



The Prevalence of Osteoporosis in Hiv Infected Patient and its Correlation with Cd4 Count/Clinical Staging in Indian Population

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Abstract

Human immunodeficiency virus (HIV) is a retroviral disease in which the viruses copy their genetic material into the genetic material of the human beings. Infected cells remain infected for the whole of their life. First discovered in the year 1981, Human immunodeficiency virus infections is considered to be a pandemic by the World Health organization.

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Introduction

Human immunodeficiency virus (HIV) is a retroviral disease in which the viruses copy their genetic material into the genetic material of the human beings. Infected cells remain infected for the whole of their life. First discovered in the year 1981, Human immunodeficiency virus infections is considered to be a pandemic by the World Health organization.

HIV/AIDS has long term and short-term complications. Infective complications include: Cytomegalovirus, Candidiasis, Herpes simplex viruses, Mycobacterium avium complex, Pneumocystis pneumonia, Toxoplasmosis and Tuberculosis. Malignancy in HIV includes: - Kaposi's sarcoma, Osteoporosis. Osteoporosis which is characterized by abnormality both in amount and in architectural arrangement of the bone tissue which can lead to increased susceptibility to the fracture causing decrease skeletal strength and leading to increased rate of morbidity and mortality^{1,2}.

Bone mineral density (BMD) can be measured through imaging modalities, such as Dual X-ray absorptiometry (DEXA), with the goal of preventing fractures with early intervention. The World Health Organization has grouped reduced BMD into two categories. Osteoporosis is defined as a bone density less than 2.5 standard deviations of the mean BMD of a sex-matched, young healthy population, i.e. a T-score less than -2.5. Osteopenia is an intermediate category of bone loss defined as a T-score between -1 and -2.5.3 Although these categories were created to classify postmenopausal women, they are often applied to other adult populations. Osteoporosis in its most common form affects the elderly (both sexes) and all racial groups of human beings. Osteoporosis is basically classified on two basic parameters it is a primary or secondary. Primary osteoporosis occurs in all ages in both sex but in females it follows after Menopause in and occurs later in the life in men. In contrary to primary osteoporosis secondary osteoporosis results from medications or other conditions or diseases^{3,4}. Diseases which causes osteoporosis includes endocrine disorders, bone marrow disorders, malabsorption disorder, inflammatory disease which were reported to be associated with osteoporosis and with increased

tendency. HIV infection is also important reported to play an important role in osteoporosis there was high incidence of osteoporosis reported in HIV infected individuals⁵.

AIDS is one of the important risk factors for osteoporosis and osteopenia⁶. Since HIV AIDS is associated with numerous metabolic and endocrine complication which can lead to decreased appetite and Hypogonadism. Medication during the therapy also causes decreased bone strength and contribute to the bone loss. Bone remodelling process is basically altered in HIV-infected individuals which can contribute to the bone loss⁷. Osteoporosis is more frequent in patients taking antiretroviral therapy for a longer duration. In HIV the main risk factor for the development of osteoporosis are protease inhibitors, longer duration of HIV therapy, high viral load, decrease CD 4 count, lower body weight before and after therapy, reduced lean body mass, weight loss and impaired functional capacity of the various factor which can further lead to osteoporosis in HIV-infected individuals.

Among HIV-infected patients receiving antiretroviral therapy (ART), reduced BMD has been reported with increasing frequency. Because of the relatively small size of these studies, investigators have generally grouped osteopenia and osteoporosis together, and have not been able to assess accurately the prevalence of osteoporosis per se and its relative risk in HIV-infected patients compared with HIV-uninfected controls^{8,9,10}.

The following questions need to be answered:

- What is the prevalence of reduced BMD, and more specifically osteoporosis in HIV-infected patients, and what is the risk of these disorders compared with HIV-uninfected control subjects?
- What is the risk of reduced BMD and osteoporosis in HIV-infected patients receiving ART compared with ART-naive patients?

Aims and Objectives

Primary Objective

- To find out the prevalence of osteoporosis in HIV infected patients.

Secondary Objective

- To find out the correlation of osteoporosis with CD4 counts/clinical staging.

Material and Methods

Study Population

This study was conducted in cases admitted to Department of Internal Medicine, K.G.M.U, Lucknow or attending the NACO-ART Centre (Medicine, outdoor patient department) for a period of one year from JUNE 2017 to April 2019. The number of the cases planned for the study was approximately 200. We managed to enrol 124 cases who fulfilled the inclusion criteria and gave consent. HIV negative attendants of the cases were enrolled as controls (total 64).

Study Design

Hospital based cross-sectional study.

Inclusion Criteria

HIV positive patients of age > 18 years (Diagnosed according to the NACO criteria).

- HIV positive patient were grouped as:
- HIV infected patients antiretroviral naive.
- HIV infected patients on antiretroviral therapy.

Exclusion Criteria

- Co-morbid conditions like neoplastic disease, rheumatoid arthritis, endocrine disorders, chronic renal disease, liver disease.
- The chronic intake of drug that was known to cause osteoporosis: oral corticosteroid, cyclosporine, cytotoxic drugs, excessive thyroxine in previous 6 months before inclusion.
- Patients immobilized and bedridden for longer duration (6 months) due to major surgery or accident.
- Patients who have refused to give consent to the study.

Detailed history and examination was done and following features were noted according to prepared questionnaire: Age, sex, BMI, date of HIV diagnosis, AIDS stage according to the NACO criteria, current CD4 count, ART regimen, duration of ART and risk factor for

osteoporosis (smoking status, alcohol consumption, the types and treatment durations of glucocorticoid or antiepileptic drugs, past history of tuberculosis treatment, current tuberculosis state, and infection with hepatitis B and C viruses).

All systems were examined thoroughly particularly musculo-skeletal system for myalgia, deformity or fracture.

- Following investigations were performed: -
- HIV by ELISA at the Integrated Counselling and Training Centre (ICTC), KGMU, Lucknow (approved by NACO).
- Complete hemogram
- Liver Function Tests (LFT), Blood Urea, Serum Creatinine, HbsAg, Anti HCV, VDRL
- CD4 count- CD4 cell counts were done by flow cytometry by using Partec-CY FLOW Counter Machine. (Department of Microbiology, KGMU, Lucknow)
- Serum Calcium, Serum Phosphorus, Random Blood Sugar, Serum Sodium, Serum Potassium.
- Thyroid Function Tests (T3, T4, TSH).
- Chest X-ray PA view
- X-ray Lumbar spine (AP, Lateral) and Proximal Femur.

Bone Mineral Density by DEXA (Dual Energy X-ray absorptiometry)- done by using the Lunar Prodigy advance DEXA system (analysis version 12.30) manufactured by GE Healthcare at the Department of Rheumatology, KGMU, Lucknow. BMD was measured at the lumbar spine [AP spine], right neck femur, left neck femur, left total femur, right total femur, left forearm radius. The AP view of L1-L4 was used for spine BMD measurement. Anatomically abnormal vertebrae were excluded from analysis when there was a T-score difference of more than 1.0 between the vertebrae in question and adjacent vertebrae. World Health Organization (WHO) classification was used for diagnostic purposes. Osteopenia was defined as a T-score between -1 SD and -2.5 SD, and osteoporosis was defined as a T-score of less than -2.5 SD. Z-score (SD below a sex- and ethnicity-matched population of

the same age) was preferred; a value less than or equal to -2.0 considered to be abnormal. The prevalence and risk factors of low BMD was determined in all patients.

Statistical analysis:

Microsoft excel was used for creating the data base, Means and standard deviation were given for continuous variables while nominal variables were described in terms of percentages.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean \pm SD.

The Following Statistical Formulas were Used

1. Mean: To obtain the mean, the individual observations were first added together and then divided by the number of observations. The operation of adding together or summation is denoted by the sign.

The individual observation is denoted by the sign X, number of observations denoted by n, and the mean by.

2. Standard Deviation: It is denoted by the Greek letter . If a sample is more than 30 then.

When Sample in Less Than 30 Then

Chi-square test: This test was used to see the association between two groups

Where O = Observed frequency

E = Expected frequency.

Analysis of Variance: Analysis of Variance (ANOVA): The ANOVA test was used to compare the within group and between group variances amongst the study groups. Analysis of variance of different groups at a particular time interval revealed the differences amongst them. ANOVA provided "F" ratio, where a higher "F" value depicted a higher inter-group difference.

: F =

Level of significance: "p" is level of significance

p > 0.05 Not significant

p <0.05 Significant

p <0.01 Highly significant

p <0.001 Very highly significant

We also reported 95% confidence interval estimates of the true means and percentages. We reported statistical results from several bivariate comparisons. For all cases in which a statistical test was conducted, a p value of less than 0.05 was considered to indicate a significant difference.

Student's t-test was used for comparison of mean and standard deviation of continuous variables. To evaluate the prevalence between ART-based regimens over time, linear by linear association and logistic regression including an interaction term was applied.

Observation & Results

The objective of this endeavour was to study the prevalence of osteoporosis in HIV infected patients in Indian population. The prevalence of osteoporosis had been studied in western countries but data from Indian population are lacking.

We included 188 subjects out of which 124 (66%) were HIV positive (diagnosed as per NACO criteria) and 64 (34%) were HIV negative controls. Out of 124 HIV positive patients 104 (83.87%) were males and 20 (16.13%) were females. In control group, 34 (53.12%) were males and 30 (46.88%) were females (Table-1). Majority of patients in both the groups were of age group 31-40 years (Table-1). Mean body mass index (BMI) was $20.03\pm 2.03\text{g/cm}^2$ in HIV positive cases while $22.65\pm 2.46\text{g/cm}^2$ in HIV negative controls. Out of 124 HIV positive patients 35 (56.4%) were taking HAART and 54 (43.6%) were HIV naïve patients. Majority of HIV positive patients were on Zidovudine+ Lamivudine+ Nevirapine regimen (77.14%). In HIV positive patients only 2 patient was >50 years while in HIV negative control 4 patients had age >50 years. Out of 124 (100%) HIV positive patients, 33.87% (n=42) patients had CD4 count in between 100-199/ μl , 29.03% (n=36) patients had CD4 count 0-99/ μl and 24.19% (n=30) patients had CD4 count greater than 300/ μl (Table 1). In 2 HIV positive patients left leg was amputated because of the trauma.

Out of 34 (100%) HIV positive patients between 21-30 years age group 14 (41.2%) patient had osteopenia and 2 (5.9%) patient was osteoporotic. While in control population between 21-30 years none

Table 1. Enrolled Variables

Variable	HIV	Non-HIV
Number (n)	124	64
Mean Age (years)	36.16±7.586	42.47±11.225
Male(n)	104	34
Female(n)	20	30
BMI (kg/m ²)	20.03±2.03	22.65±2.46
Smoking	00	00
History of fracture	00	00
Mean CD4 count (/μl)	195.69±162.41	NA
Haemoglobin (mean) (g/dl)	10.5±1.2	11.5±2.1
T3 (ng/ml)	1.52	1.15
T4 (μg/dl)	82.10	76.78
TSH (μIU/ml)	1.99	1.85
Serum Phosphorus (mg/dl)	2.99	2.83
Serum Calcium (Total) (mg/dl)	8.46	8.71
Serum Bilirubin(mg/dl)	0.9	0.76
Serum Albumin (mg/dl)	3.19	4.03
Age Group (in years)	HIV positive (n=124)	HIV negative (n=64)
20-30 years	34 (27.41%)	12 (18.75%)
31-40 years	64(51.61%)	28(43.75%)
41-50 years	24 (19.35%)	20 (31.25%)
>50 years	2(1.61%)	4 (6.25%)
HIV Positive Patients	Total (n)	Percentage (%)
ART naïve	54	43.55%
On ART*		
	70	56.45%
Z+L+N	54	43.54%
Z+L+E	2	1.61%
T+L+N	6	4.83%
T+L+E	6	4.83%
S+L+E	2	1.61%
CD 4 counts (/μl)	Total (n)	Percentage (%)
0-99	36	29.03%
100-199	42	33.87%
200-299	16	12.90%
>300	30	24.19%

had osteopenia or osteoporosis. Similarly, out of 64 HIV positive patients between 31-40 years of age, 36 (56.2%) had osteopenia and 2 (3.1%) had osteoporosis. While in HIV negative out of 28 in the same age group of 10 (35.72%) patients had osteopenia and none of them were osteoporotic. In the age group 41-50 years only 20% control population had osteopenia while 66.7% of HIV positive patients had osteopenia and 8.3% had osteoporosis (Table 1). Thus, osteoporosis occurred at younger age group in HIV positive patients as compared to HIV negative controls. The prevalence of osteoporosis was higher in HIV positive cases as compared to control group. These findings were similar to that of Arnsten JH et al, (2006)²⁴ who found that in HIV infected the prevalence of osteoporosis was higher in HIV positive cases as compared to control group compared (p value = 0.001). They reported increased fracture risk in HIV infected compared with HIV negative controls.

NACO first line regimen were used and it includes NRTI, NNRTI and NVP. Protease inhibitors were used as the second line drugs. The most of the patients (n=54) on ART were on Zidovudine (Z)+ Lamivudine (L) +Nevirapine (N) (Table 1). None of the patient was on Protease inhibitor. NACO guidelines for treatment of HIV was used which recommend protease inhibitor as the second line drug. In HIV positive patient with <2 years ART duration 45.45% (n=20) patients were normal, 45.45% (n=20) had osteopenia and 9.1% (n=4) had osteoporosis while in HIV positive patients with >2 years ART duration 53.84% (n=14) were normal, 38.46% (n=10) had osteopenia and 7.69% (n=2) had osteoporosis.

The relation was statistically non-significant (p value= 0.234). Similar results were obtain by Jones S et al, (2008)²³ who found that low BMD is prevalent in HIV infected subjects initiation of ART is associated with 2%-6% decreased in BMD over the first two years. Tebas et al, (2007)²⁴ also reported 2-6% decrease in BMD over the first two years. Thus ART itself seems not to be a risk factor for osteoporosis.

Out of the total 188 enrolled population, 124 (66%) were HIV positive of which 104 (84%) were males and 20 (16%) were females and 64(34%) were HIV negative controls out of which 34 (53%) were

males and 30 (47%) were females. All patients were non-smoker, had no history of previous fracture and there was no past history of steroid intake. In 2 patients left leg was amputated. (TABLE 1)

Out of 124 HIV positive patients 70 (56.4%) patients were taking highly active antiretroviral therapy (HAART) and the rest 54 (43.6%) were ART naive patients. (TABLE 1)

Majority of the patients in both HIV positive and HIV negative groups were of age 31-40 years with 51.61% and 43.45% respectively. In HIV positive patients only one patient was >50 years old while in HIV negative controls 2 cases had age of >50 years. (TABLE 1)

In HIV positive group 70 (56.45%) were on ART while 54 (43.55%) were ART naive patients. Among HIV positive patients' majority were on Zidovudine +Lamivudine +Nevirapine (n=54; 84.37%). No patient was on Protease inhibitor regimen. (TABLE 1)

In HIV positive patients' majority 42 (33.87%) had CD4 count between 100-199/ μ l, 30(24%) patients had CD4 count of >300/ μ l and 36 (29.03%) had CD4 count < 100/ μ l. (TABLE 1) Tab 2.

In HIV positive patients the mean T-score was minimum at lumbar spine (-1.708 \pm 1.068) and maximum at left forearm radius (-0.869 \pm 0.912). In HIV negative patients mean T-score was minimum at Left neck femur (-0.490 \pm 0.608) and maximum at lumbar spine (0.003 \pm 1.10). The mean T-score at all anatomical sites was lower in HIV positive patients as compared to HIV negative controls. (Table 2). At all anatomical sites the difference in T-score in both groups was statistically significant (p<0.05). Thus on the basis of T-score in HIV positive patients 53.22% (n=66) were osteopenic, 6.4% (n=8) were osteoporotic while in HIV negative controls 25% (n=16) were osteopenic and none of the patient was osteoporotic (Table 2). Both HIV patients (n=2) with amputated legs had normal BMD. The mean BMI of osteopenic HIV positive patients was 20.04 \pm 1.03 g/cm² while that of osteoporotic patients was 20.01 \pm 1.22 g/cm². The mean BMI of HIV positive patients with normal BMD was 20.00 \pm 1.03 g/cm².

There was no significant difference in BMI of osteopenic and osteoporotic HIV positive patients. The

Table 2. Mean Bmd and T Score

Mean BMD at various Anatomical sites		
BMD -at various sites (g/cm²)	HIV Positive (n=124)Mean BMD±SD	HIV Negative (n=64) MeanBMD±SD
BMD AP Spine	0.980±0.244	1.198±0.142
BMD Left Neck Femur*	0.869±0.170	0.987±0.082
BMD Right Neck Femur	0.886±0.152	1.027±0.147
BMD Total Left Femur*	0.880±0.156	1.049±0.081
BMD Total Right Femur	0.919±0.148	1.057±0.0963
BMD left forearm radius	0.998±0.156	1.084±0.098
Mean T-score at various anatomical sites.		
T-score at various sites	HIV Positive (n=124)Mean T-score±SD	HIV Negative (n=64) Mean T-score±SD
T-Score AP Spine	-1.708±1.068	0.003±1.198
T-Score Left Neck Femur*	-1.300±1.212	-0.490±0.608
T-Score Right Neck Femur	-1.119±1.0393	-0.1843±1.118
T-Score Total Left Femur*	-1.290±0.980	0.084±0.750
T-Score Total Right Femur	-0.985±0.924	0.062±0.826
T-Score left forearm radius	-0.869±0.912	0.162±0.834
T-score at various sites		
	HIV Positive (n=124)	HIV Negative (n=64)
Normal	50 (40.32%)	48 (75%)
Osteopenia	66 (53.22%)	16(25%)
Osteoporosis	8 (6.46%)	0 (0%)

BMI in both osteopenic and osteoporotic patients was in lower normal range. Z score was taken into consideration but as majority of the enrolled population was males and age < 50 years Z score was not used. Mean Z score of osteoporotic HIV positive patients was -1.3 ± 0.4 and -0.2 ± 0.02 in HIV negative controls. Mean Z score of osteopenic HIV positive patients was $-2.4 \pm .2$. At all anatomical sites the difference in Z-score in both groups was statistically significant ($p < 0.05$). Thus HIV positive patients had lower Z-score as compared to HIV negative controls. Z-score compares individuals results to those of an age matched population that is also matched for race and gender. The low Z-score increases the suspicion of a secondary disease/ factor in etiology of osteoporosis.

These results were similar to Brown TT et al, (2004)¹⁶ who found that HIV-infected subjects had a higher prevalence of either osteopenia or osteoporosis at the spine, hip, or forearm, compared with HIV-negative controls (63% vs. 32%, $P = 0.02$). Amorosa V et al, (2006)¹⁷ also reported high prevalence of bone demineralization among human Immunodeficiency virus (HIV)-infected patients. Similar results were obtained in the study by Dolan SE et al, (2006)¹⁸ who also reported that HIV infected subjects had lower BMD at lumbar spine (1.01 ± 0.01 vs 1.07 ± 0.01 g/cm², $p = 0.001$), hip (0.94 ± 0.01 vs 0.98 ± 0.01 g/cm² $p = 0.02$), femoral neck (0.83 ± 0.01 vs 0.87 ± 0.01 g/cm², $p = 0.02$). They also reported that HIV positive patients had higher prevalence of reduced BMD as compared to HIV negative controls. These results were also similar to that of Triant VA et al, (2008)¹⁹ who reported that HIV positive patients had higher prevalence of reduced BMD as compared to HIV negative controls. Similar finding were obtained by Teiciman J et al, (2003)²⁰ who also noted reduced BMD of lumbar spine T-score < 2.5 was found in 7 (14%) and osteopenia T-score (-1 to -2.5 SD) in 31 (62%) patients. This relationship was also observed by Libois A et al, (2009)²¹ they found that HIV-infected patients suffer more often from osteopenia and osteoporosis than age matched HIV negative subjects. Guerri-Fernandez R et al, (2013)²² found strong association between HIV infection and osteoporosis (osteoporosis evaluated in term of hip fracture incidence). They also found that duration of the HIV

infection and HAART or nadir CD4 cells count were not related to BMD loss in this population of women with no AIDS defining event. The only factor associated with BMD loss was a low BMI.

There were multiple etiologies of osteoporosis among them are primary and secondary causes. The secondary causes of osteoporosis includes neoplastic disease, rheumatoid arthritis, endocrine disorders, chronic renal disease, liver disease, chronic intake of drugs that was known to cause osteoporosis: oral corticosteroid, cyclosporine, cytotoxic drugs, excessive thyroxine in previous 6 months before inclusion. These secondary causes were excluded in the beginning of the study. Thus HIV disease itself remains one of the secondary causes of osteoporosis. In HIV patients the important factors that causes osteoporosis includes low BMI, low CD4 count, increase viral load, increased clinical staging, increased age (older age), duration of the ART and ART regimens. Mean BMD at various anatomical is TABLE 2. In HIV positive patients the mean BMD was minimum at left neck femur (0.869 ± 0.170 g/cm²) and maximum at left forearm radius (0.998 ± 0.156 g/cm²) while in HIV negative patient the BMD was minimum at left neck femur (0.987 ± 0.082 g/cm²) and maximum at lumbar spine (1.198 ± 0.142 g/cm²). (TABLE 2 MEAN BMD AND T SCORE) .

The mean BMD at all sites was lower in HIV positive patients as compared to HIV negative controls. The difference was statistically significant with p value < 0.05. (TABLE 2 MEAN BMD AND T SCORE)

The T-score in HIV positive patients was minimum at lumbar spine (-1.708 ± 1.068) and maximum at left forearm radius (-0.869 ± 0.912). In HIV negative controls the T-score was minimum at left neck femur (0.490 ± 0.608) and maximum at AP spine (0.003 ± 1.198). (TABLE 2 MEAN BMD AND T SCORE)

The average T-score at all anatomical sites was lower in HIV positive patients as compared to HIV negative controls (Table 2). The difference was statistically significant at all anatomical sites ($p < 0.05$). (TABLE 2 MEAN BMD AND T SCORE)

In HIV positive patients 50 (40.32%) were normal, 66 (53.22%) were Osteopenic, 8(6.46%) were osteoporotic while in HIV negative controls 48(75%)

were normal, 16 (25%) were Osteopenic and 0% were osteoporotic. In HIV negative control population, no patient had osteoporosis. (TABLE 3)

The prevalence of Osteopenia and osteoporosis in various age group in HIV positive and HIV negative control is given in table 3.

Out of 34(100%) HIV positive patients between 20-30 years age group 14 (41.2%) patient had osteopenia and 2(5.9%) patient had osteoporosis. While in HIV negative controls of 20-30 years age group none of them had osteopenia or osteoporosis similarly out of 64(100%) HIV positive patients between 31-40 years age groups 36 (56.2%) had osteopenia and 2 (3.1%) patient had osteoporosis. While in HIV negative out of 18 in the age group of 31-40 years 10 (35.72%) patients had osteopenia and none of them were osteoporotic in age group 41-50 years only 20% control population had osteopenia while 66.7% of HIV positive patients had osteopenia and 8.3% had osteoporosis. (TABLE 3)

Thus, the prevalence of osteoporosis in HIV positive patients was higher in all age groups as compared to HIV negative controls. The difference was statistically significant ($p=0.001$). In HIV positive Osteopenic patients had mean age of 37.27 ± 7.238 years while in HIV negative controls the mean age of patient with osteopenia was 52.62 ± 11.338 . There were no osteoporotic patients in HIV negative control group while there were 4 patients in HIV positive group with mean age of 41.25 ± 12.203 years. Thus, osteopenia and osteoporosis in HIV positive patients occurred more commonly in younger age group as compared to HIV negative controls.

Patients with lower CD4 count had higher percentage of osteopenia and osteoporosis. Thus, patients with higher CD4 count had lower prevalence of osteoporosis relation was Statistically Non-Significant ($p=0.217$) Fig 1

124 patients 50 had normal BMD (mean of $215.60/\mu\text{l}$), 8 patients had osteoporosis (mean of $179.75/\mu\text{l}$), 66 patients had osteopenia (mean of $182.55/\mu\text{l}$). Lesser the CD4 count greater was the prevalence of low BMD (osteopenia/osteoporosis). The CD4 counts in between groups and within in groups

does not show any significant relation (p -value 0.736).

Out of 124 HIV positive patients, 70 (56.4%) were on ART while rest 54 (43.6%) were ART naïve.

Among HIV positive patients on ART 32 (45.7%) were normal (Table-1) while 18 (44.3%) had reduced BMD. These results were similar to that of Brown TT et al, (2009) who found that after 96 weeks the mean percentage change for baseline in total BMD was -2.5% on Lopinavir/Reitonavir therapy and 2.3 for Efavirinz no alteration in the rate of BMD change was observed. They also found that the impact of ART initiation on bone mineral density and have generally shown a 2%–6% loss of BMD after 48–96 weeks of therapy, regardless of the type of ART initiated. This degree of bone loss is larger than what would be expected by aging alone and is comparable to the bone loss seen in women aged 50–59 years over 2 years

On basis of T-score, normal HIV positive cases ($n=50$) had mean CD4 count $215.60\pm 165.455/\mu\text{l}$, osteopenic ($n=66$) had mean CD4 count $182.55 \pm 167.906/\mu\text{l}$ and osteoporotic ($n=8$) had mean CD4 count $179.75\pm 105.396/\mu\text{l}$. Lesser the CD4 count greater was the prevalence of osteopenia and osteoporosis. The CD4 counts in between groups and within in groups does not so any significant relation with p -value 0.736 (Table-4). Similar result were obtained by Mondy K et al, (2003)²⁵ who found that amount of BMD gained depends on immune status and virological control of HIV infected as indication by correlation in between CD4 count, increased duration of HIV.

Limitations

Sample Size was Small.

In HIV positive patients males were more in number as compared to female.

None of the patient was on protease inhibitor regimen.

All predecided parameter could not be determined in all patients due to financial or other restraints.

Conclusions

We found that prevalence of osteopenia and osteoporosis is more in HIV positive patients and it starts occurring at younger age as evidenced by low

Table 3. Prevalence of osteopenia and osteoporosis in various age groups in HIV positive patients.

HIV Positive patients (Age in yrs)	Normal	Osteopenia	Osteoporosis
20-30 yrs	18(52.9%)	14(41.2%)	2(5.9%)
31-40yrs	26 (40.6%)	36 (56.2%)	2(3.1%)
41-50 yrs	6(25%)	16 (66.7%)	2(8.3%)
>50yrs	0 (0%)	0 (0%)	2 (100%)
Prevalence of osteoporosis and osteopenia in various age groups in control population.			
Type		n	Mean Age \pm SD
HIV Positive	Normal	50	33.88 \pm 6.809
	Osteopenia	66	37.27 \pm 7.238
	Osteoporosis	8	41.25 \pm 12.203
	Total	124	36.16 \pm 7.586
HIV Negative	Normal	48	41.75 \pm 9.992
	Osteopenia	16	52.62 \pm 11.338
	Osteoporosis	0	--
	Total	64	44.47 \pm 11.225

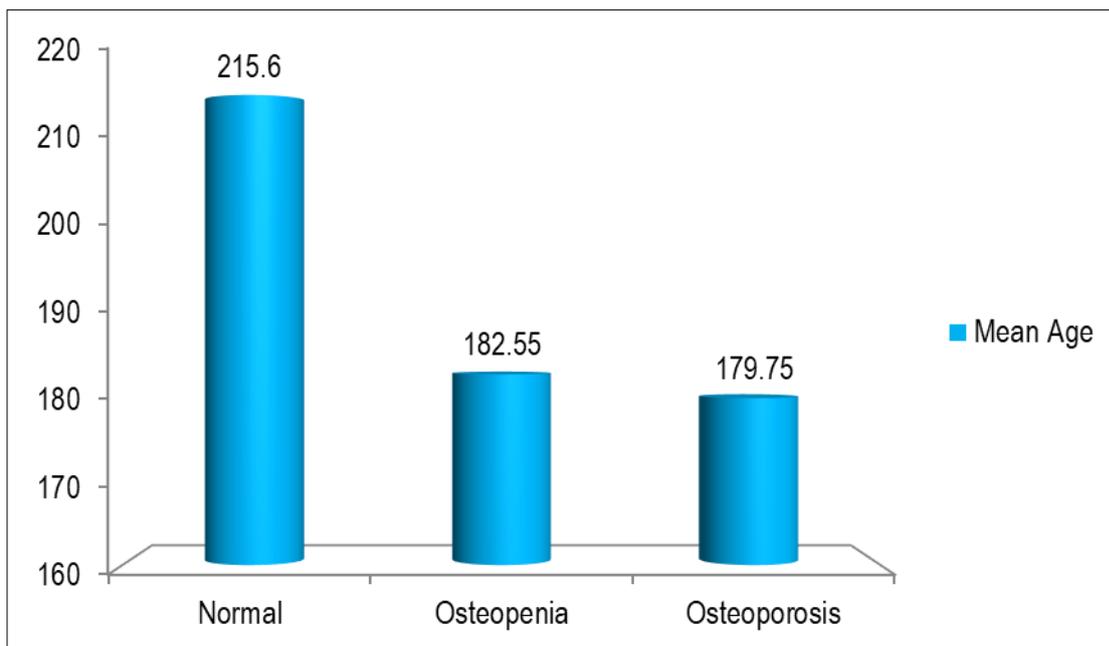


Figure 1. Prevalence of osteopenia and osteoporosis with mean CD4 count

Table 4. Prevalence Of Osteoporosis And Osteopenia

Prevalence of osteoporosis and osteopenia and CD4 count			
CD4 range (/μl)	Normal	Osteopenia	Osteoporosis
0-99	10(27.8%)	24 (66.7%)	2 (5.6%)
100-199	20 (47.6%)	20 (47.6%)	2 (4.8%)
200-299	4 (25%)	4 (50%)	4 (25%)
>300	16 (53.3%)	14 (46.7%)	0 (0.0%)
Prevalence of osteopenia and osteoporosis with mean CD4 count			
Type		n	Mean ±SD
CD4 count	Normal	50	215.60±165.455
	Osteopenia	66	182.55±167.906
	Osteoporosis	8	179.75±105.396
	Total	124	195.69±162.416
Prevalence of osteopenia and osteoporosis in study population.			
T-score at various sites	HIV Positive (n=124)	HIV Negative (n=64)	
Normal	50 (40.32%)	48 (75%)	
Osteopenia	66 (53.22%)	16(25%)	
Osteoporosis	8 (6.46%)	0 (0%)	

T-score and low Z-score in this population. In HIV positive patients mean BMD was minimum at left neck femur and maximum at left forearm radius . In HIV negative controls mean BMD was minimum at left neck femur and maximum at lumbar spine. The mean BMD at all sites was lower in HIV positive patients as compared to HIV negative controls and the difference was statistically significant (p value <0.05).

In HIV positive patients mean BMD was minimum at left neck femur and maximum at left forearm radius. In HIV negative controls mean BMD was minimum at left neck femur and maximum at lumbar spine. The mean BMD at all sites was lower in HIV positive patients as compared to HIV negative controls and the difference was statistically significant (p value <0.05).

On basis of T-score, normal HIV positive cases (n=50) had mean CD4 count 215.60±165.455/μl,

Osteopenic (n=66) had mean CD4 count 182.55 ± 167.906/μl and osteoporotic (n=8) had mean CD4 count 179.75±105.396/μl.

Lesser the CD4 count greater was the prevalence of osteopenia and osteoporosis. The CD4 counts in between groups and within in groups does not so any significant relation with p-value 0.736. Similar result was obtained by Mondy K et al, (2003)100 who found that amount of BMD gained depends on immune status and virological control of HIV infected as indication by correlation in between CD4 count, increased duration of HIV.

HIV positive patients should be screened by DEXA for BMD estimation and those with osteopenia or osteoporosis should be treated to prevent morbidity

References

1. NIH. NIH Consensus Development Panel on

- Osteoporosis, Prevention, Diagnosis, and Therapy. JAMA. 2001 ;285 :785 -95
2. Peck WA. et al. Consensus Development Conference: Diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993 ;94 :646 -650
 3. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1994; 843:1–129.
 4. Hammer SM. et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 counts of 200 per cubic millimeter or less: AIDS Clinical Trials Group 320 Study Team. N Engl J Med. 1997 ;337 :725 -33
 5. Aukurst P. et al. Decreased bone formative and enhanced resorptive markers in human immunodeficiency virus infection: indication of normalization of the bone-remodeling process during highly active antiretroviral therapy. J Clin Endocrinol Metab. 1999 ;84 :145 -150
 6. Fairfield WP. et al. Osteopenia in eugonadal men with acquired immune deficiency syndrome wasting syndrome. J Clin Endocrinol Metab. 2001;86 :2020.
 7. Corcoran C. et al. Treatments for wasting in patients with the acquired immunodeficiency syndrome. N Engl J Med. 1999 ;340 :1740 -1750.
 8. Stephens E. et al. Symptomatic osteoporosis in two young HIV-positive African women. AIDS. 1999 ;13 :2605 -2606.
 9. Grinspoon S. et al. Effects of testosterone and progressive resistance training in eugonadal men with AIDS wasting, A randomized, controlled trial. Ann Intern Med. 2000 ;133 :348 -355
 10. Kanis JA. et al. The diagnosis of osteoporosis. J Bone Miner Res. 1994;8 :1137 -1141.
 11. Schapira D, Schapira C. Osteoporosis: the evolution of a scientific term. Osteoporosis Int. 1992 ;2: 164 -167.
 12. Annapoorna N, Rao GV, Reddy NS, Rambabu P, Rao KRSS, An Increased Risk of osteoporosis during Acquired Immunodeficiency Syndrome. Int. J Med. Sci. 2004;1(3):152-164.
 13. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996; 312 (7041):1254–1259.
 14. Foundation NO. Clinician’s guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation, 2010.
 15. Bruera D, Luna N, David DO, Bergoglio LM, Zamudio J. Decreased bone mineral density in HIV-infected patients is independent of antiretroviral therapy. AIDS 2003; 17(13):1917–1923. 92.
 16. Todd T. Brown, Mary D. Ruppe, Rory Kassner, Princy Kumar, Theresa Kehoe, Adrian S. Dobs, & Joseph Timpone. Reduced Bone Mineral Density in Human Immunodeficiency Virus-Infected Patients and Its Association with Increased Central Adiposity and Postload Hyperglycemia. The Journal of Clinical Endocrinology & Metabolism 2004;89(3):1200–1206.
 17. Amorosa V, Tebas P. Bone disease and HIV infection. Clin Infect Dis. 2006 Jan 1;42(1):108-14. Epub 2005 Nov 30.
 18. Dolan SE, Kanter JR, Grinspoon S. Longitudinal analysis of bone density in human immunodeficiency virus-infected women. J Clin Endocrinol Metab 2006;91:2938-2945
 19. Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab. 2008;93(9):3499–504.
 20. Teichmann J, Stephan E, Lange U, et al. Osteopenia in HIV-infected women prior to highly active antiretroviral therapy. J Infect 2003; 46: 221–7.
 21. Libois A, Clumeck N, Kabeya K, Gerard M, De Wit S, Poll B, et al. Risk factors of osteopenia in HIV-infected women: no role of antiretroviral therapy. Maturitas. 2009;65(1):51–54.
 22. Güerri-Fernandez R, Vestergaard P, Carbonell C, Knobel H, Avilés FF, Soria CA, Nogués X, Prieto-Alhambra D, Diez-Perez A. HIV infection is strongly associated with hip fracture risk, independently of age, gender, and comorbidities: a population-based cohort study. J Bone Miner Res. 2013; 28:1259–63

23. Jones S, Restrepo D, Kasowitz A, et al. Risk factors for decreased bone density and effects of HIV on bone in the elderly. *Osteoporos Int.* 2008;19(7): 913–918
24. Tebas P, Umbleja T, Dube M. Initiation of ART is associated with bone loss independent of the specific ART regimen: Results of ACTG A5005s [abstract 837]. In: Program and abstracts of the 14th Conference on Retroviruses and Opportunistic Infections, 26 February 2007, Los Angeles, CA.
25. Mondy K, Yarasheski K, Powderly WG, et al. Longitudinal evolution of bone mineral density and bone markers in Human Immunodeficiency Virus-Infected Individuals. *Clin Inf Dis.* 2003, 36: 482–90.