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Osteoporosis after kidney transplant

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Abstract
Background: Osteoporosis is a prevalent complication in kidney transplant recipients, primarily due to the effects of immunosuppressive therapy and pre-existing bone mineral disorders associated with chronic kidney disease (CKD). This study aimed to assess changes in bone mineral density (BMD), the incidence of fractures, and the effectiveness of treatments in managing post- transplant osteoporosis.
Method: A 12-month retrospective cohort study examined 100 kidney transplant patients. DXA was used to evaluate BMD at the lumbar spine, femoral neck, and whole hip at baseline (pre-transplant) and 6 and 12 months' post-transplant. Fracture incidence, corticosteroid usage, vitamin D levels, immunosuppressive medication, and osteoporosis therapies (bisphosphonates, vitamin D) were recorded. Changes in BMD, fracture risk, and therapy efficacy were analysed statistically.
Results: Significant reductions in BMD were observed within the first year post-transplant, with an 8% decrease at the lumbar spine and a 6% decrease at the femoral neck. Fractures occurred in 8% of patients, primarily vertebral and hip fractures, with higher rates in those receiving higher cumulative corticosteroid doses and those with lower baseline vitamin D levels. Patients receiving bisphosphonates and vitamin D supplementation had better BMD retention and a lower fracture incidence compared to untreated patients.
Conclusion: In the initial year after transplantation, kidney transplant recipients are at risk for fast bone loss and fractures. Immunosuppressive medication, notably corticosteroids, causes BMD loss. Bisphosphonates and vitamin D treatment reduced this risk. Future studies are needed to assess the long-term advantages of osteoporosis therapies in kidney transplant patients.

Keywords: Osteoporosis, kidney, transplant

Introduction

Osteoporosis is a common and severe complication in kidney transplant recipients, largely stemming from the effects of chronic kidney disease (CKD) and its associated disruptions in mineral and bone metabolism, collectively termed CKD-mineral and bone disorder (CKD-MBD) [1]. CKD leads to imbalances in calcium, phosphorus, parathyroid hormone (PTH), and vitamin D [2], which contribute to increased bone turnover, loss of bone mass, and a higher risk of osteoporosis [3]. Although kidney transplantation restores kidney function and prolongs life, it does not immediately resolve the bone abnormalities associated with CKD [4]. Moreover, the immunosuppressive therapies required post-transplant introduce additional challenges, exacerbating bone deterioration and increasing the risk of osteoporosis and fractures. Immunosuppressive therapy is essential to prevent graft rejection [5]. Medications like corticosteroids (e.g., prednisone) and calcineurin inhibitors (e.g., tacrolimus, cyclosporine), though effective in controlling rejection, significantly impact bone health. Corticosteroids, in particular, accelerate bone loss by increasing resorption and decreasing formation [6]. These effects are most pronounced in the first year post-transplant, during which high doses are administered [7]. Kidney transplant recipients commonly experience declines in bone mineral density (BMD), particularly in the lumbar spine, femoral neck, and hip—areas prone to fractures. Low BMD, already present due to CKD-induced mineral imbalances, worsens with immunosuppressive therapy, leading to higher fracture rates [8]. Fractures, especially in the spine, hip, and wrist, significantly impact patients' quality of life [9]. Vitamin D deficiency is another critical factor in osteoporosis among kidney transplant recipients. CKD reduces renal synthesis of active vitamin D, impairing calcium absorption and bone remodeling [10]. Post-transplant, vitamin D metabolism often remains impaired, leading to secondary hyperparathyroidism and further bone resorption [11].

Other risk factors for osteoporosis in this population include age, gender, and hormonal status. Postmenopausal women and older men are particularly vulnerable to rapid bone loss and fractures due to these compounding factors [12]. Management of osteoporosis in kidney transplant recipients involves a multifaceted approach. Bisphosphonates have shown promise in reducing bone loss by inhibiting osteoclast-mediated resorption, but concerns remain regarding their long-term safety in patients with compromised renal function [13]. Vitamin D supplementation is widely recommended to improve calcium absorption and mitigate secondary hyperparathyroidism [14], though optimal dosing and formulations for this population are not yet standardized. Emerging therapies like denosumab, a monoclonal antibody targeting RANKL, have demonstrated efficacy in increasing BMD [15]. Similarly, teriparatide, a recombinant PTH, shows potential for treating severe osteoporosis, but its role in kidney transplant recipients requires further investigation [16]. This study aimed to assess changes in bone mineral density (BMD), the incidence of fractures, and the effectiveness of treatments in managing post- transplant osteoporosis.

Methods

This retrospective cohort study investigated changes in bone mineral density (BMD), fracture incidence, and risk factors for osteoporosis in kidney transplant recipients (KTRs) over 12 months post-transplantation. The study also evaluated the effectiveness of osteoporosis treatments in this population. Data were collected from the medical records of 100 KTRs, aged ≥18 years, with stable graft function (serum creatinine <2.0 mg/dL). Patients with primary bone diseases unrelated to CKD-MBD, requiring dialysis post-transplant, or on osteoporosis medications pre-transplant were excluded.

Data Collection

1. **Demographics:** Data included age, gender, BMI, and pre-transplant dialysis duration.
2. **BMD Measurements:** BMD at the lumbar spine, femoral neck, and hip was assessed using DXA at baseline (pre-transplant), six months, and 12 months post-transplant. Results were expressed as T-scores and Z-scores.
3. **Fracture Data:** Fracture occurrences were categorized as vertebral, hip, or wrist fractures, with radiographic confirmation and details on location and treatment.
4. **Risk Factors:** Data included corticosteroid use (categorized by cumulative dose), immunosuppressive therapy, vitamin D status (categorized as normal, insufficient, or deficient), and serum calcium and PTH levels.
5. **Osteoporosis Treatment:** Treatments like bisphosphonates, vitamin D, and calcium supplementation were tracked to assess their impact on bone health.

Statistical Analysis: BMD changes were analyzed as percentage changes from baseline, using paired t-tests ($p<0.05$). Fracture incidence was reported as a percentage. Logistic regression evaluated fracture risk, and multivariate analysis identified independent risk factors for significant BMD loss (>5%). Subgroup analyses compared BMD changes and fracture rates between patients receiving osteoporosis treatments and untreated patients, using the Mann-Whitney U test.

Results

The study included 100 kidney transplant recipients, with a median age of 50 years (range 22–70 years). Sixty percent of the study population was female. The average duration of dialysis prior to transplantation was 3.5 years. Baseline characteristics are presented in Table 1.

Table 1: Baseline characteristics of study population.

Characteristic	Value
Median Age (years)	50
Female (%)	60%
Pre-transplant Dialysis (years)	3.5
Baseline BMI (kg/m²)	25.3
Baseline Lumbar Spine BMD Z-score	-1.8
Baseline Femoral Neck BMD Z-score	-2.1

A significant reduction in BMD was observed during the first year following kidney transplantation, particularly in the lumbar spine and femoral neck. At six months' post-transplant, lumbar spine BMD decreased by an average of 4%, and femoral neck BMD decreased by 3%. By twelve months' post-transplant, lumbar spine BMD had decreased by 8%, and femoral neck BMD had decreased by 6%. Changes in BMD over time are detailed in Table 2, Figure 1.

Table 2: Changes in Bone Mineral Density (BMD) over time.

Time Point	Lumbar Spine BMD (% Change)	Femoral Neck BMD (% Change)	Hip BMD (% Change)
Baseline	0%	0%	0%
6 Months	-4%	-3%	-5%
12 Months	-8%	-6%	-9%

During the 12-month follow-up period, 8% of patients experienced fractures. Vertebral fractures were the most common, occurring in five patients (5%), while hip fractures were observed in three patients (3%). Fractures were more prevalent in patients with higher cumulative corticosteroid doses and those with lower baseline vitamin D levels. Detailed fracture data are provided in Table 3, Figure 2.

Table 3: Fracture incidence and associated risk factors.

Fracture Site	% Patients (n=100)	Significant Risk Factors
Vertebral	5%	High steroid dose, low vitamin D
Hip	3%	Age >50, low BMD

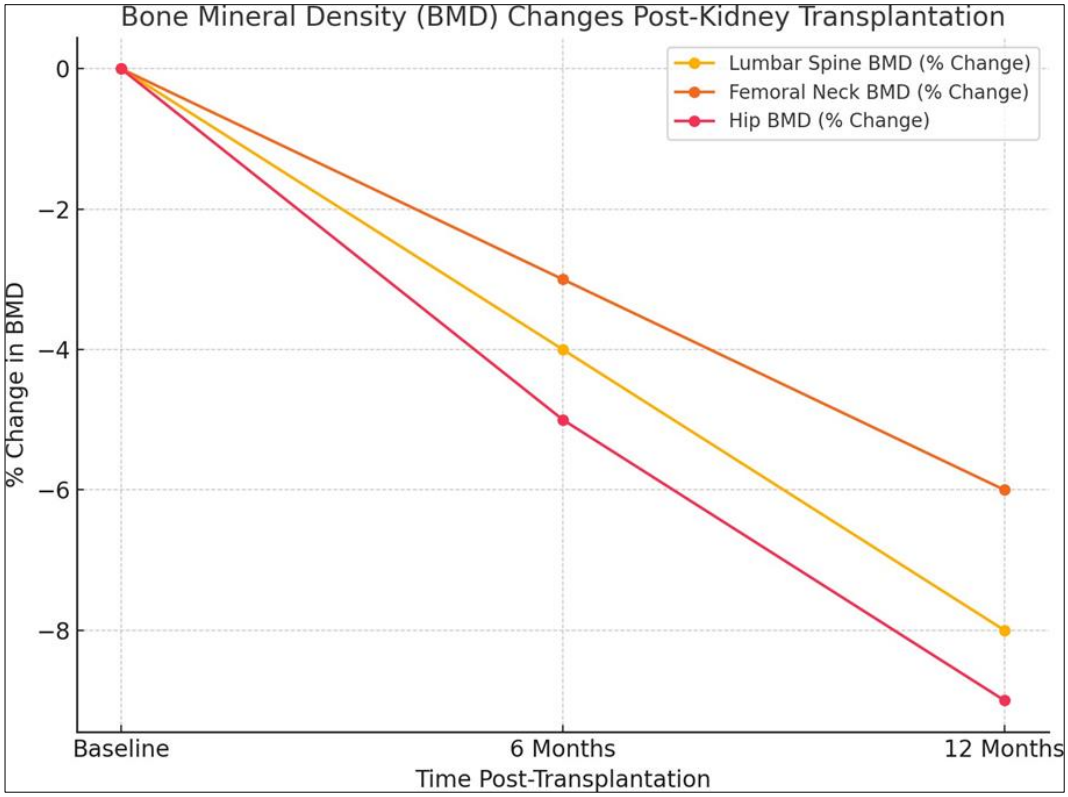

Fig 1: Shows the percentage change in bone mineral density (BMD) at different sites (lumbar spine, femoral neck, and hip) over time (baseline, 6 months, and 12 months) post-kidney transplantation.

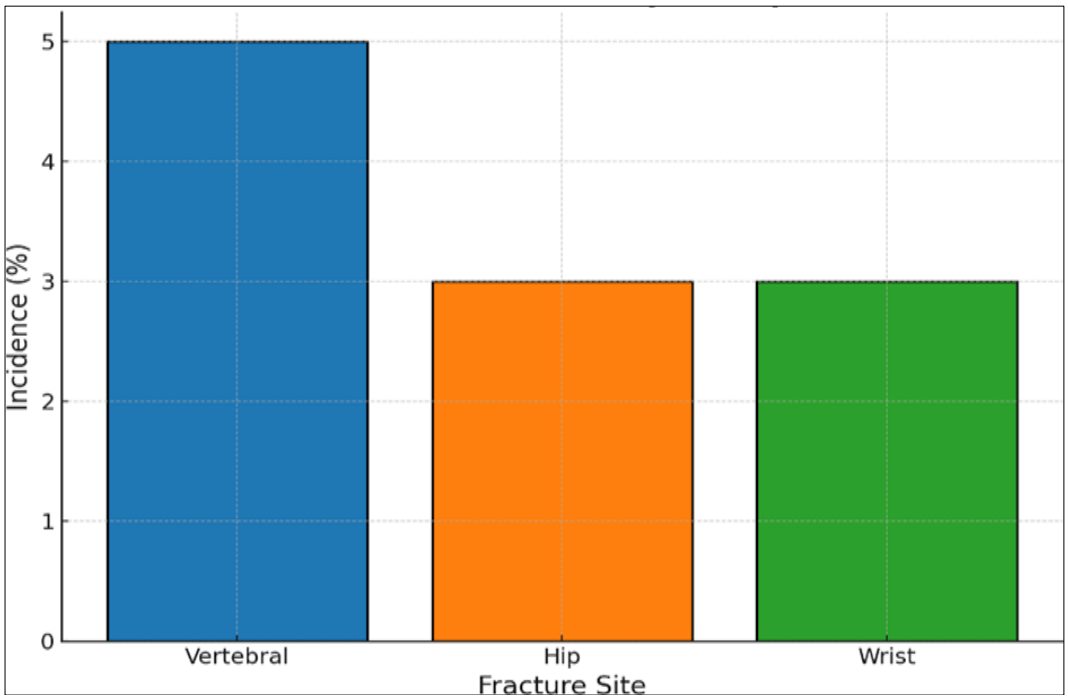

Fig 2: Incidence of fractures in kidney transplant patients

Multivariate analysis identified several significant risk factors associated with greater BMD loss, defined as a reduction of more than 5% from baseline. Patients receiving corticosteroid doses greater than 5 mg/day of prednisone experienced a significantly greater reduction in BMD compared to those receiving lower doses ($p< 0.01$). Additionally, patients with baseline vitamin D levels below 20 ng/mL had a 1.8-fold increased risk of BMD loss compared to those with normal vitamin D levels ($p< 0.05$). Patients who received bisphosphonates showed a modest improvement in BMD at the lumbar spine, with an average increase of 2% at 12 months, compared to a 5% decrease in patients who did not receive bisphosphonates ($p = 0.03$) (Figure 3-4,Table 4). Vitamin D supplementation was associated with a significantly lower fracture rate; patients who received vitamin D experienced a fracture rate of 4%, compared to 12% in patients without supplementation ($p = 0.04$). BMD loss was also significantly reduced in patients receiving vitamin D supplementation.

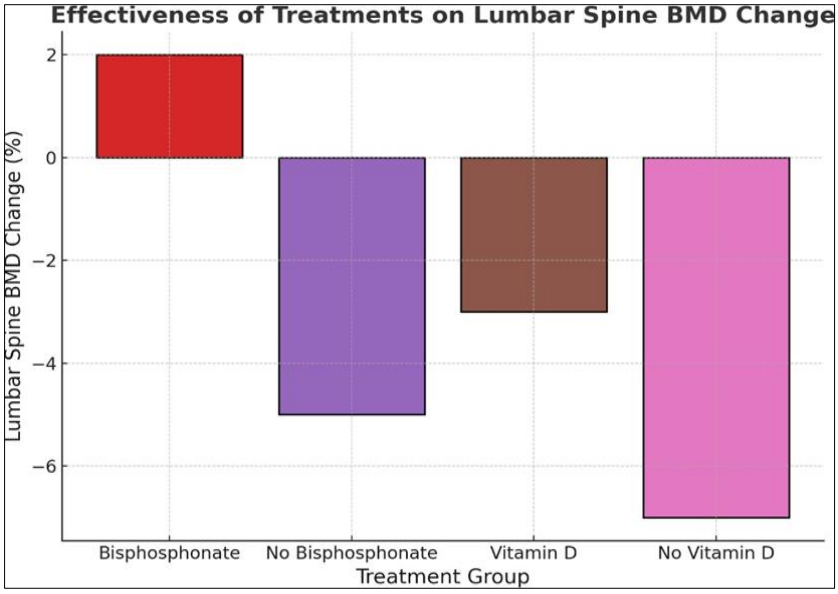

Fig 3: Effectiveness of treatments on lumbar spine BMD change.

Table 4: Comparison of BMD Loss and fracture rates between treated and untreated patients

Treatment Group	Lumbar Spine BMD Change (%)	Femoral Neck BMD Change (%)	Fracture Rate (%)
Bisphosphonate Group	+2%	-1%	3%
No Bisphosphonates	-5%	-4%	10%
Vitamin D Group	-3%	-2%	4%
No Vitamin D	-7%	-6%	12%

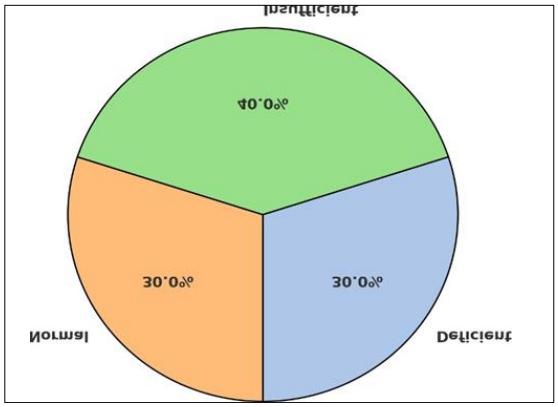

Fig 4: Vitamin D Levels in kidney transplant recipients

Discussion

Osteoporosis is a frequent and severe complication among kidney transplant recipients (KTRs), primarily due to the effects of chronic kidney disease (CKD) and immunosuppressive therapy [17]. CKD-related mineral and bone disorder (CKD-MBD) causes disturbances in calcium, phosphorus, parathyroid hormone (PTH), and vitamin D metabolism, which negatively impact bone health [18]. Although kidney transplantation restores renal function, it does not completely reverse bone impairments associated with CKD. Instead, immunosuppressive therapies exacerbate bone density loss, particularly in the first year post-transplantation. This study highlights the significant reduction in bone mineral density (BMD), with an average loss of 8% in the lumbar spine and 6% in the femoral neck during the first year post-transplant. Corticosteroids, widely used to prevent graft rejection, play a central role in post-transplant bone loss by increasing bone resorption and suppressing bone formation [19]. Calcineurin inhibitors, such as tacrolimus and cyclosporine, also contribute to reduced BMD by affecting kidney function and calcium homeostasis [20]. Fracture incidence in this cohort was 8%, with vertebral fractures being most common, followed by hip fractures. These fractures, linked to higher cumulative corticosteroid doses, underscore the need for strategies to minimize steroid exposure when feasible. Fractures significantly impact patient mobility, quality of life, and even graft survival, necessitating effective preventive measures. Vitamin D deficiency was a notable risk factor, observed in 30% of the study population. Vitamin D plays a critical role in calcium absorption and bone metabolism, and its deficiency leads to secondary hyperparathyroidism, further exacerbating bone resorption [21]. The strong association between vitamin D deficiency and fracture risk highlights the importance of routine vitamin D screening and supplementation in KTRs to stabilize BMD and reduce fractures. This study also demonstrated the effectiveness of bisphosphonates and vitamin D supplementation in mitigating bone loss and fracture risk. Bisphosphonates inhibit osteoclast-mediated bone resorption, and their use was associated with stabilization or slight improvement in lumbar spine BMD compared to substantial declines in untreated patients. Vitamin D supplementation further reduced fractures and improved calcium balance, highlighting its role in addressing vitamin D deficiency and associated hyperparathyroidism. These findings emphasize the importance of initiating bisphosphonates and vitamin D in high-risk KTRs, particularly those with severe bone density loss or prolonged corticosteroid use. Age and gender were additional risk factors for osteoporosis, with older adults and postmenopausal women being particularly vulnerable due to reduced baseline bone mass and estrogen deficiency. Immunosuppressive therapy exacerbates this vulnerability, increasing the urgency for targeted interventions in these subgroups. Despite its insights, this study has limitations. Its retrospective and cross-sectional design precludes

establishing causality between risk factors and BMD changes. The 12-month follow-up period may not fully capture the long-term impacts of bone loss or the effectiveness of treatments like bisphosphonates and vitamin D. Future research should focus on longitudinal studies to evaluate the durability of these interventions and explore newer therapies, such as denosumab and teriparatide, which show promise in osteoporosis management.

Conclusion

This study confirms that kidney transplant recipients are at increased risk for osteoporosis and fractures in the first year. The same decline in BMD at critical vertebral column and hip locations shows that immunosuppressive regimens, especially corticosteroids, damage bone. In this patient population, fractures, especially vertebral and hip fractures, increase the importance of early bone density testing and therapy. Bisphosphonates and vitamin D supplementation assist organ transplant patients preserve BMD and minimise fracture risk, according to certain studies. Given the higher correlation between cumulative corticosteroid dosage and BMD loss, limiting it as much as feasible is critical. Thus, this study advises bone densitometry and bisphosphonates or vitamin D medication for kidney transplant recipients at risk for osteoporosis to prevent bone loss and fractures. Longer-term research is needed to evaluate the effectiveness of therapies and develop novel treatments to reduce osteoporosis burden in senior adults.

Conflict of Interest

Not available

Financial Support

Not available

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