

# Fragility Fractures in HIV-Infected Subjects: an area for improvement

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**ABSTRACT**

**Background:** Despite a high prevalence of decreased bone mineral density (BMD) in HIV infected patients (pts), reports of fragility fractures are rare. We performed an analysis of such cases.

**Methods:** Cases of fragility fractures were reviewed from 9 large HIV clinics (~8,600 pts). Clinical presentations, antiretroviral (ARV) data, laboratory and radiological work-up, and therapeutics were reviewed.

**Results:** 49 pts were identified with fractures which occurred after no (n=28) or minor (n=21) trauma. Median date of fracture was 8/01 (2/91-8/03); only one case occurred before 10/97. Twenty seven patients were white, 10 blacks and 12 females. Median age at the time of fracture was 45 years (range 25-75). Forty eight % (20/42) were current smokers and 15% (6/40) current excessive alcohol users. Median BMI (n=40) was 23.29 kg/m2 (range 15.81-32.25). At the time of fracture, the median (range) HIV-1 RNA and CD4 (n=48) were 782 cps/mL (<50->750,000) and 216.5 cells/mm3 (7-908), respectively. Information regarding ARV therapy at the time of fracture was available on 46 pts; 2 were ARV-naïve and 38 were receiving therapy, including PI(s) in 31. Median cumulative duration of ARV and of PI therapy (n=43) were 37 months (0-142) and 25 months (0-83), respectively. The median nadir CD4 was 50 cells/mm3 (range 0-498) and median duration of HIV 6 years (0.1-19). Seven pts had a history of steroid use (chronic use including at the time of fracture in only 2). Fractures occurred in vertebrae alone (22) or with foot, femur, or pelvis (in 1 case each); ribs (4); lower extremities (15); upper extremities (3); clavicle (2). Only 10 pts had documented 25-OH Vitamin D levels; 30% (3/10) had levels <15 ng/mL. Only 10 cases had documented DEXA scan; median (range) of lumbar spine and hip t-scores were -2.43 (0.11 to -5.6) and -2.21 (-0.5 to -3.58), respectively. Calcium supplementation was prescribed in 16 pts, either alone (n=3), with vitamin D (n=7) or with alendronate (n=6); 3 others were prescribed calcitonin spray. In 9 pts, fractures re-occurred at the same or different site(s).

**Conclusion:** The prevalent decreased BMD found in HIV infected pts may predispose them to fragility fractures. Fragility fractures appear to be under-reported. Given the low rates of appropriate evaluation and treatment, further education is needed for HIV providers to ensure management consistent with current standards of care.

**BACKGROUND AND OBJECTIVES**

**BACKGROUND**

- Reports of high prevalence of decreased bone mineral density in HIV infected subjects
- Very few case reports of fragility fractures
- Optimal screening and management of decreased bone density in HIV is unclear, in part because consequences of this finding have not been defined

**OBJECTIVES**

- To describe factors associated with fragility fractures, including antiretroviral therapy composition, time on therapy, concomitant medications, co-morbidities, CD4 cell count history, viral load history, and demographic characteristics.
- To describe the clinical course of fragility fractures.
- To correlate the fragility fractures and lumbar spine t-score, as measured by DEXA scan

**METHODS**

- Retrospective analysis of identified cases of fractures in HIV-infected subjects that occurred after no or minimal trauma.
- Setting: 9 large HIV clinics (~8,600 pts).
- Data Collected:
  - Patient demographics
  - Antiretroviral history, steroids
  - Body Mass Index, pt & family history of bone disorders
  - Smoking, ETOH, drugs
  - CD4, HIV-1RNA
  - TSH, FSH, PTH, lactate, vitD, Ca, Ph, Alk Phos
  - Bone DEXA results
  - Fracture site, circumstances, management
  - Recurrence of fractures

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**RESULTS**

**DEMOGRAPHICS (n=49)**

- Median date of fracture 8/01 (2/91-8/03); only 1 case before 10/97
- Race: n=40: White 27, Black 10, Hisp 3
- Males 37 (76%)
- Median age at fracture: 45 years (range 25-75)
- Current smokers: 20/42 (48%)
- Current excessive alcohol use 6/40 (15%)
- Median BMI (n=40) was 23.29 kg/m2 (range 15.81-32.25)
- Seven pts had a history of steroid use (chronic use including at the time of fracture in only 2)

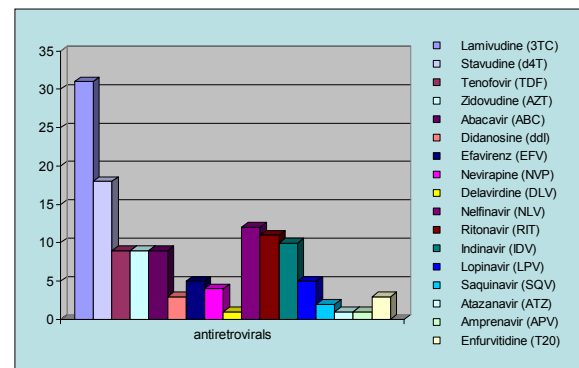
**HIV-RELATED INDICES**

- Median duration of HIV 6 years (0.1-19)
- Median nadir CD4: 50 cells/mm3 (range 0-498)
- At the time of fracture (n=48):
  - Median HIV-1 RNA: 782 cps/mL (range <50- >750,000); 22/48 (46%) were < 400 copies/mL
  - Median CD4 216.5 cells/mm3 (range 7-908)
- ARV history (n=46)
  - ARV-naïve: 2
  - Receiving ARV at time of fracture: 38 (PI in 31)
  - Median cumulative duration of ARV: 37 months (0-142)
  - Median cumulative duration of PI therapy: 25 months (0-83)

**ARV THERAPY AT TIME OF FRACTURE**

	Cases		Cases
Lamivudine (3TC)	31	Delavirdine (DLV)	1
Stavudine (d4T)	18	Nelfinavir (NLV)	12
Tenofovir (TFV)	9	Ritonavir (RIT)	11
Abacavir (ABC)	9	Indinavir (IDV)	10
Zidovudine (AZT)	9	Lopinavir (LOP)	5
Didanosine (ddl)	3	Saquinavir	2
Zalcitabine (ddC)	1	Amprenavir (AMP)	1
Emtricitabine (FTC)	1	Atazanavir (ATZ)	1
Efavirenz (EFV)	5	Enfuvirtidine (T20)	3
Nevirapine (NVP)	4		

**ARV Exposure at Time of Fracture**



**BONE DEXA RESULTS**

- Median date of fracture was no different between cases with and those without DEXA (8/02 vs. 7/01)
- Documented DEXA lumbar spine t-score (n=10)
  - Only 4/10 (40%) were osteoporotic (t-score< 2.5)
  - 5/10 (50%) were osteopenic (t-score -1 to -2.5)
- Median (range) of lumbar spine t-score -2.43 (0.11 to -5.6)
- Documented DEXA hip t score (n=10)
  - Only 4/10 (40%) osteoporotic (t-score < -2.5)
  - 4/10 (40%) osteopenic (t-score -1 to -2.5)
- Median (range) of hip t-score -2.21 (-0.5 to -3.58)

**BONE-RELATED LABORATORY INDICES**

- Documented 25-hydroxyvitamin D in 10/49 (20%): <15 ng/mL in 3/10 (30%)
- Documented lactate in 17/49 (35%): > 2 mmol/L in 1/17 (6%)
- Documented FSH in 2/12 (17%) females: both pre-menopausal
- Documented TSH in 26/49 (53%)- no cases of hyperthyroidism
- Documented PTH in 10/49 (20%): 2 had elevated levels (both to > 3ULN), one of whom had low 25-hydroxyvitamin D level
- Documented Alkaline phosphatase in 48/49 (98%): >130 IU/L in 21/48 (44%)

**FRACTURE CHARACTERISTICS**

- Fracture circumstances:
  - No trauma: n= 28
  - Minor trauma: n=21

- Location of fractures:
  - Vertebrae alone: 22
  - Vertebrae and foot: 1
  - Vertebrae and femur: 1
  - Vertebrae and pelvis: 1
  - Ribs: 4
  - Lower extremities: 15
  - Upper extremities: 3
  - Clavicle: 2

**TREATMENT AND OUTCOME**

- Treatment: *only 39% (19/49) had some bone-related tx*
  - Calcium supplementation alone: 3 cases
  - Calcium and Vitamin supplementation: 7
  - Calcium and alendronate: 6
  - Calcitonin spray: 3
  - None changed ARV
- Outcome (N = 36)
  - Median duration of follow-up 10 months (range <1- 143)
  - Recurrence of fracture in 9 cases (7 of whom at different bone sites)

**SUMMARY**

- The majority of HIV infected subjects with fragility fractures did not have a documented DEXA scan nor standard laboratory investigation to rule out secondary causes of osteoporosis
- Fragility fractures can happen with DEXA-measured BMD in the range of osteopenia, and not necessarily osteoporosis
- Management of the identified cases of fragility fractures was suboptimal and did not reach the standard of care of fragility fractures in the general population
- Despite a short duration of follow-up (10 months), 18% had already suffered from recurrence of fragility fracture, usually at a different bone site

**CONCLUSIONS**

- The prevalent decreased BMD found in HIV infected subjects may predispose them to fragility fractures.
- Fragility fractures appear to be under-reported
- Fragility fractures may occur at t-scores which are not considered diagnostic of osteoporosis
- More research is needed to determine optimal screening and management strategies for HIV infected individuals
- Given the suboptimal management of HIV infected subjects with fragility fractures in our study population, further education is needed for HIV providers to ensure management consistent with current standards of care.