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Original Article

Prevalence and Risk Factors of Osteoporosis in Kidney Transplant Recipients: Dual-Energy X-Ray Absorptiometry Scan Study

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Abstract

Background: Osteoporosis is one of the major bone diseases that affect kidney transplant (KT) recipients; it causes significant long-term morbidity and increases the risk of fractures. The aim of this study was to investigate the prevalence and risk factors of osteoporosis in KT recipients. **Materials and Methods:** A cross-sectional study enrolled 70 KT recipients followed in the Nephrology Unit at Hawler Teaching Hospital, Erbil, Iraq, over a period of 6 months from December 15, 2017, to June 14, 2018. All patients were subjected to comprehensive history, clinical examination, relevant investigations, and measurement of bone mineral density (BMD) in the hip and lumbar spines using dual-energy X-ray absorptiometry. A T-score of –1 to + 1 standard deviation (SD) indicates normal BMD whereas a T-score of −1 to −2.5 SD was considered as osteopenia and T-score of <−2.5 SD was regarded as osteoporosis. **Results:** Osteoporosis was seen in 52.9% of the studied patients; statistically significant positive associations were detected between osteoporosis and low body mass index (BMI), diabetes mellitus (DM), second KT, pretransplant steroid treatment, and Vitamin D deficiency ($P < 0.05$), whereas no significant relationship was observed with age, gender, smoking, hypertension, and serum levels of calcium, phosphate, and parathyroid hormone. **Conclusion:** Osteoporosis is common among KT recipients. Low BMI, Vitamin D deficiency, DM, pretransplant steroid therapy, and second KT are the contributing factors. BMD measurement at pre- and post-transplant period is warranted for early recognition and management of this condition.

Keywords: Iraq, kidney transplant, osteopenia, osteoporosis

Introduction

Posttransplant bone disease is a major cause of morbidity in kidney transplant (KT) recipients, with a fundamentally higher risk of fractures, as well as expanded healthcare costs, hospitalization, and mortality.[1] The range of bone diseases in KT recipients includes renal osteodystrophy, osteoporosis, bone fracture, and osteonecrosis characterized by decreased bone mass, impeded bone quality, and inclination to fracture.[2] Back pain, vertebral fractures, and osteopenia on plain films are recognized as the clinical characteristics of osteoporosis. After transplantation, bone mineral density (BMD) declines by 4%–10% in the first 6 months with a further decrease of 0.4%–4.5% in lumbar BMD between 6 and 12 months as reported by earlier studies.[2,3] BMD remains relatively stable with no more declines after 1 year but at significantly lower levels than healthy people.[2] Osteopenia after renal transplantation has been demonstrated to be associated with several factors, including preexisting bone diseases, low BMD due to advanced age and/or Vitamin D deficiency, secondary hyperparathyroidism as well as posttransplant immunosuppressive therapy, dose of steroid, and ongoing disorder in the phosphate-calcium-parathyroid hormone-Vitamin D axis.[4,5] Dual-energy X-ray absorptiometry (DXA) scan is generally a noninvasive, accurate, cost-effective screening technique for evaluating bone mass, and it appears to help expecting fracture risk in KT recipients.[6] The aim of this study was to investigate the prevalence and risk factors of osteoporosis in KT recipients.

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Materials and Methods

This cross-sectional study enrolled 70 KT recipients in the Nephrology Unit at Hawler Teaching Hospital in Erbil, Iraq, over a period of 6 months from December 15, 2017, to June 14, 2018.

The patients were randomly assigned with a transplantation vintage of at least 1 year. The exclusion criteria were age below 18 years, pregnancy, abnormal renal indices, history of pretransplantation osteoporosis, and postmenopausal women. The data were collected through direct interview using a special questionnaire, and the following information was obtained from each patient: age, gender, history of smoking, hypertension and diabetes mellitus (DM), existence of pretransplant steroid therapy, and hyperparathyroid bone disease. Clinical examination was done including height and weight to calculate body mass index (BMI) (normal range [NR] 18.5–24.9 kg/m^2). All participants were subjected to serum measurements of creatinine (NR 0.6–1.3 mg/dL), calcium (NR 8.5–10.5 mg/dL), phosphate (NR 2.48–4.34 mg/dL), parathyroid hormone (NR 16–75 pg/ml), and 25 OH-Vitamin D (NR >50 nmol/L). BMD was measured in the hip and lumbar spines using DXA scan. A T-score of −1 to +1 standard deviation (SD) indicate a normal BMD. A T-score of −1 to −2.5 SD was considered as osteopenia and T-score of <−2.5 SD (i.e., ≥2.5 SDs below the mean BMD of a normal young-adult reference population) was regarded as osteoporosis according to the WHO criteria.[7]

The study was conducted according to the Helsinki ethical guidelines and has been approved by the Ethical Committee of Kurdistan Board of Medical Specialties. The written consent forms were obtained from all patients before recruitment and guarantees were given for confidentiality of their personal information.

The data were analyzed using Statistical Package for the Social Sciences version 25 (SPSS, IBM Company, Chicago, USA). The data were presented as mean, SD, and ranges. Categorical data were presented by frequencies and percentages. Pearson's Chi-square test was used to assess statistical association between bone density levels (BDLs) and studied variables. A $P < 0.05$ was considered statistically significant.

Results

This study included 70 KT recipients. The mean age of them were 48.9 ± 11.8 years. The participants' characteristics are presented in Table 1.

Laboratory investigations revealed that the highest proportion of patients had normal level of serum calcium, phosphorus, and 25 OH-Vitamin D (61.4%, 87.1%, and 54.3%, respectively), whereas 57.1% of them showed high parathyroid hormone level. According to the DXA scan results, the patients were distributed according to BDL, and more than half of them have osteoporosis [Table 2].

Regarding immunosuppressive drugs, all participants were on steroid, mycophenolate mofetil, and calcineurin inhibitors (either cyclosporine or tacrolimus). However, 13 patients (18.6%) were on pretransplantation steroid therapy.

The highest prevalence of osteoporosis was found among underweight patients, diabetics, second renal transplantation, pre transplantation steroid therapy and those with vitamin D deficiency ($P < 0.05$) [Table 3].

Table 1: Patients characteristics*

Characteristics	Frequency (%)
Age (years) (%)	
<40	19 (27.1)
40-59	41 (58.6)
≥60	10 (14.3)
Gender (%)	
Male	37 (52.9)
Female	33 (47.1)
BMI (kg/m^2) (%)	
Underweight	14 (20.0)
Normal	28 (40.0)
Over weight	21 (30.0)
Obese	7 (10.0)
Smoking (%)	
Smoker	34 (48.6)
Hypertension, *n* (%)	32 (45.7)
Diabetes mellitus, *n* (%)	22 (31.4)
Number of renal transplantation	
First (%)	59 (84.3)
Second (%)	11 (15.7)
Transplantation vintage (years) (%)	
1-3	59 (84.3)
>3	11 (15.7)

*Values are expressed as *n* or (%). BMI: Body mass index

Table 2: Patients distributions according to certain variables

	n (%)
Serum calcium	
Normal	43 (61.4)
Low	27 (38.6)
Serum phosphate	
Normal	61 (87.1)
Low	9 (12.9)
Serum 25(OH) Vitamin D	
Normal	38 (54.3)
Low	32 (45.7)
Serum intact parathyroid hormone	
Normal	30 (42.9)
High	40 (57.1)
Bone mineral density	
Osteoporosis	37 (52.9)
Osteopenia	29 (41.4)
Normal	4 (5.7)

Discussion

Post-KT bone diseases commonly develop, with a significantly

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Table 3: Relationship between bone density level and patient's variables

Variable	Osteoporosis (*n*=37), *n* (%)	Osteopenia (*n*=29), *n* (%)	Normal (*n*=4), *n* (%)	Total (*n*=70), *n* (%)	*P*
Age group (years)					
<40	8 (42.1)	9 (47.4)	2 (10.5)	19 (27.1)	0.444
40-59	23 (56.1)	17 (41.5)	1 (2.4)	41 (58.6)	
≥60	6 (60.0)	3 (30)	1 (10.0)	10 (14.3)	
Gender					
Male	20 (54.0)	15 (40.6)	2 (5.4)	37 (52.9)	0.885
Female	17 (51.5)	14 (42.5)	2 (6.0)	33 (47.1)	
BMI level					
Underweight	12 (85.7)	2 (14.3)	0 (0)	14 (20.0)	0.029
Normal	17 (60.7)	10 (35.7)	1 (3.6)	28 (40.0)	
Overweight	6 (28.6)	13 (61.9)	2 (9.5)	21 (30.0)	
Obese	2 (28.6)	4 (57.1)	1 (14.3)	7 (10.0)	
Smoking					
Smoker	20 (58.8)	12 (35.3)	2 (5.9)	34 (48.6)	0.591
Nonsmoker	17 (47.2)	17 (47.2)	2 (5.6)	36 (51.4)	
Hypertension					
Yes	20 (62.5)	11 (34.4)	1 (3.1)	32 (45.7)	0.295
No	17 (44.7)	18 (47.4)	3 (7.9)	38 (54.3)	
Diabetes					
Yes	17 (77.3)	5 (22.7)	0 (0)	22 (31.4)	0.016
No	20 (41.7)	24 (50.0)	4 (8.3)	48 (68.6)	
Number of KT					
First	27 (45.8)	28 (47.5)	4 (6.8)	59 (84.3)	0.022
Second	10 (90.9)	1 (9.1)	0 (0)	11 (15.7)	
Transplantation vintage (years)					
1-3	32 (54.2)	25 (42.4)	2 (3.4)	59 (84.3)	0.152
>3	5 (45.5)	4 (36.4)	2 (18.2)	11 (15.7)	
Pretransplant steroid therapy					
Yes	12 (92.3)	1 (7.7)	0 (0)	13 (18.6)	0.006
No	25 (43.9)	28 (49.1)	4 (7.0)	57 (81.4)	
Serum calcium					
Low	15 (55.6)	10 (37)	2 (7.4)	27 (38.6)	0.784
Normal	22 (51.2)	19 (44.2)	2 (4.7)	43 (61.4)	
Serum phosphate					
Low	2 (22.2)	7 (77.8)	0 (0)	9 (12.9)	0.057
Normal	35 (57.4)	22 (36.1)	4 (6.6)	61 (87.1)	
25(OH) Vitamin D					
Low	26 (81.3)	5 (15.6)	1 (3.1)	32 (45.7)	0.001
Normal	11 (28.9)	24 (63.2)	3 (7.9)	38 (54.3)	
iPTH					
High	25 (62.5)	14 (35)	1 (2.5)	40 (57.1)	0.11
Normal	12 (40.0)	15 (50.0)	3 (10.0)	30 (42.9)	

KT: Kidney transplant, iPTH: Intact parathyroid hormone

higher risk of morbidity and mortality. Osteoporosis is associated with low bone mass and enhanced skeletal fragility.

The current study demonstrates a high prevalence (52.9%) of osteoporosis among Iraqi KT recipients, which was comparable with studies conducted in Turkey (42.9%)[8] and South Korea (47.3%)[9] but higher than that reported in other studies as 26% in Iran[10] and 26.4% in Thailand,[11] which may be explained by complex pathophysiology underlying bone disorders, including preexisting renal osteodystrophy.[6] Our results showed that low BMI level was positively associated with osteoporosis that is in line with some studies[11,12] and disagreed with others.[10,13]

The present study revealed that Vitamin D deficiency had significant impact on the development of osteoporosis; a similar finding was reported in other regions across the world, as in Turkey,[8] the UK,[14] Denmark,[15] the Netherlands,[16] and the USA.[17] Vitamin D deficiency may be due to the low sunlight exposure, using sun protectors and immunosuppressive

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drugs, especially high doses of steroid and impaired kidney function.[18]

This study showed that osteoporosis associated significantly with pretransplant steroid treatment, this is consistent with a China study[13] but disagreed with other,[10] and this might be explained by the fact that corticosteroid can suppress bone formation, inhibit osteoblastogenesis, stimulate bone resorption, promote osteoblast apoptosis, and attenuate calcium absorption from the intestine.[19]

In congruence with our observation, other study showed a high rate of osteoporosis among diabetics.[6] Cumulative dosage of steroid may explain the high prevalence of osteoporosis in second KT recipients.[2,11]

In agreement with other studies, no significant relationship was observed between osteoporosis and age, gender, smoking, hypertension, and serum levels of calcium, phosphate, and parathyroid hormone.[8,10,13] The sample size of the present study does not allow us to generalize the findings to patients in other settings across the country.

Conclusion

Osteoporosis is common among Iraqi KT recipients. Low BMI, Vitamin D deficiency, DM, pretransplant steroid therapy, and second KT are the contributing factors. BMD measurement at pre- and post-transplant period is warranted for early recognition and management of this condition.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nair SS, Lenihan CR, Montez-Rath ME, Lowenberg DW, Chertow GM, Winkelmayer WC, *et al.* Temporal trends in the incidence, treatment and outcomes of hip fracture after first kidney transplantation in the united states. Am J Transplant 2014;14:943-51.
2. Malluche HH, Monier-Faugere MC, Herberth J. Bone disease after renal transplantation. Nat Rev Nephrol 2010;6:32-40.
3. Brandenburg VM, Politt D, Ketteler M, Fassbender WJ, Heussen N, Westenfeld R, *et al.* Early rapid loss followed by long-term consolidation characterizes the development of lumbar bone mineral density after kidney transplantation. Transplantation 2004;77:1566-71.
4. Borchhardt K, Sulzbacher I, Benesch T, Födinger M, Sunder-Plassmann G, Haas M. Low-turnover bone disease in hypercalcemic hyperparathyroidism after kidney transplantation. Am J Transplant 2007;7:2515-21.
5. Gwinner W, Suppa S, Mengel M, Hoy L, Kreipe HH, Haller H, *et al.* Early calcification of renal allografts detected by protocol biopsies: Causes and clinical implications. Am J Transplant 2005;5:1934-41.
6. Bouquegneau A, Salam S, Delanaye P, Eastell R, Khwaja A. Bone disease after kidney transplantation. Clin J Am Soc Nephrol 2016;11:1282-96.
7. Bone Health. World Health Organization Criteria for Diagnosis of Osteoporosis; 2018. Available from: http://www.4bonehealth.org/education/world-health-organization-criteria-diagnosis-osteoporosis/. Last accessed on 2018 Jul 05].
8. Unal A, Kocyigit I, Sipahioglu MH, Tokgoz B, Kavuncuoglu F, Oymak O, *et al.* Loss of bone mineral density in renal transplantation recipients. Transplant Proc 2010;42:3550-3.
9. Park WY, Han S, Choi BS, Park CW, Yang CW, Kim YS, *et al.* Progression of osteoporosis after kidney transplantation in patients with end-stage renal disease. Transplant Proc 2017;49:1033-7.
10. Ahmadpoor P, Reisi S, Makhdoomi K, Ghafari A, Sepehrvand N, Rahimi E. Osteoporosis and related risk factors in renal transplant recipients. Transplant Proc 2009;41:2820-2.
11. Techawathanawanna N, Avihingsanon Y, Praditpornsilpa K, Kingpetch K, Suwanwalaikorn S, Kanjanabuch T, *et al.* The prevalence and risk factors of osteoporosis in Thai renal-transplant patients. J Med Assoc Thai 2005;88 Suppl 4:S103-9.
12. Coskun Y, Paydas S, Balal M, Soyupak S, Kara E. Bone disease and serum fibroblast growth factor-23 levels in renal transplant recipients. Transplant Proc 2016;48:2040-5.
13. Wong HS, Chau KF, Wong KM, Chan YH, Liu YL, Chan HW, *et al.* Prevalence of osteoporosis in patients after renal transplantation. Hong Kong J Nephrol 2005;7:70-6.
14. Stavroulopoulos A, Cassidy MJ, Porter CJ, Hosking DJ, Roe SD. Vitamin D status in renal transplant recipients. Am J Transplant 2007;7:2546-52.
15. Ewers B, Gasbjerg A, Moelgaard C, Frederiksen AM, Marckmann P. Vitamin D status in kidney transplant patients: Need for intensified routine supplementation. Am J Clin Nutr 2008;87:431-7.
16. Keyzer CA, Riphagen IJ, Joosten MM, Navis G, Muller Kobold AC, Kema IP. Associations of 25(OH) and 1,25(OH)2 Vitamin D with long-term outcomes in stable renal transplant recipients. J Clin Endocrinol Metab 2015;100:81-9.
17. Lee JR, Dadhania D, August P, Lee JB, Suthanthiran M, Muthukumar T. Circulating levels of 25-hydroxyvitamin D and acute cellular rejection in kidney allograft recipients. Transplantation 2014;98:292-9.
18. Kulshrestha S, Ojo AO, Luan FL. Metabolic syndrome, Vitamin D deficiency and hypoadiponectinemia among nondiabetic patients early after kidney transplantation. Am J Nephrol 2013;37:399-404.
19. Canalis E. Mechanisms of glucocorticoid-induced osteoporosis. Curr Opin Rheumatol 2003;15:454-7.