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

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Abstract

Background The introduction of antiretroviral therapy (ART) has signi□cantly 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 e□ectiveness 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 e□ectiveness 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 di□erences of BMD between the two groups. Statistical signi□cance 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 e□ectiveness: 12.5%). However, among 43 PLHIV with normal BMD at baseline, 7 PLHIV had low BMD at the follow-up visit (cumulative

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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 e□ectiveness 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-speci□c factors and BMI may in□uence susceptibility to low BMD.

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

Introduction

e advent of antiretroviral therapy (ART) has made a signi cant change in the lives of people living with HIV (PLHIV). is medical breakthrough has led to a signi cant 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. e 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], signi cantly 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 identi ed 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 intensi es 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]. e rate of BMD decrease is particularly signi cant 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 e ective 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]. erefore, 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 e ectiveness of a standard treatment among PLHIV who su ered 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

is longitudinal study was conducted from September 2021 to September 2023 at a Voluntary Counseling and Testing Center (VCT) in Kerman, Iran. e 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.

e 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). erapeutic options included alendronate, zoledronic acid, denosumab, and teriparatide, tailored speci cally for each participant with low BMD. ose 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 e ectiveness in the treatment group. Additionally, bone turnover markers were measured during this phase.

Outcome variables

e primary outcome variable was de ned as a combination of low BMD and osteoporosis. is variable was used to measure the cumulative incidence of low BMD among the normal BMD population and measure the treatment e ectiveness 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 de ned 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 de ned 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 de ned 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 de nition to include both age groups by combining the aforementioned de nitions.

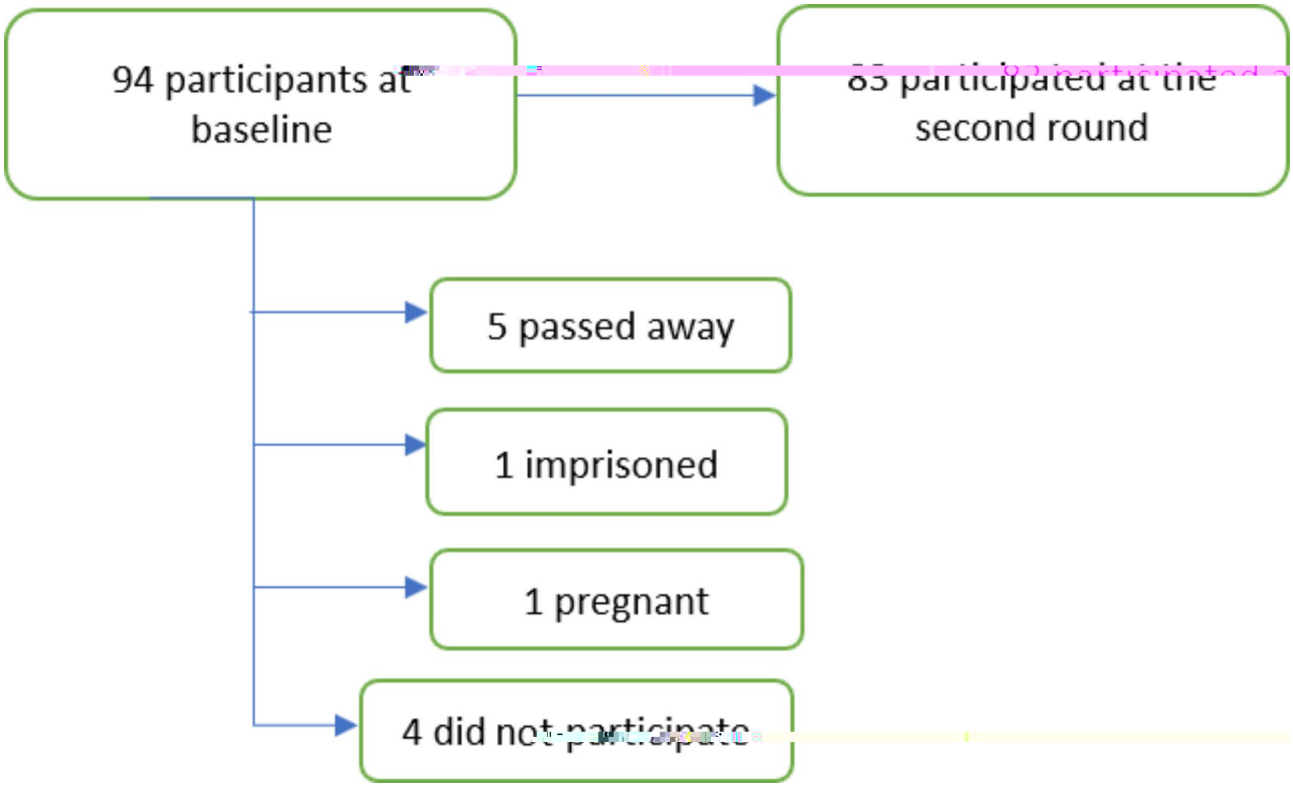

Fig. 1 Flowchart of participants

According to the Committee of Scienti c 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. e di erences were calculated for each site.

We also measured bone turnover markers, including osteocalcin and β-CTx levels, at the baseline and follow-up visits. ese 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).

e levels of hormones and markers related to bone health and metabolism were measured by laboratory tests. e bone turnover markers osteocalcin and β-CTx, baseline CD4+cell counts (as ≤350 vs. >350 cells/mm³) [19], and viral load (detectable vs. undetectable (<50 copies/mL)) [20] were also measured. ART regimens were obtained from medical les. BMI was calculated as weight in kilograms divided by the square of height in meters. We de ned 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 signi - cant. All statistical analyses were performed using Stata 17 software.

Ethical consideration

e 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. e mean (SD) age was 49.3 (7.7) years old. e mean (SD) of BMI was 24.8 (5.7). e median (IQR) of ART usage was 90 (53–113) months at the baseline. A total of 20 (25%) of participants were smokers. e prevalence of low BMD in the total sample of the follow-up visit was 50.6% (95% con dence 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. e 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. e mean (SD) BMI in the low BMD group was 21.4 (2.3), signi cantly lower than that in the normal BMD group, which had a mean BMI of 28.1 (5.5) (p-value: 0.003) (Table 1).

e TBS mean (SD) in the low BMD group at the baseline was 1.38 (0.04), and it was not signi cantly higher than that in the normal group, which had a mean of 1.34 (0.08) (p-value: 0.733). e baseline osteocalcin median (IQR) in the low BMD group was 16.1 (11.4–21.3), signi cantly higher than the normal BMD group, which had a median of 3.6 (2.6–7.7) (p-value: 0.004). e baseline β-CTx median (IQR) was 0.9 (0.7–1.3) in the low BMD group, which was signi cantly 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. e cumulative treatment e ectiveness of low BMD was 12.50% (95% CI: 4.19–26.80%) in 11 months of follow-up. e 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). e lumbar spine BMD measurement did not show a signi cant increase, with the baseline and follow-up measurements being 0.856 (0.168) and 0.861 (0.173), respectively (p-value: 0.393). e 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 signi cant decrease in BMD was observed in the femoral neck and total hip, while lumbar spine BMD showed an

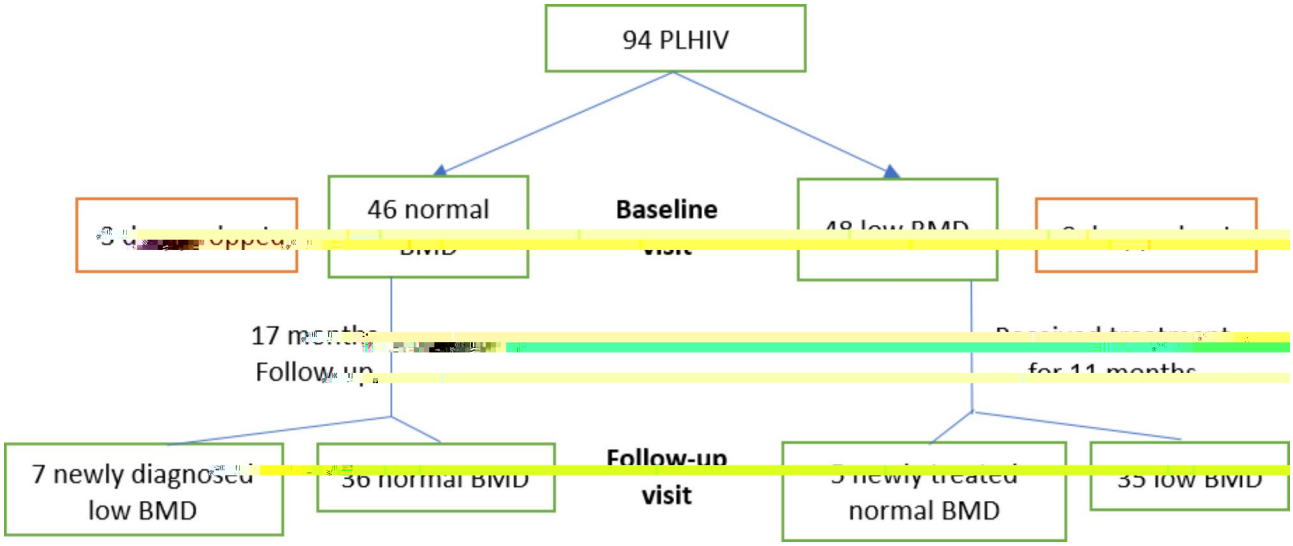

Fig. 2 Flowchart of BMD measurement and low BMD frequency in baseline and follow-up visit

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

e 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 signi cant (p-value: 0.117). e osteocalcin mean (SD) in the baseline measurement was 10.15 (10.25), and in the follow-up measurement, it increased signi cantly to 18.41 (16.05) (p-value: 0.001) (Table 2).

Discussion

e ndings of this study o er 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. e 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 signi - cant incidence and prevalence of low BMD in PLHIV. is study also showed that the e ectiveness of a standard treatment among those with low BMD at baseline was around 12.5%.

e cumulative incidence of low BMD during 17 months of follow-up was measured at 16.3%. e cumulative incidence of osteoporosis among PLHIV who were 41–50 in 10 years follow-up was 18.3% [22]. is shows a higher observed cumulative incidence of low BMD in this study. is notable disparity in cumulative incidence may be attributed to the low socio-economic context of our participants as it a ects 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.

e treatment e ectiveness 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-speci c and prescribed by a rheumatologist, this e ectiveness cannot be directly compared to the treatment rates of speci c 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 e ectiveness of the treatment in this population, further supporting its consideration.

In the follow-up measurement, gender di erences in the low BMD group were marginally signi cant, indicating that men are more prone to developing low BMD compared to women. e lack of statistical signi cance 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: de nition 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. is 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 ndings 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. is 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. is could be attributed to increased overall bone metabolism, with a speci c increase in bone resorption activity. e magnitude of this increase may contribute to the elevated levels of osteocalcin.

e β-CTx level decreased in all the participants. e 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 re ects bone resorption activities, the reduction in its levels indicates

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

e 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. us, 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.

is study had two limitations. First, due to the low sample size and running the study only in one center, the ndings 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. ird, 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

is 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. is highlights the high treatment rate of low BMD in this population. is dynamic state of high incidence and treatment e ectiveness of low BMD emphasizes the imperative to identify individuals at risk of developing low BMD. Moreover, it underscores the potential bene ts of treatment for this population, as the study indicates that treatment e ectively reverses low BMD status among these individuals.

Abbreviations

BMD	Bone mineral density
PLHIV	People living with HIV
ART	Antiretroviral therapy
SD	Standard deviations
CI	Con dence 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

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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.

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Data availability
Data will be available upon request from the senior author (Hamid Shari; shari hami@gmail.com).

Declarations

Ethics approval and consent to participate
Before the study, the study's objectives, bene ts, 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.

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