AIDS Research and Therapy

RESEARCH

Open Access

Cumulative incidence and treatment effectiveness of low bone mineral density among people living with HIV in Iran (2021–2023)

Hamidreza Rashidi[1,2], Soheil Mehmandoost[2], Noushin Fahimfar[1,3*†], Seyed Mohammad Hosseinian[4], Mohammad Reza Shakibi[4], Tarlan Hasan Aghaei[4], Farzaneh Yazdi Yahaabadi[4], Pouriya Salajegheh[5], Willi Mcfarland[6], Afshin Ostovar[7] and Hamid Sharifi[2,8*†]

Abstract

Background The introduction of antiretroviral therapy (ART) has significantly improved the life expectancy of people living with HIV (PLHIV), leading to an increased prevalence of age-related comorbidities such as osteoporosis. This study investigates the incidence and characteristics of low bone mineral density (BMD) and the treatment effectiveness of low BMD participants among PLHIV in Kerman, Iran.

Methods A longitudinal study utilized dual-energy X-ray absorptiometry (DEXA) to screen 94 PLHIV in Kerman, Iran, for low BMD. Participants were aged 30 or older and had received antiretroviral therapy (ART) for at least 12 months. Those with low BMD were entered into a single-arm clinical trial and received the appropriate treatment. These people were checked to assess the treatment effectiveness 11 months after completion of the treatment. Those with normal BMD entered a cohort study and were checked to determine the cumulative incidence of low BMD. Data on demographics, medical history, and laboratory tests were collected. A chi-square test was used to assess the association between the categorical variables. A t-test (for normally distributed variables), or Mann-Whitney U (for non-normally distributed variables) was used to assess the differences of BMD between the two groups. Statistical significance was set at $p \leq 0.05$, with analyses conducted in Stata 17.

Results Among 94 PLHIV at baseline, 48 participants (51%) had low BMD. During the follow-up, 11 participants (11.7%) missed the follow-up visits. In the follow-up, 83 PLHIV (40 with low BMD and 43 with normal BMD at baseline) were available. Among 40 participants who received treatment, 5 had normal BMD (treatment effectiveness: 12.5%). However, among 43 PLHIV with normal BMD at baseline, 7 PLHIV had low BMD at the follow-up visit (cumulative

†Noushin Fahimfar and Hamid Sharifi contributed equally to this work.

*Correspondence:
Noushin Fahimfar
n.fahimfar@gmail.com
Hamid Sharifi
sharifihami@gmail.com; hsharifi@kmu.ac.ir

Full list of author information is available at the end of the article

Incidence 16.3%). Those with lower body mass index (BMI) had a higher prevalence of low BMD than those with normal BMI during the follow-up (*p*-value: 0.003). Lumbar spine BMD increased modestly (0.005 g/cm^2), while femoral neck and total hip BMD declined in total participants (0.011, 0.007 g/cm^2, respectively). Osteocalcin and β-isomerized C-terminal telopeptides (β-CTx) levels were higher in the low BMD group in the follow-up, indicating increased bone turnover.

Conclusions The study highlights the high cumulative incidence of 16.3% and treatment effectiveness of 12.5% of low BMD among PLHIV in Kerman, Iran, with implications for fracture risk. Despite a steady state in spine BMD decline, the risk of fracture remains elevated due to continued femoral neck and total hip BMD reduction. Gender-specific factors and BMI may influence susceptibility to low BMD.

Keywords Bone density, HIV infections, Anti-retroviral agents, Osteoporosis, Comorbidities

Introduction

The advent of antiretroviral therapy (ART) has made a significant change in the lives of people living with HIV (PLHIV). This medical breakthrough has led to a significant increase in the life expectancy of this population, bringing it closer to that of the general population [1]. However, this increased longevity led to some novel challenges among PLHIV. The diseases related to older adults have become an important health-related problem for this group. For example, chronic diseases such as low bone mineral density (BMD) and bone fractures have become more prevalent [2], significantly contributing to the comorbidities associated with HIV [3].

Osteoporosis is a condition known for low bone density, leading to an elevated risk of bone fractures [4]. Approximately 18.3% of the general population are suffering from osteoporosis all around the world [5]. While in Iran, the prevalence of osteoporosis was approximately 17% in the general population [6], and around 34% of individuals aged 60 and older experience this condition [7]. Osteoporosis and low BMD are of particular concern in PLHIV. Factors such as HIV infection, aging, and the use of ART have been identified as the risk factors for osteoporosis [8–10]. While the decrease in BMD among PLHIV is more pronounced compared to the general population, the commencement of ART further intensifies the extent of the BMD decrease [11, 12]. Studies have shown that PLHIV who use ART experience a greater decrease in spine BMD (-2.7% annually), compared to the rate observed during the initial stages of menopause (-2.0% annually) [13]. The rate of BMD decrease is particularly significant in ART regimens that include Tenofovir Disoproxil Fumarate (TDF), a commonly used ART medication [14].

Low BMD treatment is a major concern in the PLHIV population. Given the elevated risk of low BMD among PLHIV, implementing effective treatment strategies becomes imperative to maintain bone health, enhance quality of life, and reduce the burden of associated complications. Treatment with bisphosphonates (alendronate and zoledronate) has improved BMD in PLHIV. Some studies even suggest that zoledronate can counteract the bone mineral loss seen after initiation of antiretroviral treatment [15]. Therefore, exploring and implementing targeted low BMD treatment approaches tailored to the unique needs of PLHIV are pivotal steps toward ensuring optimal health outcomes and improving their overall well-being.

In light of this evidence, the primary objectives of our study were to evaluate the effectiveness of a standard treatment among PLHIV who suffered from low BMD and assess the cumulative incidence of low BMD among PLHIV with normal BMD 17 months after the evaluation. Additionally, we aimed to evaluate the rate of BMD decline over time. Furthermore, we sought to examine the dynamic changes in bone turnover markers and alterations in BMD among PLHIV with low BMD in Kerman, southeast Iran.

Methods

Study design

This longitudinal study was conducted from September 2021 to September 2023 at a Voluntary Counseling and Testing Center (VCT) in Kerman, Iran. The study participants were PLHIV aged 30 years or older and had been using ART for at least 12 months before including in this study. VCT serves as a referral center for PLHIV, where they attend routine checkups. Over three months, an interviewer was present at VCT. Participants were approached anonymously, introduced to the study, and enrolled if they agreed to participate. All participants were provided with written informed consent forms to participate in the study.

The study was conducted in two phases. In the baseline phase, a cross-sectional study was carried out to assess the BMD status of the participants. PLHIV with low BMD at the baseline entered into the second phase, a single-arm clinical trial and received the appropriate treatment of low BMD under the supervision of a rheumatologist based on clinical judgment for each patient, which by average had 11 months interval to the follow-up measurement (time from treatment initiation to

follow-up). Therapeutic options included alendronate, zoledronic acid, denosumab, and teriparatide, tailored specifically for each participant with low BMD. Those with normal BMD at the baseline entered a cohort study to measure the cumulative incidence of low BMD. After 17 months, all participants were recruited for follow-up laboratory exams (beta C-terminal telopeptide (β-CTx), osteocalcin, CD4+cell counts, and viral load) and for measuring BMD using Dual-energy X-ray absorptiometry (DEXA). Of the 94 participants in the baseline phase, 83 were visited for DEXA (11.7% loss to follow-up). For more information, see Fig. 1.

At the baseline, a face-to-face interview was conducted in a private room to collect sociodemographic factors including age, gender and education, medical history, medication use, and some behavioral variables like smoking status. Physical activity was assessed using the short form of the International Physical Activity Questionnaire (IPAQ-SF). Physical examinations, including height and weight, were performed by a trained nurse using a standard protocol. Laboratory samples, including CD4+cell counts, viral load, and bone turnover markers, were collected at the VCT center. Biochemical parameters were measured while in a fasting state, following standard protocols.

In the follow-up visit, DEXA results were used to assess participants' BMD. Our objectives included monitoring BMD changes, identifying the cumulative incidence of low BMD, and evaluating treatment effectiveness in the treatment group. Additionally, bone turnover markers were measured during this phase.

Outcome variables

The primary outcome variable was defined as a combination of low BMD and osteoporosis. This variable was used to measure the cumulative incidence of low BMD among the normal BMD population and measure the treatment effectiveness of low BMD among those with low BMD at the baseline. BMD measurements were performed by a trained operator at the lumbar spine (L1-L4), femoral neck, and total hip in a standard position, using a DXA HORIZON® Discovery Wi (S/N 301657 M). Osteoporosis was defined as having a BMD of 2.5 standard deviations (SD) or greater below the average value of young Caucasian women aged 20–29 years, at the femoral neck, lumbar spine (L1-L4), or total hip [16, 17], in participants aged 50 years or older. Total osteoporosis was defined as having osteoporosis at any of these sites. For participants younger than 50 years, low BMD was measured using Z-scores at these sites, with total low BMD defined as having a Z-score ≤ -2 SD at any of these sites [17]. Because our participants' ages ranged from 33 to 69 years, we used the low BMD definition to include both age groups by combining the aforementioned definitions.

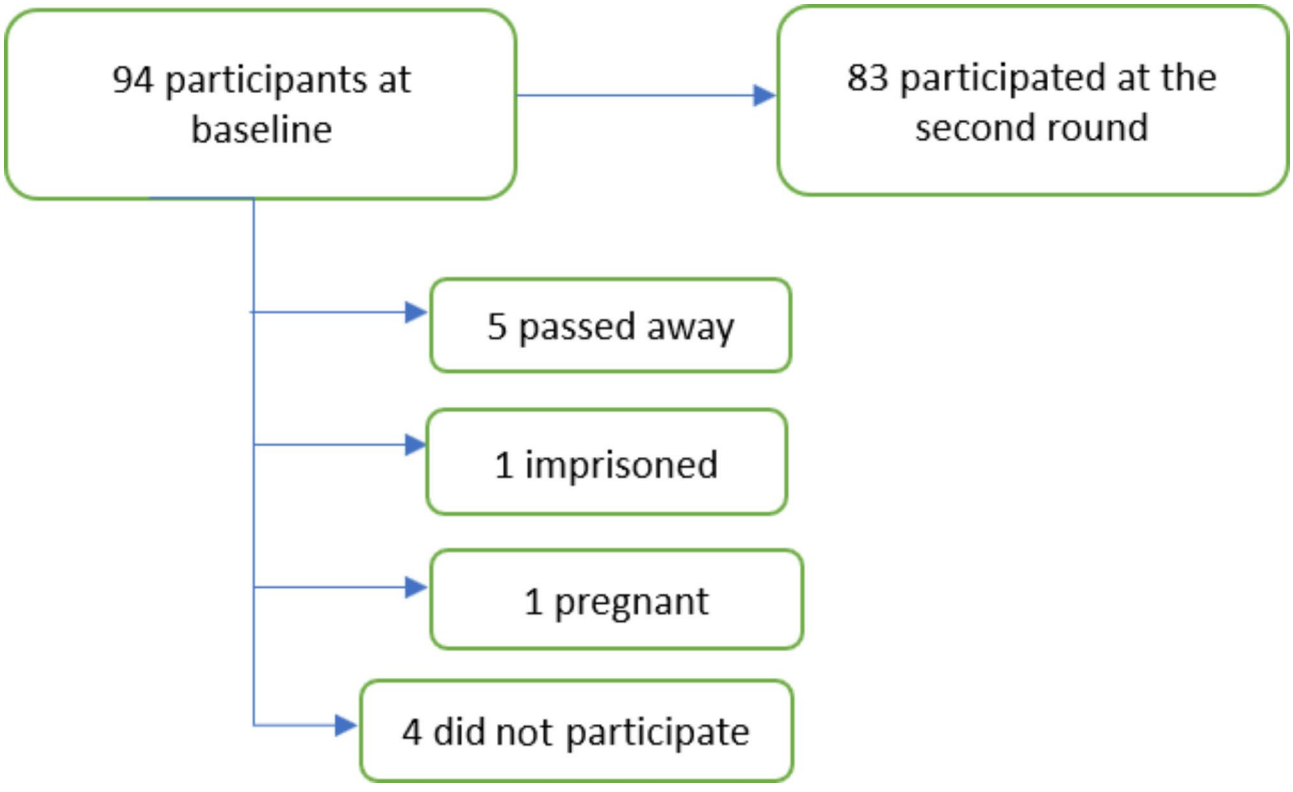

Fig. 1 Flowchart of participants

According to the Committee of Scientific Advisors of the International Osteoporosis Foundation recommendations, we used the National Health and Nutrition Examination Survey (NHANES) III reference database for femoral neck measurements in Caucasian women aged 20–29 years [18].

We also assessed the BMD changes at various sites. At the baseline visit, BMD was measured, and after 17 months, these measurements were repeated at the follow-up visit. The differences were calculated for each site.

We also measured bone turnover markers, including osteocalcin and β-CTx levels, at the baseline and follow-up visits. These markers serve as indicators of osteoblast and osteoclast activity, respectively, which were considered the fourth outcome for this study.

Predictor variables

Predictor variables measured at the baseline and follow-up were: demographic variables, smoking and physical activities, current CD4+cell counts and viral load, ART regimens, hypogonadism, and body mass index (BMI). The levels of hormones and markers related to bone health and metabolism were measured by laboratory tests. The bone turnover markers osteocalcin and β-CTx, baseline CD4+cell counts (as ≤350 vs. >350 cells/mm^3) [19], and viral load (detectable vs. undetectable (<50 copies/mL)) [20] were also measured. ART regimens were obtained from medical files. BMI was calculated as weight in kilograms divided by the square of height in meters. We defined hypogonadism as the summation of men with testosterone levels of under 10 nmol/L [21] and women who were post-menopause.

Statistical analysis

Descriptive statistics, frequency (percentage) for categorical variables, mean and standard deviation (SD) for normally distributed continuous variables, and median with interquartile range (IQR) for variables not normally distributed were used to describe the data. Pearson's chi-square test was used to assess the association of categorical variables. Independent sample t-tests and Mann-Whitney U tests were used for normally and not normally distributed continuous variables, respectively. A p-value of ≤0.05 was considered statistically significant. All statistical analyses were performed using Stata 17 software.

Ethical consideration

The study protocol and consent form were reviewed and approved by the Ethical Committee of Tehran University of Medical Sciences (Approval Number: IR.TUMS.EMRI.REC.1400.002) and Kerman University of Medical Sciences (Approval Number: IR.KMU.REC.1400.129).

Results

Out of 83 participants at the second visit, 52 (62.6%) were women. The mean (SD) age was 49.3 (7.7) years old. The mean (SD) of BMI was 24.8 (5.7). The median (IQR) of ART usage was 90 (53–113) months at the baseline. A total of 20 (25%) of participants were smokers. The prevalence of low BMD in the total sample of the follow-up visit was 50.6% (95% confidence intervals [CI]: 39.4–61.7) (n=42).

Out of the 46 participants who had normal BMD at the baseline, 43 were assessed for the follow-up visit. The mean (SD) time between measurements was 17 [2] months. Seven new cases of low BMD were detected in the follow-up period. So, the cumulative incidence of low BMD was 16.3% (95% CI: 6.81–30.70%) (Fig. 2). Of the seven new participants with abnormal BMD, four were men, three had lower than a high school diploma degree, two were smokers, four had hypogonadisms, and one had a CD4+T cell count of ≤350 cells/mm3. The mean (SD) BMI in the low BMD group was 21.4 (2.3), significantly lower than that in the normal BMD group, which had a mean BMI of 28.1 (5.5) (p-value: 0.003) (Table 1).

The TBS mean (SD) in the low BMD group at the baseline was 1.38 (0.04), and it was not significantly higher than that in the normal group, which had a mean of 1.34 (0.08) (p-value: 0.733). The baseline osteocalcin median (IQR) in the low BMD group was 16.1 (11.4–21.3), significantly higher than the normal BMD group, which had a median of 3.6 (2.6–7.7) (p-value: 0.004). The baseline β-CTx median (IQR) was 0.9 (0.7–1.3) in the low BMD group, which was significantly higher than the normal BMD group, with a median of 0.4 (0.3–0.8) (p-value: 0.011) (Table 1).

Out of the 48 participants with low BMD at the baseline, 40 were assessed for the follow-up visit, of which 5 were treated. The cumulative treatment effectiveness of low BMD was 12.50% (95% CI: 4.19–26.80%) in 11 months of follow-up. The mean (SD) treatment time was 11 [2] months among those participants with abnormal BMD who received treatment for osteoporosis (Fig. 1).

Among the three sites of BMD measurement, the femoral neck exhibited the highest decrease, with the baseline measurement at 0.749 (0.151) compared to the follow-up measurement at 0.737 (0.144) (p-value: 0.009). The lumbar spine BMD measurement did not show a significant increase, with the baseline and follow-up measurements being 0.856 (0.168) and 0.861 (0.173), respectively (p-value: 0.393). The total hip BMD also decreased, with the baseline measurement 0.874 (0.162) versus the follow-up measurement 0.868 (0.159) (p-value: 0.066) (Table 2).

Among the normal subgroup at the baseline, a significant decrease in BMD was observed in the femoral neck and total hip, while lumbar spine BMD showed an

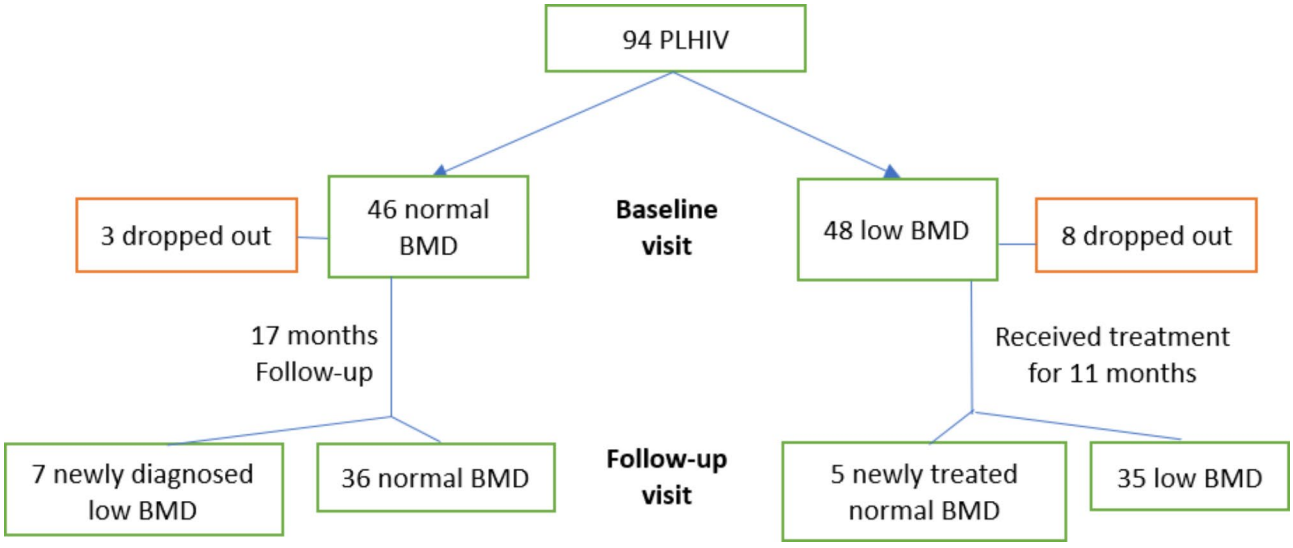

Fig. 2 Flowchart of BMD measurement and low BMD frequency in baseline and follow-up visit

insignificant increase. Conversely, in the subgroup of participants who used low BMD treatment, the decrease in BMD in the femoral neck and total hip became insignificant, and the increase in lumbar spine BMD, though more prominent, remained statistically insignificant (Table 2).

The decrease in B-Ctx between the follow-up and baseline measurements was observed as 0.597 (0.393) and 0.726 (0.561), respectively, which was not statistically significant (p-value: 0.117). The osteocalcin mean (SD) in the baseline measurement was 10.15 (10.25), and in the follow-up measurement, it increased significantly to 18.41 (16.05) (p-value: 0.001) (Table 2).

Discussion

The findings of this study offer valuable insights into the high cumulative incidence and prevalence of low BMD among PLHIV under the treatment of ART, illuminating potential contributing factors to this condition. The results revealed a cumulative incidence of 16.3% over a 17-month follow-up period. Moreover, the observation that more than half of the participants exhibited low BMD during the follow-up round underscores a significant incidence and prevalence of low BMD in PLHIV. This study also showed that the effectiveness of a standard treatment among those with low BMD at baseline was around 12.5%.

The cumulative incidence of low BMD during 17 months of follow-up was measured at 16.3%. The cumulative incidence of osteoporosis among PLHIV who were 41–50 in 10 years follow-up was 18.3% [22]. This shows a higher observed cumulative incidence of low BMD in this study. This notable disparity in cumulative incidence may be attributed to the low socio-economic context of our participants as it affects poor nutrition intake that can contribute to osteoporosis development [23], and the widespread use of antiretroviral therapy (ART), which has been associated with an increased cumulative incidence of osteoporosis compared to the pre-ART era [22]. Additionally, it is noteworthy that osteoporosis diagnosis in the referenced study relied primarily on osteoporotic fractures rather than DEXA scans. Newer antiretroviral drugs, such as tenofovir alafenamide, have been shown to have a less detrimental impact on BMD compared to conventional options like tenofovir [24]. Healthcare providers should consider incorporating these newer, less harmful medications into treatment plans to preserve patients' BMD better.

The treatment effectiveness in this study was recorded at 12.5% in an 11-month follow-up period. As the treatment of the participants in this study was case-specific and prescribed by a rheumatologist, this effectiveness cannot be directly compared to the treatment rates of specific protocols, as it encompasses various treatment approaches tailored for each participant. However, it can be inferred that the treatment positively impacts osteoporosis management in this population. Other studies have indicated that the response rate to osteoporosis treatment in PLHIV is comparable to that of the general population [13]. Our results also demonstrated the effectiveness of the treatment in this population, further supporting its consideration.

In the follow-up measurement, gender differences in the low BMD group were marginally significant, indicating that men are more prone to developing low BMD compared to women. The lack of statistical significance may be attributed to the small sample size in this study. However, men are more prone to developing low BMD, as other studies showed [25]. Additionally, the BMI of the low BMD group was lower than that of the normal BMD

Table 1 Characteristics of participants with normal BMD[a] at the baseline and their BMD status at the follow-up visit

Variable	Total Normal BMD at baseline	Normal BMD at the follow-up	Low BMD at the follow-up	*P*-value
	n (%)	*n* (%)	*n* (%)	
Sex				
Women	31 (72.1)	28 (90.3)	3 (9.7)	0.059
Men	12 (27.9)	8 (66.7)	4 (33.3)	
Education				
Lower than high school diploma	29 (69.1)	26 (89.7)	3 (10.3)	0.101
Diploma and higher	13 (30.9)	9 (69.2)	4 (30.8)	
Current tobacco use				
Yes	7 (16.7)	5 (71.4)	2 (28.6)	0.355
No	35 (83.3)	30 (85.7)	5 (14.3)	
Hypogonadism				
Yes	16 (38.1)	12 (75.0)	4 (25.0)	0.256
No	26 (61.9)	23 (88.5)	3 (11.5)	
Activity level				
Inactive	23 (54.8)	20 (87.0)	3 (13.0)	0.764
Minimally active	15 (35.7)	12 (80.0)	3 (20.0)	
HEPA[b] active	4 (9.5)	3 (75.0)	1 (25.0)	
Baseline CD4+				
≤ 350	3 (7.0)	2 (66.7)	1 (33.3)	0.407
> 350	40 (93.0)	36 (85.0)	6 (15.0)	
Undetectable baseline HIV viral load (< 50 copies/ml)				
Yes	37 (86.1)	30 (81.1)	7 (18.9)	0.244
No	6 (13.9)	6 (100.0)	0 (0.0)	
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
Age (years)				
	48.05 (7.51)	47.54 (7.70)	50.63 (6.32)	0.326
Body mass index				
	26.99 (5.67)	28.07 (5.51)	21.45 (2.29)	0.003
ART[c]use duration at baseline (months)				
	78.63 (33.84)	76.17 (32.03)	91.29 (42.49)	0.285
TBS[d]score at baseline				
	1.34 (0.08)	1.34 (0.08)	1.38 (0.04)	0.270
WBC[e]				
	6.47 (1.79)	6.31 (1.68)	7.29 (2.22)	0.188
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	
CD4 + at diagnosis				
	204 (123–427)	198 (107-393.5)	321 (170–462)	0.324
Baseline Osteocalcin (ng/mL)				
	4.2 (2.6–10.1)	3.6 (2.6–7.7)	16.1 (11.4–21.3)	0.004
Osteocalcin (ng/mL)				
	15.1 (7.3–25.5)	12.3 (5.3–24.1)	23.8 (20.6–42.9)	0.038
Baseline β-CTx[f](ng/mL)				
	0.5 (0.3–0.8)	0.4 (0.3–0.8)	0.9 (0.7–1.3)	0.011
β-CTx[f](ng/mL)				
	0.5 (0.3–0.8)	0.4 (0.3–0.8)	0.7 (0.5–0.9)	0.161

a: definition was based on "T score ≤-2.5, 50 years & above 50 years, and Z score≤-2 under 50 years"

b: HEPA: health-enhancing physical activity

c: ART: antiretroviral therapy

d: TBS: trabecular bone score

e: WBC: white blood cell (thousand cells per cubic millimeter)

f: β-CTx: β-isomerized C-terminal telopeptides

Table 2 Variable measurements at baseline and follow-up measurements

Variable	baseline measurement (g/cm^2)	follow-up measurement (g/cm^2)	*P*-Value	Power (sample size required for 80% power)
Total sample (*n* = 83)				
	Mean (SD)	**Mean (SD)**		
Femoral neck BMD[a]	0.749 (0.151)	0.737 (0.144)	0.009	0.76 (93)
Lumbar spine BMD	0.856 (0.168)	0.861 (0.173)	0.393	0.14 (868)
Total hip BMD	0.874 (0.162)	0.868 (0.159)	0.066	0.45 (191)
β-CTx[b]	0.726 (0.561)	0.597 (0.393)	0.117	0.35 (192)
Osteocalcin	10.15 (10.25)	18.41 (16.05)	0.001	0.98 (32)
TBS[c]	1.319 (0.091)	1.314 (0.084)	0.426	0.12 (993)
Normal BMD (*n* = 43)				
Femoral neck BMD	0.830 (0.134)	0.812 (0.127)	0.002	0.90 (33)
Lumbar spine BMD	0.969 (0.134)	0.971 (0.141)	0.712	0.07 (2335)
Total hip BMD	0.957 (0.139)	0.949 (0.138)	0.048	0.51 (84)
β-CTx	0.610 (0.329)	0.522 (0.261)	0.217	0.23 (150)
Osteocalcin	7.200 (5.534)	17.518 (15.263)	0.001	0.98 (16)
TBS	1.347 (0.080)	1.331 (0.081)	0.105	0.37 (119)
Used low BMD treatment (*n* = 28)				
Femoral neck BMD	0.656 (0.125)	0.648 (0.119)	0.371	0.14 (268)
Lumbar spine BMD	0.740 (0.120)	0.750 (0.132)	0.344	0.15 (240)
Total hip BMD	0.786 (0.139)	0.781 (0.135)	0.560	0.09 (634)
β-CTx	0.888 (0.767)	0.662 (0.514)	0.236	0.21 (130)
Osteocalcin	12.938 (11.358)	16.273 (13.833)	0.392	0.13 (250)
TBS	1.282 (0.079)	1.278 (0.072)	0.743	0.06 (2008)
Needed low BMD treatment but didn't use (*n* = 12)				
Femoral neck BMD	0.675 (0.093)	0.676 (0.109)	0.943	0.05 (17770)
Lumbar spine BMD	0.743 (0.091)	0.743 (0.105)	1.000	---
Total hip BMD	0.787 (0.137)	0.781 (0.133)	0.586	0.08 (302)
β-CTx	0.671 (0.435)	0.694 (0.385)	0.859	0.05 (1590)
Osteocalcin	13.243 (17.981)	29.517 (23.478)	0.005	0.94 (6)
TBS	1.313 (0.122)	1.340 (0.096)	0.151	0.29 0.80

a, BMD: bone marrow densitometry

b, β-CTx: β-isomerized C-terminal telopeptides

c, TBS: Trabecular bone score

group. This suggests a potential association between lower BMI and the development of low BMD. Low BMI has also been found to be a risk factor in developing low BMD [25].

During 17 months of follow-up, Lumbar spine BMD increased by 0.58% in total participants, while total hip BMD decreased by 0.74%, and femoral neck BMD decreased by 1.51%. With a median ART use duration of 90 months in the participants, the decline in spine BMD, which predominantly contributes to low BMD, has ceased and reached a steady state. Our findings align with those of other studies [26]. Femoral neck BMD and total hip BMD continued their decline, which was more prominent in the group that didn't need the osteoporosis medicine. As the prevalence of low BMD in our study didn't change substantially, the BMD of the femoral neck and total hip still decreased, which can cause an increased risk of fracture in the participants.

Baseline β-CTx was found to be higher in the low BMD group, indicating increased osteoclast activity. This higher osteoclast activity may contribute to the lower BMD observed in this group. Interestingly, baseline osteocalcin, a bone formation marker, was also higher in the low BMD group. This could be attributed to increased overall bone metabolism, with a specific increase in bone resorption activity. The magnitude of this increase may contribute to the elevated levels of osteocalcin. The β-CTx level decreased in all the participants. The decrease was more pronounced in the group that used the osteoporosis medicine. At the same time, there wasn't any decrease in the group that needed the osteoporosis drug but didn't use the medicine. As β-CTx reflects bone resorption activities, the reduction in its levels indicates

improved bone metabolism in participants. Although β-CTx changes were not statically significant, it can be related to the low power of the analysis.

The osteocalcin level in total participants increased. As osteocalcin activity can be attributed to increased bone turnover, higher osteocalcin levels may suggest increased bone formation activities. Thus, we can conclude that bone formation was increased in the participants. Osteocalcin usage was due to the limitation of providing procollagen type 1 N-terminal propeptide (P1NP), which is a more widespread bone turnover marker used for bone formation activity.

This study had two limitations. First, due to the low sample size and running the study only in one center, the findings may not be generalizable to all PLHIV in Iran. Second, some variables like activity level were collected by asking the participants, which introduces the possibility of recall bias. Third, using this study design, we could not measure the predisposing factors associated with low BMD. We recommend that future studies include a broader evaluation of additional risk factors.

Conclusion

This study showed a high cumulative incidence (16.3% in 17 months follow-up) of low BMD among PLHIV under the treatment of ART. Also, we found that 12.5% of the participants with low BMD responded to the appropriate treatment in an 11-month follow-up after osteoporosis treatment. This highlights the high treatment rate of low BMD in this population. This dynamic state of high incidence and treatment effectiveness of low BMD emphasizes the imperative to identify individuals at risk of developing low BMD. Moreover, it underscores the potential benefits of treatment for this population, as the study indicates that treatment effectively reverses low BMD status among these individuals.

Abbreviations

BMD	Bone mineral density
PLHIV	People living with HIV
ART	Antiretroviral therapy
SD	Standard deviations
CI	Confidence intervals
BMI	Body mass index
TDF	Tenofovir disoproxil fumarate
VCT	Voluntary counseling and testing
TBS	Trabecular bone score
IPAQ –SF	International Physical Activity Questionnaire Short Form
DXA	Dual-energy X-ray absorptiometry
β-CTx	beta Isomerized C-terminal telopeptides

Acknowledgements

We would like to thank the participants for their valuable time in this study and all the staff of VCT of Kerman City, Iran. We would also like to express our gratitude to the Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Author contributions

Study design: NF, HSH, AO, HR, WM. Data collection: HR, SMH, MRSH, FYY, PS, THA. Analysis: HR, SM. Manuscript drafting: HR, SM. Manuscript editing: NF, HSH, WM, AO, HR, SM, SMH, MRSH, FYY, PS, THA. Project managing: HR. Supervising: HSH, NF.

Funding

The Iran Ministry of Health financially supported this project (#400000091).

Data availability

Data will be available upon request from the senior author (Hamid Sharifi; sharifihami@gmail.com).

Declarations

Ethics approval and consent to participate

Before the study, the study's objectives, benefits, and potential risks of participating in the study were explained to eligible participants, and they were asked to sign a written informed consent form. The study protocol and consent form were reviewed and approved by the Ethical Committee of Tehran University of Medical Sciences (Number: IR.TUMS.EMRI.REC.1400.002).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[2]HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
[3]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[4]Rheumatology Department, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
[5]Pediatric Department, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
[6]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
[7]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[8]Institute for Global Health Sciences, University of California, San Francisco, San Francisco, CA, USA

Received: 3 August 2024 / Accepted: 27 November 2024
Published online: 18 December 2024

References

1. Hogg RS, Yip B, Kully C, Craib KJ, O'Shaughnessy MV, Schechter MT, Montaner JS. Improved survival among HIV-infected patients after initiation of triple-drug antiretroviral regimens. CMAJ. 1999;160(5):659–65.
2. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS. 2006;20(17):216574.
3. Lewiecki EM, Laster AJ. Clinical applications of vertebral fracture assessment by dual-energy X-ray absorptiometry. J Clin Endocrinol Metabolism. 2006;91(11):421522.
4. Föger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P. Osteoporosis: pathophysiology and therapeutic options. Excli j. 2020;19:1017–37.
5. Salari N, Ghasemi H, Mohammadi L, Rabieenia E, Shohaimi S, Mohammadi M. The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. J Orthop Surg Res. 2021;16(1):120.
6. Irani AD, Poorolajal J, Khalilian A, Esmailnasab N, Cheraghi Z. Prevalence of osteoporosis in Iran: a meta-analysis. J Res Med Sci. 2013;18(9):759–66.
7. Nourmohammadi H, Abdan Z, Hashemipour SMA, Sarokhani D, Abdan M, Fakhri M, Dehkordi AH. Prevalence of osteoporosis and osteopenia in people over 60 years in Iran: a systematic review and meta-analysis. Int J Prev Med. 2022;13(1):11.

8. Ofotokun I, Titanji K, Vikulina T, Roser-Page S, Yamaguchi M, Zayzafoon M, et al. Role of T-cell reconstitution in HIV-1 antiretroviral therapy-induced bone loss. Nat Commun. 2015;6(1):8282.
9. Ofotokun I, Titanji K, Vunnava A, Roser-Page S, Vikulina T, Villinger F, et al. Antiretroviral therapy induces a rapid increase in bone resorption that is positively associated with the magnitude of immune reconstitution in HIV infection. AIDS. 2016;30(3):40514.
10. Pouresmaeili F, Kamalidehghan B, Kamarehei M, Goh YM. A comprehensive overview on osteoporosis and its risk factors. Therapeutics and clinical risk management. 2018;14(null):2029_49.
11. Starup-Linde J, Rosendahl SB, Storgaard M, Langdahl BL. Management of osteoporosis in patients living with HIV—A systematic review and Meta-analysis. JAIDS J Acquir Immune Defic Syndr. 2020;83(1):18.
12. McComsey GA, Tebas P, Shane E, Yin MT, Overton ET, Huang JS, et al. Bone disease in HIV infection: a practical review and recommendations for HIV care providers. Clin Infect Dis. 2010;51(8):937–46.
13. Biver E. Osteoporosis and HIV infection. Calcif Tissue Int. 2022;110(5):62440.
14. Han WM, Wattanachanya L, Apornpong T, Jantrapakde J, Avihingsanon A, Kerr SJ, et al. Bone mineral density changes among people living with HIV who have started with TDF-containing regimen: a five-year prospective study. PLoS ONE. 2020;15(3):e0230368.
15. Starup-Linde J, Rosendahl SB, Storgaard M, Langdahl B. Management of osteoporosis in patients living with HIV—A systematic review and Meta-analysis. JAIDS J Acquir Immune Defic Syndr. 2020;83(1):1–8.
16. World Health Organization. Prevention and management of osteoporosis: report of a WHO scientific group. World Health Organization; 2003. p. 921. Report No.: 9241209216 Contract No.
17. Lewiecki EM, Gordon CM, Baim S, Leonard MB, Bishop NJ, Bianchi M-L, et al. International Society for Clinical Densitometry 2007 adult and pediatric official positions. Bone. 2008;43(6):111521.
18. Kanis JA, Adachi JD, Cooper C, Clark P, Cummings SR, Diaz-Curiel M, et al. Standardising the descriptive epidemiology of osteoporosis: recommendations from the Epidemiology and Quality of Life Working Group of IOF. Osteoporos Int. 2013;24:27634.
19. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach-2010 revision. World Health Organization; 2010.
20. Gallant JE, DeJesus E, Arribas JR, Pozniak AL, Gazzard B, Campo RE, et al. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. N Engl J Med. 2006;354(3):25160.
21. Wu FC, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, et al. Identification of late-onset hypogonadism in middle-aged and elderly men. N Engl J Med. 2010;363(2):12335.
22. Jespersen NA, Axelsen F, Dollerup J, Nørgaard M, Larsen CS. The burden of non-communicable diseases and mortality in people living with HIV (PLHIV) in the pre-, early- and late-HAART era. HIV Med. 2021;22(6):478–90.
23. Weiser SD, Young SL, Cohen CR, Kushel MB, Tsai AC, Tien PC, et al. Conceptual framework for understanding the bidirectional links between food insecurity and HIV/AIDS. Am J Clin Nutr. 2011;94(6):1729S39S.
24. Moran CA, Weitzmann MN, Ofotokun I. Bone loss in HIV infection. Curr Treat Options Infect Dis. 2017;9(1):52–67.
25. Goh SSL, Lai PSM, Tan ATB, Ponnampalavanar S. Reduced bone mineral density in human immunodeficiency virus-infected individuals: a meta-analysis of its prevalence and risk factors. Osteoporos Int. 2018;29(3):595–613.
26. Bolland MJ, Wang TKM, Grey A, Gamble GD, Reid IR. Stable bone density in HAART-Treated individuals with HIV: a Meta-analysis. J Clin Endocrinol Metabolism. 2011;96(9):2721–31.

Publisher's note