Bone Mineral Density was measured using a DXA scan (HOLOGIC device) of the lumbar spine in all patients from the lumbar spine (first to fourth vertebrae) and the results are given as BMD (g/cm²). The female National Health and Nutrition Examination Survey (NHANES) III data was used as the reference standard for lumbar spine t-scores as there are no baseline reference values in Zambia.[8] The results were categorized according to WHO as normal, osteopenia, and osteoporosis. Reduced bone mineral density in this study was regarded as either osteopenia and/or osteoporosis.

The clinical Assessments, International Physical Assessment Questionnaire, laboratory results and Bone Mineral density findings were compiled and put in one Standard Data Collection sheet. Data collected was directly entered into Statistical Package for Social Sciences (SPSS) version 23.0 software. The Shapiro-Wilk test was used to test for normality and normally distributed variables were reported using means and medians for none normally distributed. To test association and correlations, the Chi-Square test (Fisher's exact test when numbers were small) was carried out for categorical variables. The Mann Whitney U test was used to test differences between two medians. Univariate Logistic Regression analysis was used for the associations with each dependent outcome. To explain confounding, we developed one model using multivariate logistic regression to predict osteoporosis that included clinically important (such as sex) or significant covariates at univariate analysis. A p-value less than 0.05 were considered statistically significant.

Ethical considerations

Informed consent was obtained from eligible and willing participants who had come for their routine reviews or drug refill. Participation was voluntary and there was no compensation for any inconveniences/ time lost. All ethical procedures were followed and privacy and confidentiality were ensured by allocating codes to the participants. Ethical approval (IRB00001131 of IORG0000774 with No. 750-2020) was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC).

Results

Prevalence of reduced bone mineral density

The study included 315 PLHIV that were on ART. The median age was 55 years (IQR 60–51), and 44.0% (138) of participants were female. The proportion of osteopenia and osteoporosis was 34.0% and 48.5% respectively. Nearly two thirds (63.5%) of the participants had undetectable viral load and only 7.0% (22) were not suppressed (viral load ≥1000 copies/mL). The proportion of participants with CD4 cell count <500 cells/mm^3 was 40.0% (126). Three quarters (76%) of participants were on a TDF-based regimen, 12.7% on Zidovudine based regimen, 5.0% on Abacavir based regimen while only 6.0% were on Tenofovir Alafelamide (TAF-based) regimen as shown in table 1.

The following factors were significantly different between participants with osteoporosis and those without; median age (P<0.001), age 55 years and older versus age <55 years (P<0.001), median age at menopause (p<0.033), duration of menopause ≥4 years versus duration <4 years (p<0.001), alcohol intake (P<0.046), HIV duration ≥10 years versus <10 years (P=0.009), ART duration ≥10 years versus duration <10 years (p=0.017), median CD4 cell count (p<0.001), CD4 count ≥500 cells/m^3 versus CD4 <500 cells/m3 (p<0.001), median viral load (p<0.001), viral load ≥ 20 copies/mL versus viral load <20 copies/mL (P<0.001) and IPAQ Score (P=0.050)

Age ≥55 years, duration of menopause ≥4 years, duration of HIV ≥10 years, duration of ART ≥10 years, and a viral load ≥ 20 copies/mL showed a positive association with osteoporosis. On the other hand, a CD4 count ≥500 cells/mm^3 and an increase in BMI were significantly associated with decreased odds of osteoporosis.

After adjusting for age, sex, alcohol intake, BMI, HIV duration, ART duration, viral load, and CD4 count, only age 55 years and older (AOR 5.87, 95% CI 3.34-10.30, p=**<0.001**) was independently associated with increased odds of osteoporosis. CD4 ≥500 cells/mm^3 (AOR 0.21, 95% CI 0.08-0.55, p=**<0.001**) and increase in BMI (AOR 0.94, 95% CI 0.90-0.99, p=0.008) were independently associated with reduced odds of osteoporosis.

Discussion

In this study, the proportion of osteopenia and osteoporosis was respectively 34.0% and 48.6% and age, CD4 cell count and BMI were positive predictors of bone mineral disease (BMD). There have been variations in prevalence amongst PLWHIV from one region/ country to the other.[6] Previously studies have reported higher rates of up to 85% reduced BMD amongst PLWHIV in low- and middle-income countries.[19] However, recent studies conducted in the sub-Saharan Africa (SSA) reported 20% lower rates of BMD.[11-13] The prevalence low BMD obtained in this study of 82.5 % is markedly high and it consistent with previous findings[5,19] The problems such as malnutrition, low BMI, and longer duration without ART treatment after the diagnosis of HIV are usually common challenges seen in this region in SSA.[20] This is also the region worst affected by HIV/ AIDS and also have similar challenges in the management of this pandemic

Of the studies that have been done in this region, they mostly were conducted in HIV patients aged 18 to 49 years and age could be the main factor to explain this huge difference.[9] Other studies in SSA that were performed in similar age group in Senegal showed comparable osteopenia val-

Table 1. Fisher's exact test for association between type of drugs and t - score

Variable	Category	Bone Mineral density			P-Value
		Normal	Osteopenia	Osteoporosis	
Current regimen	TDF Based	43	78	119	0.016
	AZT Based	9	20	11	
	ABC Based	3	3	10	
	TAF Based	0	6	13	
Previous regimen	TDF Based	26	57	86	0.077
	AZT Based	5	6	17	
	ABC Based	0	6	3	
	ATVr Based	0	3	0	

ABC; Abacavir, ATVr; Atazanavir/ritonavir, AZT;Zidovudine, TAF; Tenofovir alafelamide,; TDF;Tenofovir disoproxil fumarate

ues.[5] This shows the importance in factoring age in analysis of BMD. However, osteoporosis values in this study were still higher than what was pertaining in Senegal ten years ago. This could be because of the time duration that has passed or other factors especially related in the management of HIV.

In this age range, the national age specific prevalence of HIV is higher in females than in males.[14] The effect on HIV either as a virus on bone metabolism or even effects of various ART drugs could be the cause of this osteopenia.[1] Most likely, it could also be effect of menopause (estrogen) on the bone metabolism.[8] However, males have a higher prevalence of osteopenia (36.7%) than females (30.4%). A United States study reported 42.0% of postmenopausal women living with HIV had osteoporosis.[21] In contrast, some studies have found overall low BMD in males than in females.[22]

Currently, there is no data on low BMD in the Zambian general population. The lack of age-matched control group in our study also precludes comparisons with HIV negative subjects. In general, low BMD is more common among PLHIV compared to HIV negative individuals.[1] In Nigeria, a setup similar to Zambia, the prevalence of osteoporosis was 9.0% in the general population compared to 31.9% in PLHIV.[19] However, data from a South African study among black women shows no difference in BMD DEXA measurements by HIV infection status.[23] Of concern, although with unknown clinical implication, is the very high combined prevalence of 82.5% of low BMD (osteopenia 34% and osteoporosis 48.6%) in our study which warrants further intervention measures.

In this present study, older age ≥55 years was associated with nearly 6-fold-odds for having osteoporosis in PLHIV. This finding agrees with existing information that biological age is significantly related to low BMD.[8] PLHIV have seen high quality and increased life expectancy due to improved care including ART[1,5] and as a result, it exposes them to the consequences of aging including low BMD.[5] As the population of PLHIV in Zambia ages, so will the individuals with complications of BMD loss increase.

Of the known modifiable factors, an increase in BMI was associated with reduced odds of low BMD. This confirms results from other studies including Sub-Saharan Africa that have shown this relationship between BMI and low BMD in PLHIV.[5] There is evidence that PLHIV are lighter in weight than comparable HIV negative controls which is mainly explained by BMI between the two groups.[5] Changes in weight or BMI are associated with changes in BMD in various studies.[1,5] As one loses weight (or BMI), BMD reduces with some lag time. Likewise, as one gains weight (or BMI), BMD rises, again with a similar lag time.[20] In PLHIV, ART naive with stage 3 or 4 disease, there is significant weight loss, but once on ART, they regain their lost weight.[24] Therefore, it is imperative to have weight monitoring programs for people with PLHIV to keep their BMI in the normal range to prevent BMD.

Height is part of the BMI formula and therefore, a negative significant association with BMD is expected. An increase in one's height is likely to lead to an increase in BMD loss.[25] The association between height (or BMI) and BMD suggests that growth is an important factor other than weight alone. Several studies have shown that taller individuals have an increased risk of fractures in multiple body regions that have no biomechanical predisposition.[26] Although height is not a modifiable risk factor, preventative measures could be put in place to protect these individuals from developing osteoporotic fractures.

There is also evidence that PLHIV have low BMD beyond what is expected when compared to those with traditional risk factors alone.[1,5] Studies on PLHIV ART-naïve have shown that longer duration of HIV infection, more advanced HIV stage, and high levels of viremia are associated with greater BMD loss, suggesting that the virus itself and the inflammation associated with HIV infection have an effect on BMD.[27]

In our study, duration of HIV infection ≥10 years, duration of ART ≥10 years, CD4 count < 500cells/mL, viral load ≥20 copies/mL and a viral load ≥1000 copies/mL were all associated with an increased odds of osteoporosis at univariate analysis. However, in multivariate analysis, only

Table 2. Baseline Characteristics of Participants stratified by Osteoporosis status

Variables		Osteoporosis		P value
		Absent	Present	
Age in years	Median (IQR)**	51(56-50)	59(64-53)	**<0.001**
	Age < 55, N (%)	119 (69)	54 (31)	**<0.001**
	Age ≥ 55, N (%)	43 (30)	99 (70)	
Sex	Male N (%)	92 (52)	85 (48)	0.825
	Female N (%)	70 (51)	68 (49)	
Age at menopause	Median (IQR)**	49(49-47)	49(50-48)	**0.033**
	Age <49, N (%)	26 (53)	23 (47)	0.109
	Age ≥49, N (%)	28 (38)	45 (62)	
Menopause duration in years	Median (IQR)**	2(1-3)	11(7-14)	**<0.001**
	Duration <4, N (%)	57 (84)	11 (16)	**<0.001**
	Duration ≥4, N (%)	6 (10)	53 (90)	
Smoking	Yes, N (%)	9 (56)	7 (44)	0.692
	No, N (%)	153 (51)	146 (49)	
Alcohol	Yes, N (%)	12 (35)	22 (65)	**0.046**
	No, N (%)	150 (53)	131(47)	
HIV duration in years	Median (IQR)**	10(14-5)	12(14-6)	0.250
	Duration <10, N (%)	97 (58)	69 (42)	**0.009**
	Duration ≥10, N (%)	65 (44)	84 (56)	
ART duration in years	Median (IQR)	10(14-5)	11(14-6)	0.705
	Duration <10, N (%)	98 (58)	72 (42)	**0.017**
	Duration ≥10, N (%)	64 (44)	81 (56)	
ART type	TDF based, N (%)	121(50.4)	119 (49.6)	0.52
	Non-TDF based, N (%)	41 (55)	34 (45)	
Change of regimen	Yes. N (%) No, N (%)	103(49.3) 59 (56)	106(50.7) 47 (44)	0.285
CD4 Count (cells/mm^3)	Median (IQR)**	608(782-501)	472(606-306)	**<0.001**
	CD4 Count <500, N (%)	38 (30)	88 (70)	**<0.001**
	CD4 Count ≥500, N (%)	124 (66)	65 (34)	
Viral load (copies/mL)	Median (IQR)	<20 (<20-0)	58(303-≥20)	**<0.001**
	Viral Load <20, N (%)	129 (64.5)	71 (35.5)	**<0.001**
	Viral Load ≥20, N (%)	33 (29)	82 (71)	
BMI (Kg/m^2)	Median (IQR)**	25(29-22)	24 (28-21)	0.41
	BMI < 18.5, N (%)	7(37)	12 (63)	0.189
	BMI ≥18.5, N (%)	155 (52)	141(48)	
IPAQ Score*	Mild, N (%)	120 (49.8)	121 (50.2)	**0.050**
	Moderate, N (%)	36 (53)	32 (47)	
	Highly active, N (%)	6 (100)	0 (0)	

*Fisher's exact test used; ** Mann Whitney U test used; BMI, Basal Mass Index; BMD, Bone Mineral Density; IPAQ, International Physical Activity Questionnaire; IQR, Interquartile Range; ART, Antiretroviral therapy; CD4, Cluster of Differentiation 4.P values for the Mann-Whitney U test and chi-square/ Fishers' exact test comparisons between groups are in the right most.

CD4 count <500cells/mL was associated with low BMD. There is conflicting data on CD4 count and low BMD with some studies showing a significant relationship while others demonstrating that immune activation led to low BMD despite good virologic suppression.[1,5] In our study a CD4 count <500 cells/mm^3 was independently associated with low BMD.

In PLHIV who are ART naive, literature shows that increased duration of HIV infection is associated with increased BMD loss.[20,26] In our study, the duration of HIV ≥10 years was not associated with osteoporosis at multivariate analysis. The fact that our population was on ART with excellent virologic suppression; this may have offset the impact of long-term viremia on BMD. The gain in BMI because of ART may also have had an impact of the dura-

Table 3. Crude predictors of Osteoporosis

Variables		Crude OR	95% CI	P value
Age in years	Age ≥ 55	5.07	3.12-8.21	**<0.001**
	Age <55	1		
Sex	Female	1.05	0.67-1.64	0.825
	Male	1		
Age at menopause in years	Age ≥49	1.82	0.87- 3.78	0.110
	Age <49	1		
Duration of Menopause in years	Duration ≥4	45.77	15.82-132.48	**<0.001**
	Duration <4	1		
Viral Load, copies/mL	Viral load ≥20	4.52	2.75-7.42	**<0.001**
	Viral load <20	1		
Duration of HIV in years	Duration ≥ 10	1.82	1.16 - 2.84	**0.009**
	Duration > 10	1		
Duration of ART in years	ART Duration ≥10	1.72	1.10-2.69	**0.017**
	ART Duration <10	1		
ART Regimen	TDF based ART	0.84	0.50 - 1.42	0.521
	Non-TDF Based	1		
CD4 count cells/mm^3	CD4 ≥500	0.23	0.14-0.37	**<0.001**
	CD4<500	1		
BMI in Kg/m^2	Median	0.94	0.90 - 0.99	**0.008**
Smoking	Yes	1.23	0.45 - 3.38	0.692
	No	1		
Alcohol Intake	No	0.476	0.23 - 1.00	**0.050**
	Yes	1		
IPAQ Score*	Mild	1		0.900
	Moderate	0.882		0.647
	Highly Active	0.000		0.999

BMI, Basal Mass Index; BMD, Bone Mineral Density; IPAQ, International Physical Activity Questionnaire; IQR, Interquartile Range; ART, Antiretroviral therapy; CD4, Cluster of Differentiation 4. Crude OR, Crude Odds Ratio; 95% CI, 95% confidence Interval. P-value ≤ 0.050 was considered significant

tion of HIV infection on BMD. Therefore, weight or BMI loss in PLHIV during the untreated period may cause BMD loss that continues into the early period of ART initiation, but which stabilizes after continued ART intake with subsequent body weight or BMI gain.[27]

The effect of ART on BMD loss is universal across antiretroviral drug classes even though the magnitude of BMD loss may vary by drug regimen.[27] TDF based regimens have been associated with BMD loss compared to other regimens.[28] The mechanisms by which TDF causes BMD loss includes direct effects on osteoblasts and osteoclast gene expression[28] and phosphate wasting that is caused by proximal renal tubular dysfunction.[28]

We did not demonstrate any association between a TDF based regimen and low BMD. Three quarters (76%) of participants were on a TDF-based regimen in our study and 71.5% had been previously switched from a TDF based regimen. Therefore, some patients who were previously switched from a TDF regimen were currently on a non-TDF regimen. The washout period after the switch was not considered. This could have confounded our findings and thus this result should be interpreted with caution. On the other hand, the overall benefit of ART on BMI and viremia may lead to BMD gain and stabilization in the long term.[27]

Traditional predictors for BMD loss such as smoking, alcohol use, hypogonadism, thyroid disease, CKD, post menopause, vitamin D deficiency and glucocorticoid use are more common in PLHIV.[27] We did exclude (although not completely) most of the participants who had underlying co-morbidities that may predispose to BMD loss. Smoking was not associated with osteoporosis in our study. The reason could be that the prevalence of smoking was very low in this study. Only 4.8% (16 out of 315) were smokers. We also found that the duration of menopause was associated with increased odds of osteoporosis. Nevertheless, further statistical analysis revealed that duration of menopause was confounded by age (the group which was menopause for ≥4 years was statistically older than the group which was menopause <4 years). Alcohol intake was associated with low BMD at univariate level but marginally non-significant at multivariate level. None of our participants reported previous fractures. Hence, we cannot report

Table 4. Adjusted predictors of Osteoporosis

Variables		AOR	AOR 95% C.I	P-value
Sex	Female Male	1.52 1	0.83 - 2.78	0.175
Alcohol Intake	Yes No	2.44 1	097 - 5.88	**0.057**
BMI in Kg/m^2	BMI	0.91	0.86 - 0.97	**0.002**
Age in years	Age ≥55 Age <55	5.87 1	3.34 - 10.30	**<0.001**
HIV Disease Duration in years	Duration ≥10 Duration <10	5.63 1	0.81 - 39.35	0.082
ART Duration in years	Duration ≥ 10 Duration > 10	0.32 1	0.05 - 2.18	0.243
Viral Load, copies/mL	Viral Load ≥20 Viral Load <20	1.50 1	0.58 - 3.89	0.407
CD4 count cells/mm^3	CD4 ≥500 CD4 <500	0.21 1	0.08 - 0.55	**<0.001**

BMI, Basal Mass Index; BMD, Bone Mineral Density; IPAQ, International Physical Activity Questionnaire; IQR, Interquartile Range; ART, Antiretroviral therapy; CD4, Cluster of Differentiation 4. 95% CI, 95% confidence Interval; AOR Adjusted Odds Ratio; P-value ≤ 0.050 was considered significant

on fracture risk in this population. All these factors may affect BMD in PLHIV on ART but to explain early BMD loss after ART initiation followed by BMD increases and stability in the presence of all these factors remains a puzzle.

Our study is without limitations. Despite an optimal sample size, it lacked a comparison group. As this was a cross sectional study, we could not compare our findings with the pre-ART BMD. Some patients who were previously switched from a TDF regimen were currently on a non-TDF regimen. The washout period after the switch was not considered. This could have confounded our findings. We did not perform the following tests in all the patients to rule out other factors or co morbid conditions associated with low BMD like 25-Hydroxy vitamin D, parathyroid hormones, thyroid hormones, and alkaline phosphatase.

Conclusions

We report a high prevalence of low BMD in our study. A CD4 count ≥500 cells/mm^3 and an increase in BMI were associated with reduced odds of osteoporosis. Age was the only unmodifiable risk factor associated with osteoporosis.

Recommendations

There is need to enhance BMI and CD4 count monitoring of the older HIV patients in Zambia to enhance preventive intervention of BMD disorders.

Submitted: March 14, 2022 EAT, Accepted: November 01, 2023 EAT

References

1. Compston J. HIV infection and bone disease. *Journal of internal medicine*. 2016;280(4):350-358. doi:10.1111/joim.12520

2. Salari N, Ghasemi H, Mohammadi L, Rabieenia E, Shohaimi S, Mohammadi M. The global prevalence of oste-oporosis in the world: a comprehensive systematic review and meta-analysis. *Journal of orthopaedic surgery and research*. 2021;16(1):1. doi:10.1186/s13018-021-02772-0

3. Paruk F, Tsabasvi M, Kalla AA. Osteoporosis in Africa—where are we now. *Clinical rheumatology*. 2021;40:3419-3428. doi:10.1007/s10067-020-05335-6

4. Atiase Y, Quarde A. A call to action for osteoporosis research in sub-saharan Africa. *Ghana Medical Journal*. 2020;54(1):58-67. doi:10.4314/gmj.v54i1.8

5. Cournil A, Eymard-Duvernay S, Diouf A, et al. Prevalence of Osteoporosis among HIV-1-Infected Men and Women Aged 50 years and Older in Dakar, Senegal: A Cross-Sectional Study. *J AIDS Clin Res*. 2015;6(443):2. doi:10.4172/2155-6113.1000443

6. Negredo E, Domingo P, Gutiérrez F, et al. Executive summary of the consensus document on osteoporosis in HIV-infected individuals. *Enfermedades Infecciosas y Microbiología Clínica*. 2018;36(5):3124. doi:10.1016/j.eimc.2017.03.010

7. Carr A, Grund B, Neuhaus J, et al. Prevalence of and risk factors for low bone mineral density in untreated HIV infection: a substudy of the IN-SIGHT Strategic Timing of Anti-Retroviral Treatment (START) trial. *HIV medicine*. 2015;16:137-146. doi:10.1111/hiv.12242

8. Thompson SR, Miller MD, eds. *Miller's Review of Orthopaedics*. Elsevier, Incorporated; 2016.

9. Aydın OA, Karaosmanoglu HK, Karahasanoglu R, Tahmaz M, Nazlıcan O. Prevalence, and risk factors of os-teopenia/osteoporosis in Turkish HIV/AIDS patients. *Brazilian Journal of Infectious Diseases*. 2013;17(6):707-711. doi:10.1016/j.bjid.2013.05.009

10. Zebaze RM, Seeman E. Epidemiology of hip and wrist fractures in Cameroon, Africa. *Osteoporosis international*. 2003;14(4):301-305.

11. Chisati EM, Constantinou D, Lampiao F. Reduced bone mineral density among HIV infected patients on anti-retroviral therapy in Blantyre, Malawi: Prevalence and associated factors. *PloS one*. 2020;15(1):e0227893. doi:10.1371/journal.pone.0227893

12. Mwaka ES, Munabi IG, Castelnuovo B, et al. Low bone mass in people living with HIV on long-term anti-retroviral therapy: A single center study in Uganda. *Plos one*. 2021;16(2):e0246389. doi:10.1371/journal.pone.0246389

13. Dave JA, Cohen K, Micklesfield LK, Maartens G, Levitt NS. Antiretroviral therapy, especially efavirenz, is associated with low bone mineral density in HIV-infected South Africans. *PloS one*. 2015;10(12):e0144286. doi:10.1371/journal.pone.0144286

14. Zambia Population-Based HIV/AIDS Impact Assessment (ZAMPHIA 2021), Summary sheet. December 2022.

15. Ikachana SJ. *Prevalence of Postmenopausal Osteoporosis Fractures among Women Presenting with Fractures to the University Teaching Hospital, Lusaka*. The University of Zambia, School of Medicine, Lusaka; 2015.

16. McComsey GA, Tebas P, Shane E, et al. Bone disease in HIV infection: a practical review and recommendations for HIV care providers. *Clinical infectious diseases*. 2010;51(8):937-946. doi:10.1086/656412

17. Lewiecki EM, Gordon CM, Baim S, et al. International Society for Clinical Densitometry 2007 adult and pediatric official positions. *Bone*. 2008;43(6):1115-1121. doi:10.1016/j.bone.2008.08.106

18. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. *International journal of behavioral nutrition and physical activity*. 2011;8(1):1-1. doi:10.1186/1479-5868-8-115

19. Alonge TO, Okoje-Adesomoju VN, Atalabi OM, Obamuyide HA, Olaleye D, Adewole IF. Prevalence of ab-normal bone mineral density in HIV-positive patients in Ibadan, Nigeria. *Journal of the west african college of surgeons*. 2013;3(4):1.

20. Matovu FK, Wattanachanya L, Beksinska M, Pettifor JM, Ruxrungtham K. Bone health and HIV in resource-limited settings: a scoping review. *Current Opinion in HIV and AIDS*. 2016;11(3):306. doi:10.1097/COH.0000000000000274

21. Yin M, Dobkin J, Brudney K, et al. Bone mass and mineral metabolism in HIV+ postmenopausal women. *Osteoporosis International*. 2005;16(11):1345-1352. doi:10.1007/s00198-005-1845-0

22. Neto LF, Ragi-Eis S, Vieira NF, et al. Low bone mass prevalence, therapy type, and clinical risk factors in an HIV-infected Brazilian population. *Journal of Clinical Densitometry*. 2011;14(4):434-439. doi:10.1016/j.jocd.2011.06.004

23. Hamill MM, Ward KA, Pettifor J, Norris SA, Prentice A. Bone mass, body composition and vitamin D status of ARV-naïve, urban, black South African women with HIV infection, stratified by CD4 count. *Osteoporosis International*. 2013;24(11):2855-2861. doi:10.1007/s00198-013-2373-y

24. Bolland MJ, Wang TK, Grey A, Gamble GD, Reid IR. Stable bone density in HAART-treated individuals with HIV: a meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*. 2011;96(9):2721-2731. doi:10.1210/jc.2011-0591

25. Hamill MM, Ward KA, Pettifor J, Norris SA, Prentice A. Bone mass, body composition and vitamin D status of ARV-naïve, urban, black South African women with HIV infection, stratified by CD4 count. *Osteoporosis International*. 2013;24(11):2855-2861. doi:10.1007/s00198-013-2373-y

26. Carr A, Grund B, Neuhaus J, et al. Prevalence of and risk factors for low bone mineral density in untreated HIV infection: a substudy of the IN-SIGHT Strategic Timing of AntiRetroviral Treatment (START) trial. *HIV medicine*. 2015;16:137-146. doi:10.1111/hiv.12242

27. Bolland MJ, Wang TK, Grey A, Gamble GD, Reid IR. Stable bone density in HAART-treated individuals with HIV: a meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*. 2011;96(9):2721-2731. doi:10.1210/jc.2011-0591

28. Grigsby IF, Pham L, Mansky LM, Gopalakrishnan R, Carlson AE, Mansky KC. Tenofovir treatment of prima-ry osteoblasts alters gene expression profiles: implications for bone mineral density loss. *Biochemical and bi-ophysical research communications*. 2010;394(1):48-53. doi:10.1016/j.bbrc.2010.02.080