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Original Research Paper

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A RETROSPECTIVE STUDY OF BONE MINERAL DENSITY AMONG PEOPLE LIVING WITH HIV AND ITS CORRELATION WITH CD4 COUNT.

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ABSTRACT

Background: Very less studies are found with data on prevalence of Bone Mineral Disease (BMD) in PLHIV among Indian population. This study was done to find out the prevalence of osteoporosis in HIV infected population and its correlation with CD4 counts. **Methods:** This Retrospective observational study was conducted in NACO- ART centre of tertiary care hospital. Total 47 PLHIV subject were included in this study. 47 HIV negative age and sex matched controls were enrolled. All subjects were analyzed for BMD by DEXA scan and correlation of BMD with a CD4 count was studied. **Results:** BMD was found to be low in PLHIV group compared to control group. T score in PLHIV in our study was -1.7 ± 0.7 which was significantly lower ($p<0.05$) as compared to 1.5 ± 0.8 in HIV negative control group. In our study we found osteopenia in 76.6% and osteoporosis in 10.6% among PLHIV, as compared to 23.4% and 4.2 % respectively in HIV negative controls. For every 100 cells/mm3 increase in CD4 count, the BMD T-score increases by 0.07 ($p = 0.014$) **Conclusions:** The prevalence of Bone mineral disease in form of osteopenia and osteoporosis in people living with HIV was higher and even presents earlier as compared to HIV negative controls. BMD levels show direct correlation with CD4 count. We recommend that all PLHIV especially with low CD4 count, multiple musculoskeletal symptoms and female sex should be screened for osteoporosis and started on anti-osteoporotic measures.

KEYWORDS : PLHIV, HAART, DEXA, CD4 Counts, Osteoporosis

INTRODUCTION

Human Immunodeficiency Virus (HIV)infection is a pandemic disease affecting millions of people. HIV infection is an inflammatory state, associated with chronic immune dysregulation. It's a multisystem disease and involves almost all system including pulmonary, cardiovascular, hematologic, central nervous system, musculoskeletal system, gastro intestinal and skin.(1)

With the advancement in efficacy of antiretroviral therapies (ART) combinations, life expectancy of people living with HIV (PLHIV) is now close to that of the HIV-uninfected population, this results in PLHIV being an aging population, with an increasing proportion of patients over the age of 50 years. Therefore, PLHIV are at greater risk of developing age-related non-communicable diseases, including osteoporosis and fractures.(2,3)

Along with traditional risk factors like postmenopausal status, elderly population, weight loss, malnutrition, physical inactivity, suboptimal intake of calcium and vitamin D, HIV-associated risk factors like antiretroviral therapy (ART) medications, duration of HIV infection, chronic illness may be associated with decreased bone mineral density.(4)

METHODS

This is a retrospective study, carried out at the NACO-ART center of a tertiary care centre in Pune, Maharashtra over a period of six months from January 2022 to June 2022. Data from medical records of People living with HIV visiting ART center for follow-up were taken and for control group data was taken from patient meeting inclusion criteria who underwent DEXA scan in Medicine OPD. Data of DEXA scan of Calcaneum Bone was collected. Demographic parameters, information regarding duration and type of HAART, CD4 count and Viral load, BMI and other parameters were collected.

Sample size:

Our study has two group with 1st group of 47 People living with HIV and 47 age and gender matched controlled were enrolled in 2nd group with total sample size of 94.

Inclusion criteria :

All diagnosed HIV-positive patients with age more than 18 years visiting ART clinic who were willing to participate in the study were included. The patients were diagnosed as per the criteria specified by National AIDS Control Organization (NACO), India. (2)

Exclusion criteria :

- All subjects with neoplastic diseases, rheumatoid arthritis, endocrine disorders, chronic renal disease, and liver disease were excluded from the study.
- Pregnant females and patients immobilized and bedridden for 6 months or more and those who refused to give consent were also excluded.

For all those 94 patient's data was collected regarding BMD which was measured by DEXA (dual-energy X-ray absorptiometry) scan. Those with BMD T-score >1 was considered to be normal. Osteopenia was defined as a BMD T-score between -1.0 and -2.5, and osteoporosis was defined as a BMD T-score ≤-2.5 using WHO criteria.(5) During analysis, variables from DEXA scan were treated as ordinal (normal values, osteopenia, or osteoporosis).

RESULTS

A total of 94 patients were recruited in a tertiary care teaching hospital in suburban Pune. 47 patients were recruited from the anti-retroviral therapy centre (NACO- ART) while 47 served as controls. Mean age of PLHIV is 47.5±9.5 years and that of control population is 42.7±11.7 years.

Mean Body Mass Index (BMI) of PLHIV group is 24.2 ± 4.1 kg/m^2 and that of control group is 26.5 ± 4.7 kg/m^2.Bone mineral density was measured with help of DEXA scan and T score was calculated. Mean T score among PLHIV group was -1.7±0.7 and among control group was 1.5±0.8. Mean CD4 count of PLHIV group was 544 cells per mm^3.

Mean duration of PLHIV on HAART was 6.4 ± 3.5 years. (Table 1).

Out of 47 PLHIV, 8 (17%) had muscle pain, 16 (34%) had bone pain, 30 (63.8%) had backache, 4 (8.6%) had a history of a stress fracture, and 12 (25.6 %) had joint pain. A total 34 (72.3 %) patients had at least one musculoskeletal symptom during time of data collection.

Table 1: Comparison between PLHIV and Control

Variable	PLHIV Group (n=47)	Controls Group (n=47)	p-value
Mean age (±SD) – years	45.7 ± 9.5	42.7 ± 11.7	.167
Gender – n (%) • Males • Females	 24 (51.1%) 23 (48.9%)	 27 (57.4%) 20 (42.6%)	.679
Mean BMI (±SD) – (kg/m2)	24.2 ± 4.1	26.5 ± 4.7	.011
Co-morbidities – n (%) • DM • HTN • IHD • Hypothyroidism	 8 (17%) 11 (23.4%) 0 (0%) 0 (0%)	 11 (23.4%) 10 (21.3%) 1 (2.1%) 2 (4.3%)	–
Mean BMD (±SD) – T-score	-1.7 ± 0.7	1.5 ± 0.8	.039
BMD categories – n (%) • Normal • Osteopenia • Osteoporosis	 6 (12.8%) 36 (76.6%) 5 (10.6%)	 33 (70.2%) 11 (23.4%) 2 (4.2%)	.049
Mean CD4 count (±SD) – cells/mm3	544 (437 – 703)	-	-
Cd4 ranges – n (%) • ≤200 cells/mm3 • 201-499 cells/mm3 • ≥500 cells/mm3	 1 (2.1%) 18 (38.3%) 28 (59.6%)	-	-
Mean duration on ART (±SD) – years	6.4 ± 3.5	-	-
Latest viral load – n (%) • ≤20/TND copies/mm3 • 21-199 copies/mm3 • ≥200 copies/mm3	 44 (93.6%) 3 (6.4%) 0 (0%)	-	-

The overall multivariate regression model was statistically significant (R^2 = 0.478, F [6, 87] = 13.27, p = <.001). CD4 counts, age, and gender significantly predict BMD when adjusted for other variables. For every 100 cells/mm^3 increase in CD4 count, the BMD T-score increases by 0.07 (beta = 0.07, 95% CI: 0.02 to 0.13, p = .014) (Figure 1). Similarly, for every year increase in age,

Table 2: Results of univariate and multivariate logistic regression

Variable	Univariate		Multivariate	
	Beta-coefficient [95% CI]	p-value	Beta-coefficient [95% CI]	p-value
Cd4 count (in hundreds)	0.11 [0.04 to 0.17]	.002	0.07 [0.02 to 0.13]	.014
Duration on ART	-0.01 [-0.05 to 0.03]	.543	0.04 [-0.01 to 0.09]	.085
PLHIV group	-0.25 [-0.55 to 0.05]	.099	-0.23 [-0.62 to 0.16]	.244
Age	-0.03 [-0.04 to -0.01]	<.001	-0.02 [-0.03 to -0.01]	<.001
Males	0.84 [0.59 to 1.09]	<.001	0.71 [0.48 to 0.95]	<.001
BMI	0.03 [0.001 to 0.07]	.044	0.01 [-0.02 to 0.03]	.600
Significant p value <0.05.				

the BMD T-score decreases by 0.02 (beta = -0.019, 95% CI: -0.03 to -0.009, p <.001). For males, keeping all other variables constant, the average BMD was better by a T-score of 0.711 than females (beta = 0.811, 95% CI:

0.477 to 0.946, p <.001). Results of univariate and multivariate regression are shown in Table 2(Table 2). Adjusted size of the effect of variables in multivariate analysis is graphically represented in Figure 2 (Figure 2).

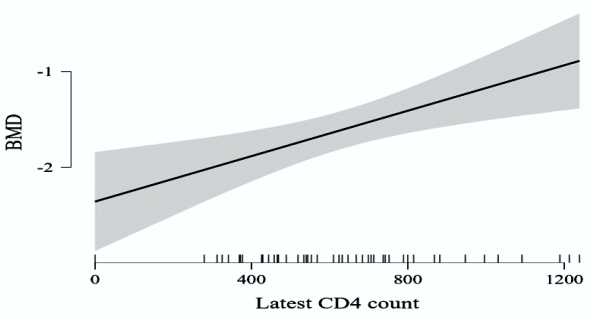

Figure 1: Correlation between CD4 count and Bone Mineral Density.

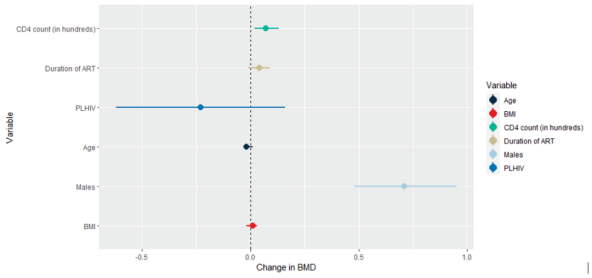

Figure 2: Forest plot of beta coefficients with 95% confidence intervals for their effects.

DISCUSSION

HIV infection affects each and every system of the body with primary involvement of the immunological system. Musculoskeletal system and bone metabolism are overlooked in a patient with PLHIV. Altered bone metabolism in PLHIV lead to reduced bone size, reduced bone mass, and reduced muscle and bone strength.(6) Many international studies revealed changes in BMD in these people. Borderi et al and Duvivier et al found that HIV infection of osteoblasts is associated with a negative balance of bone remodelling. (7) Decline in BMD following HIV, and its treatment leading to osteopenia and osteoporosis in both male and female patients with HIV as compared with non-HIV controls were reported.(8)

The rates of osteopenia and osteoporosis were found to be as high as 67 and 15% respectively, whilst the magnitude of BMD reduction was 6.4-fold higher, and that of osteoporosis 3.7-fold higher in HIV-positive patients, as reported in a meta-analysis.(9) Cazavane et al. indicated that more than half the HIV-infected patients had osteopenia, and approximately a third had osteoporosis, results which were verified by a study from McComsey et al.(10)

HIV infection leads to chronic T-cell activation and increased production of proinflammatory cytokines that enhance osteoclast activity. The cytokine Receptor Activator of Nuclear Factor kappa-B Ligand (RANKL) induces bone loss, while osteoprotegerin (OPG) counteracts its activity. In individuals with HIV, RANKL expression is increased and OPG expression is decreased in immune cells, leading to accelerated bone loss.(11) Furthermore, HIV proteins decrease bone formation by promoting osteoblast apoptosis (programmed cell death). Additionally due to chronic inflammatory state and malabsorption there is deficiency of vitamin D, calcium and

phosphorus which also add to the above mechanism of bone loss in patient with PLHIV.

One of the studies conducted in tertiary care centre in India shows prevalence of osteopenia and osteoporosis in PLHIV was 50.4% and 29.6% respectively.(12) In present study we found osteopenia in 76.6% of the study population and osteoporosis in 10.6%.

In our study we also collected data regarding musculoskeletal symptoms like Low back ache, arthralgia, myalgia, among PLHIV where we found that patient with a greater number of musculoskeletal symptoms have lower BMD and vice-versa.

Without doubt present study shows that HIV patients have significantly higher percentage of osteoporosis and osteoporosis as compare to healthy controls of same mean age. Among PLHIV Osteoporosis and osteopenia was found in 87.2% of study population and among control group in 26.6% population. This shows that in people Living with HIV are more prone to Bone mineral disease than normal population.

In our study in relation to CD4 counts we found that for every 100 cells/mm^3 increase in CD4 count, the BMD T-score increases by 0.07 ($p = .014$). There are many studies which shows CD4 counts and its correlation with BMD in PLHIV.(13,14) Similarly, for every year increase in age, the BMD T-score decreases by 0.02 ($p < .001$). We also found difference in BMD in PLHIV on basis of gender i.e. For males, keeping all other variables constant, the average BMD was better by a T-score of 0.711 than females ($p < .001$). few studies shows that BMD in PLHIV female declines twice as quickly compared to males.(15)

To conclude in present study, we found prevalence of osteopenia and osteoporosis is much higher, around three times age and sex matched control population. People living with HIV who have low CD4 count have a greater number of musculoskeletal symptoms and lower BMD (T score) on DEXA scan. As the duration of PLHIV increases, BMD reduces. BMD was found to be on lower side in female population than male population. Our study suggests screening of all PLHIV with age >45 years, longer duration of infection or therapy, female sex, those with musculoskeletal symptoms and also suggest use of supplementary therapy by anti-osteoporotic drugs to PLHIV especially with Tenofovir backbone, Low CD4 count and female sex.

Declarations
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Ethical approval: *Not required*

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