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Femur Fracture Risk in HIV-Positive Patients with End-Stage Renal Disease: A Comparative Analysis from 2004–2013 to 2014–2023

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Abstract

Background: While femur fractures typically affect the elderly, HIV-positive patients with end-stage renal disease (ESRD) are at an accelerated risk due to prolonged antiretroviral therapy (ART) use and bone loss. The combined impact of these factors on fracture trends remains under-explored.

Objective: To evaluate the association between femur fractures and the coexistence of HIV and ESRD, and to analyze trends in fracture incidence and prevalence from 2004–2013 to 2014–2023 by age, sex, and race.

Methods: This retrospective cohort study used the TriNetX database to analyze data from 2,429 patients with HIV and ESRD receiving ART. The cohort was divided into two time periods: 2004–2013 and 2014–2023. Chi-square tests and Poisson regression were used to assess differences in fracture incidence and prevalence.

Results: Femur fracture incidence increased from 1.52% to 2.61% (a 71% increase), while prevalence grew from 1.67% to 3.80% (a 127% increase). This rise was most pronounced in females, with incidence increasing from 1.53% to 3.24% versus 1.84% to 2.25% in males. Racial disparities were also observed, with incidence in Asian patients rising from 0.0% to 45.45% and in Black or African American patients from 1.42% to 2.1%. The increase in fractures was also evident in younger patients.

Conclusion: The incidence of femur fractures in HIV-positive ESRD patients has significantly increased, with fractures occurring at earlier ages and disproportionately impacting women and certain racial minorities. These findings underscore the urgent need for early and routine bone health screening and tailored prevention strategies in this vulnerable population.

Keywords: HIV; End-Stage Renal Disease; Femur Fracture; Antiretroviral Therapy; Bone Fragility

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Introduction

Fractures of the hip and femur typically affect elderly patients due to increased fall risk and osteoporosis [1]. However, HIV-positive patients, especially those with end stage renal disease (ESRD), are also at heightened risk for these fractures due to accelerated bone loss [2, 3]. While antiretroviral therapy (ART) has significantly improved life expectancy, prolonged use of medications like tenofovir increases fracture risk by reducing bone mineral density (BMD) [4]. Early and widespread ART use has led to prolonged exposure in younger HIV-positive patients, making early-onset femur fractures an increasingly important issue. Despite independent studies on HIV, ESRD, and ART's effects on fractures, the combined impact of these factors remains underexplored. This study aims to evaluate the association between femur fractures and the coexistence of HIV and ESRD, focusing on how prolonged ART use and bone loss in ESRD contribute to increased fracture rates. The study will analyze trends in femur fracture incidence and prevalence from 2004–2013 to 2014–2023, and observe differences in age, sex, and race.

Methods

Study Design

This retrospective cohort study utilized the TriNetX database to analyze the incidence and

prevalence of femur, hip, and lower leg fractures in patients with ESRD and HIV receiving ART. Data were collected from January 2004 to December 2023, with a cohort of 2,429 patients diagnosed with both HIV and ESRD who were receiving ART. The fractures of interest included femur fractures (proximal femur and femoral shaft), hip fractures (femoral neck and intertrochanteric region), and lower leg fractures. The cohort was divided into two time periods: 2004–2013 and 2014–2023, to assess changes in fracture incidence and prevalence.

Cohort Definition

The cohort was defined by patients diagnosed with both HIV and End-Stage Renal Disease (ESRD) and receiving Antiretroviral Therapy (ART) during the study period. Out of a total population of 159,174,429 individuals, 2,429 patients met the inclusion criteria for femur, hip, and lower leg fractures in these populations.

Fracture Types Analyzed

This study analyzed femur fractures (including proximal femur and femoral shaft fractures), hip fractures (specifically femoral neck and intertrochanteric region fractures), and lower leg fractures including the ankle.

Data Extraction and Analysis

Fracture diagnoses, demographic details (age, sex, and race), and comorbidity information were extracted from the TriNetX database. The analysis evaluated the incidence proportion, prevalence, and incidence rate of fractures using Poisson regression for rate analysis and chi-square tests for proportions.

Statistical Analysis

Chi-square tests for proportions were used to assess differences in fracture incidence and prevalence between the two time periods (2004–2013 *vs*. 2014–2023). To evaluate the incidence rates of fractures over time, Poisson regression and rate ratio analysis were employed, adjusting for potential confounders including age, sex, and race.

Results

See Tables and Figures.

Discussion

This study demonstrates a significant increase in femur fracture incidence and prevalence among HIV-positive patients with End-Stage Renal Disease (ESRD) when comparing the decades of 2004–2013 and 2014–2023. The observed trends reflect the growing burden of bone fragility within this population, driven by the combined effects of prolonged ART exposure and ESRD-related metabolic bone disease [5]. While the advancement in HIV treatment has extended patient survival, prolonged exposure to ART, particularly Tenofovir Disoproxil Fumarate (TDF), accelerates bone loss, which heightens fracture risk [6, 7]. The increased incidence and prevalence of femur fractures are especially evident in younger patients, highlighting an emerging fracture risk in individuals who may not traditionally be considered at high risk. This earlier onset of bone loss suggests that prolonged ART exposure, along with ESRD-related bone fragility, accelerates skeletal deterioration [5, 8]. These findings emphasize the need for earlier osteoporosis screening and targeted preventive interventions, particularly in younger HIV-positive ESRD patients.

Sex differences were significant, with women showing a more pronounced increase in both fracture incidence and prevalence compared to men between 2004–2013 and 2014–2023. This aligns with existing literature demonstrating that women are at higher risk for osteoporosis and fractures due to hormonal factors, including reduced estrogen levels, which are compounded by ESRD and ART [9]. In contrast, although men experienced a smaller increase in fracture risk, the burden remains considerable, highlighting the need for preventive strategies for both sexes. These findings underscore the importance of sex-specific approaches to fracture prevention, including early bone density screening, calcium and vitamin D supplementation, and in some cases, hormone replacement therapy [10].

Racial disparities emerged in both decades, with Asian patients exhibiting a significant rise in fracture rates from 2004–2013 to 2014–2023. This sharp increase may reflect small population sizes and heightened sensitivity to individual cases, potentially leading to disproportionately large changes in incidence. These findings highlight the need for caution in interpreting the data and underscore the importance of targeted bone health interventions for Asian patients with ESRD and HIV, particularly considering potential genetic factors that may increase susceptibility to bone loss and fractures [11]. Other racial groups also showed increases in incidence, likely due to small population sizes. These findings suggest the need for further exploration of unique risk factors and healthcare disparities to guide tailored interventions. Black patients, while experiencing more moderate increases in fracture risk, continue to face heightened vulnerability due to the higher prevalence of HIV-associated nephropathy and ESRD [11]. White patients showed a slight increase in fracture incidence but a more significant rise in prevalence, suggesting longer survival and continued concerns regarding bone fragility. This underscores the need for ongoing fracture prevention strategies and bone health monitoring in this group.

These findings reinforce the importance of race-specific

Age Group	2004–2013 Incidence (%)	2014–2023 Incidence (%)	2004–2013 Prevalence (%)	2014–2023 Prevalence (%)	2004–2013 Incidence Rate (cases/person-day)	2014–2023 Incidence Rate (cases/person-day)
20-24	0.0	15.38	0.0	15.38	3.39E-05	5.86E-05
25-29	6.62	9.01	6.62	9.01	2.37E-05	3.73E-05
30-34	4.81	6.67	4.81	6.67	1.35E-05	2.61E-05
35-39	3.02	5.81	3.02	5.81	1.1E-05	2.15E-05
40-44	2.5	4.05	2.49	4.03	1.57E-05	1.61E-05
45-49	3.61	2.79	3.61	2.75	1.87E-05	1.1E-05
50-54	4.31	2.36	4.29	3.03	4.44E-05	4.44E-05
55-59	10.64	5.59	10.64	8.47	8.47E-05	2.35E-05
60-64	0.0	4.95	0.0	5.38	5.38E-05	2.18E-05
65-69	55.56	11.24	10.75	10.75	9.2E-06	9.2E-06
80-84	0.0	100.0	0.0	100.0	0.0000	3.64E-05

Table 1: Femur Fracture Incidence, Prevalence, and Rate by Age Group (2004-2013, 2014–2023).

Sex	2004–2013 Incidence Proportion (%)	2014–2023 Incidence Proportion (%)	2004–2013 Prevalence (%)	2014–2023 Prevalence (%)	2004–2013 Incidence Rate (cases/person-day)	2014–2023 Incidence Rate (cases/person-day)
Female	1.53	3.24	1.52	3.95	6.80×10^{-6}	1.30×10^{-5}
Male	1.84	2.25	1.91	3.69	8.60×10^{-6}	9.30×10^{-6}

Table 2: Femur Fracture Incidence, Prevalence, and Rate by Sex ((2004-2013, 2014–2023).

Race	2004–2013 Incidence (%)	2014–2023 Incidence (%)	2004–2013 Prevalence (%)	2014–2023 Prevalence (%)	2004–2013 Incidence Rate (cases/person-day)	2014–2023 Incidence Rate (cases/person-day)
Asian	0.0	45.45	40.0	45.45	0.0	0.000137
Black or African American	1.42	2.1	1.49	3.15	7.02E-06	8.62E-06
Unknown Race	3.26	3.58	3.25	4.52	1.3E-05	1.48E-05
White	3.1	3.32	3.1	5.6	1.3E-05	1.39E-05
Other Race	0.0	22.22	0.0	22.22	0.0	8.86E-05

Table 3: Femur Fracture Incidence, Prevalence, and Rate by Race (2004–2013, 2014-2023).

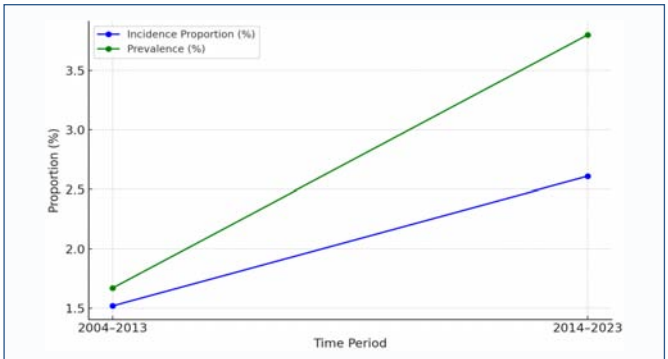

Figure 1: Incidence and prevalence of femur fractures in ESRD patients with HIV increased over two decades (2004–2013 *vs*. 2014–2023). The incidence proportion rose from 1.52% to 2.61%, reflecting a 71% increase, while prevalence grew from 1.67% to 3.80%, a 127% increase.

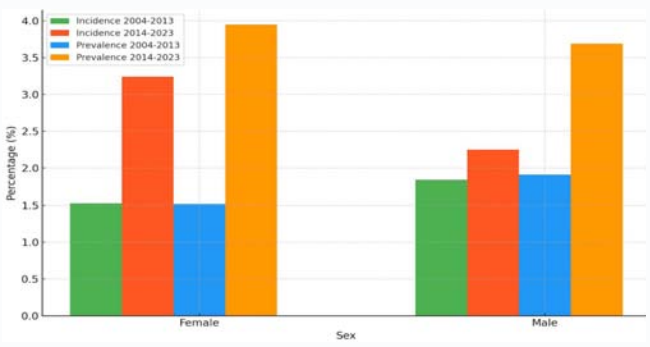

Figure 3: Incidence and prevalence of femur fractures in ESRD patients with HIV by sex for 2004–2013 and 2014–2023. The incidence increased from 1.53% to 3.24% in females and from 1.84% to 2.25% in males. Prevalence increased from 1.52% to 3.95% in females and from 1.91% to 3.69% in males.

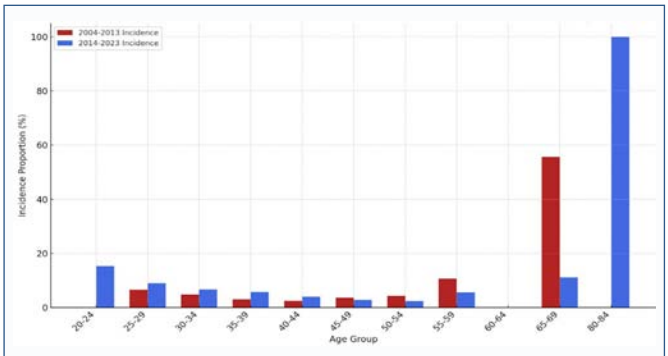

Figure 2: Incidence of femur fractures in ESRD patients with HIV for the periods 2004–2013 and 2014–2023 by age group. The graph displays the proportion of femur fractures across different age groups in each time period.

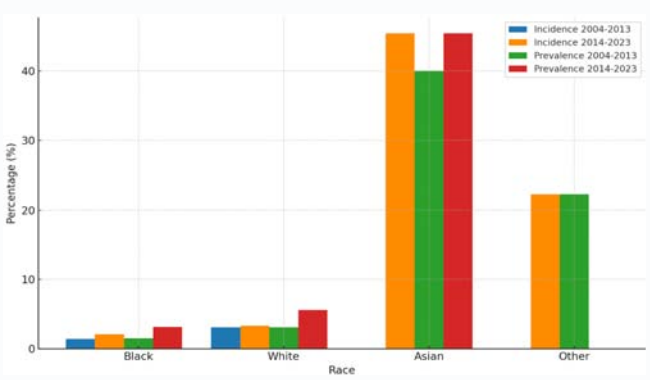

Figure 4: Incidence and prevalence of femur fractures in ESRD patients with HIV increased from 2004–2013 to 2014–2023. Incidence for Asian patients rose from 0.0% to 45.45%, while Other race increased from 0.0% to 22.22%. Black or African American patients saw incidence rise from 1.42% to 2.1%, with prevalence increasing from 1.49% to 3.15%. White patients had a slight increase in incidence from 3.1% to 3.32%, with prevalence growing from 3.1% to 5.6%.

interventions, such as early osteoporosis screening and adjustments to ART regimens to minimize bone loss, along with equitable osteoporosis screening and fracture prevention for all HIV-positive ESRD patients. Additionally, the increasing incidence of femur fractures in both younger and older patients highlights the critical need for proactive bone health management across the lifespan. Regular DXA screening should be implemented for high-risk groups, particularly those on long-term ART, along with fracture prevention strategies, including fall prevention, lifestyle modifications, and appropriate pharmacologic interventions, with a focus on both sex-specific and race-specific factors.

This study is limited by its retrospective design and the absence of direct bone mineral density measurements, which would provide more precise correlations between BMD and fracture risk. Moreover, the analysis did not account for confounders such as steroid use, diabetes, or co-infections, which may also impact bone health. Future prospective studies should focus on evaluating the effectiveness of early osteoporosis screening, fracture risk stratification, and long-term skeletal outcomes in this high-risk population [12].

Conclusion

The incidence of femur fractures in HIV-positive ESRD patients has significantly increased, with fractures occurring at earlier ages and disproportionately impacting women and racial minorities. These findings highlight the growing burden of skeletal fragility in this vulnerable population, underscoring the urgent need for early and routine DXA screening to identify bone loss at earlier stages. Proactive fracture prevention strategies, including tailored interventions based on sex and race, are critical to reducing the associated morbidity and improving patient outcomes. A comprehensive, individualized approach to bone health management is essential to address the evolving risk of femur fractures in HIV-positive ESRD patients.

Declaration of Conflicting Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval and Informed Consent Statements

This study utilized de-identified data from the TriNetX database and, therefore, was exempt from institutional review board (IRB) approval. As no identifiable patient information was accessed, the requirement for informed consent was waived.

Data Availability Statement

The data used in this study were obtained from the TriNetX database, a global federated research network. Access to the database is available to subscribing institutions, and data are not publicly available due to licensing agreements. However, aggregated results generated during this study are available from the corresponding author upon reasonable request.

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