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Effect of Chronic Kidney Disease on Bone Mineral Density

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Abstract

INTRODUCTION: Chronic kidney disease (CKD) leads to significant metabolic and nutritional changes that impact mineral metabolism and bone health, collectively referred to as CKD-mineral and bone disorders. AIM: To study effect of chronic kidney disease on bone mineral density. ***METHODOLOGY:*** This observational cross-sectional hospital-based study was conducted in the Department of Medicine, Rheumatology Division, at S.P. Medical College and Associated Groups of P.B.M. Hospitals in Bikaner, Rajasthan. ***RESULT:*** In our study, 36.92% of CKD patients were aged 51–60, with significant osteoporosis and osteopenia associated with disease stage, while metabolic parameters indicated reduced bone density, and the prevalence of osteoporosis was notably higher compared to other studies, likely due to differing population characteristics and confounding factors. ***CONCLUSION:*** Our study showed a 9.23% prevalence of osteoporosis in CKD patients, significantly associated with disease stage and metabolic abnormalities, highlighting the need for cost-effective BMD measurements and biochemical assessments for timely intervention in resource-limited settings.

Keywords: CKD, BMD, osteoporosis

INTRODUCTION

Chronic kidney disease (CKD) leads to significant metabolic and nutritional changes that impact mineral metabolism and bone health, collectively referred to as CKD-mineral and bone disorders (CKD-MBD). This condition is marked by imbalances in phosphate and calcium levels, alongside alterations in critical regulators such as parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23). CKD-MBD is thus thought to be a major contributor to the high mortality among patients with CKD1.BMD is a well-established key parameter for monitoring bone disease in CKD patients, although it should be noted that, there are many common factors affecting BMD not specifically related to CKD-MBD, such as age, gender, menopause, estrogen, body mass, cigarette smoking, alcohol abuse, excess glucocorticoid exposure, physical activity and genetic factors2.Disruption in mineral metabolism occur already at early stages of CKD, leading as the disease progresses to alterations in bone mass, bone turnover, mineralization and bone health3. Disorders of bone structure and mass can cause severe osteoporosis and fractures, while also contributing to vascular calcification linked to cardiovascular disease and increased mortality.The following brief review which in part is based on a recent review article from our group4 summarizes the current understanding of causes of CKD-MBD, and its consequences for clinical outcome in CKD patients.BMD decreases progressively in patients during the course of progression from mild to severe degrees of renal failure and the decrease in BMD is thus most pronounced in patients with the lowest glomerular filtration rate (GFR)5. Bianchi et al. reported that patients with pre-dialysis renal failure have reduced BMD which correlated to the reduction of renal function6 BMD measured in the lumbar bone decreased significantly after six months of transplantation7, which seemed to be mediated primarily by glucocorticoid usage after transplantation8. On the other hand, it will be reported that in patients on dialysis treatment, BMD did not change during the first year of dialysis treatment, neither in patients on hemodialysis (HD) nor in patients treated by peritoneal dialysis (PD)9. There is a positive correlation between body weight and BMD in the general population10. Similarly, several studies demonstrated that the body size relates with BMD also in CKD and ESRD patients11-13.Obesity also is associated with elevated BMD of weight-bearing bones and ribs, suggesting that obesity per se or indirectly via the increase of body mass may prevent bone loss14. On the other hand, reduced lean body mass and sarcopenia associated with bone loss as demonstrated in elderly people15,

putatively due to reduced impact on bone remodeling which through increased mechanical load forces of lean tissue may serve to strengthen bone16. In CKD patients17, higher body mass correlates with increased bone mineral density (BMD), influenced by adipose tissue metabolism and hormonal changes, while regular weight-bearing exercise is crucial for maintaining muscle mass, improving bone quality, and reducing fracture risk18-22. In CKD patients, the regulation of bone mineral density (BMD) is complicated by abnormal metabolism of calcium, phosphorus, PTH, and vitamin D23, with serum markers like intact PTH, ionized calcium, phosphate, alkaline phosphatase, and vitamin D serving as indicators of bone status and turnover24

AIM

To study effect of chronic kidney disease on bone mineral density.

MATERIALS AND METHODS

This observational cross-sectional hospital-based study was conducted in the Department of Medicine, Rheumatology Division, at S.P. Medical College and Associated Groups of P.B.M. Hospitals in Bikaner, Rajasthan. The study took place over a one-year period, from January 1, 2023, to December 30, 2023. A total of 130 chronic kidney disease (CKD) patients were included in the study, drawn from those attending the outpatient department or admitted to the hospital during this timeframe. The sample size for the study was thus set at 130 participants.

Formula: $n = \frac{z^2 * p(1-p)}{e}$

i.e. $((1.96*1.96)*(0.072)*(1-0.072))/(0.05*0.05) = 102.6721$

i.e. n=103 (nearest rounding off) and with 20% attrition the minimum sample size was130.

where – Z is the z score

e is the margin of error

n is the population size

p is the population proportion

The sampling technique used for this study was convenience sampling. The inclusion criteria consisted of chronic kidney disease (CKD) patients in stages 1 to 5 who were pre-dialytic and not on maintenance hemodialysis. Conversely, the exclusion criteria encompassed patients already receiving maintenance dialysis, transplant patients, and those with known parathyroid abnormalities. Additionally, individuals taking nonsteroidal anti-inflammatory drugs (NSAIDs), anti-epileptics, or those with known liver diseases, rickets, or osteomalacia were also excluded from the study.

RESULTS

Table- 1 Distribution of subjects according to their age

AGE	Frequency	Percent
21 – 30	7	5.38
31 – 40	10	7.69
41 – 50	21	16.15
51 – 60	48	36.92
61 – 70	34	26.15
71 – 80	10	7.69
TOTAL	130	100.00%
Mean	59.75 ± 6.55	

Maximum 36.92% patients belonged to 51 – 60 year age group followed by 61-70 yr had 26.15% patients whereas minimum 5.38% were in 21 – 30 yr followed by 7.69% in 31 – 40 yr. the mean age was 59.75± 6.55 yr.

Table – 2 Distribution of subjects according to grade of CKD

CKD stage	Frequency	Percent	Mean BMD
1	48	36.92	0.91 ± 0.15
2	32	24.62	0.88 ± 0.10
3	26	20.00	0. 84± 0.10
4	14	10.77	0.82 ± 0.13
5	10	7.69	0.80 ± 0.11
Total	130	100.00	**Mean BMD**

Maximum 36.92% patients had stage1 kidney disease followed by stage 2 (24.62%) and stage 3 (20.00%) whereas minimum 7.69% cases were in stage 5 followed by 10.77% in stage 4 of CKD.Mean value of BND in CKD stage 1 was 0.91 ± 0.15 and 0.88 ± 0.10in stage 2, 0.84±0.10in stage 3, 0.82 ± 0.13in stage 4 and 0.80 ± 0.11 in stage 5cases. The mean BMD level decreases as the stage of CKD increases and was found statistically significant. ($p<0.0001$**)

Table – 3 Distribution of subjects according to Hematological investigation

Haematological	Mean	SD
Hb	8.02	1.98
TLC	8.93	1.63
PLT	233	81.23
ALP	186.95	110.86
S. Albumin	3.25	0.79

In our study, Mean hemoglobin level was 8.02 ± 1.98 gm/dl, Total leucocyte count was 8.93 ± 1.63 103/mm3 and mean platelets were 233 ± 81.23 103/mm3. Mean Alkaline phosphatase was 186.95 ± 110.86 IU/L and serum albumin was 3.25 ± 0.79 g/dL.

Table – 4 Distribution of subjects according to renal investigation

Renal function test	Mean	SD
S. Urea	130.3	47.58
S. Creatinine	6.8	3.31
Electrolyte	**Mean**	**SD**
S. Sodium	134.85	7.24
S. Potassium	4.75	0.86
S. calcium	7.73	1.85
Variable	**Mean**	**SD**
HbA1c	8.4	3.26
Vit D	14.07	5.70

Mean Serum urea level was 130.3 ± 47.58 mg/dl, and serum creatinine was 6.8 ± 3.31 mg/dl.Mean Serum sodium level was 134.85 ± 7.24 IU/dl, serum potassium was 4.75 ± 0.86 IU/dl, and serum calcium was 7.73 ± 1.85 IU/dl.Mean HbA1c level was 8.4 ± 3.26 %, serum Vit D3 was 14.07 ± 2.70 ng/ml.

Table – 5 Distribution of subjects according to Z score

Z score	No.	%
Normal	71	54.62
Osteopenia	42	32.31
Osteoporosis	12	9.23
Sever Osteoporosis	5	3.85
Mean ± SD	-1.19 ± 2.17	

Maximum 32.31% cases had osteopenia followed by osteoporosis (9.23%) whereas minimum 3.85% cases had sever osteoporosis. 54.62% were having normal Z score. Mean Z score was -1.19 ± 2.17.

Table – 6 Association of grade of CKD with BMD

CKD stage	Normal		Osteopenia		Osteoporosis		Severe osteoporosis	
1	35	49.30	12	28.57	1	8.33	0	0.00
2	23	32.39	8	19.05	1	8.33	0	0.00
3	12	16.90	10	23.81	3	25.00	1	20.00
4	1	1.41	9	21.43	3	25.00	1	20.00
5	0	0.00	3	7.14	4	33.33	3	60.00
Total	71	100	42	100	12	100	5	100
P value	0.001**							

Maximum 60% patients had severe osteoporosis in stage4 kidney disease followed by stage 3 (33.33%) and osteopenia in stage 3and 4 (25.00%) and normal cases were in stage 1 (49.30%). ($p<0.0001$**)

DISCUSSION

In our study, maximum 36.92% patients belonged to 51 – 60 year age group followed by 61-70 yr had 26.15% patients whereas minimum 5.38% were in 21 – 30 yr followed by 7.69% in 31 – 40 yr. the mean age was 59.75± 6.55 yr. Maximum 80% patients with severe osteoporosis belonged to 41 – 60 year age group, 41.67% had osteoporosis and 57.14% had osteopenia were in in 51-60yr age group (P>0.05). Similarly Jin-Feng Huang et al. (2020)25 they studied 11050 participants aged ≥20 years. Also Sunil K. Patro et al. (2022)26 found that the mean age of the study population was (53.14 ± 9.81) years. Also Jana Uhlinova et al. (2022)27 observed that ninety patients had median age 64 years (range 29–87).

In our study, Maximum 36.92% patients had stage1 kidney disease followed by stage 2 (24.62%) and stage 3 (20.00%) whereas minimum 7.69% cases were in stage 5 followed by 10.77% in stage 4 of CKD. Maximum 60% patients had severe osteoporosis in stage4 kidney disease followed by stage 3 (33.33%) and osteopenia in stage 3and 4 (25.00%) and normal cases were in stage 1 (49.30%). Similarly H. K. Aggarwal et al. (2013)28 study was planned to evaluate the BMD in 75 predialysis patients, 25 each from CKD stage III, IV and V, respectively. As severity of CKD increased, the total number of patients with reduced bone density (osteopenia and osteoporosis) increased from 9 in stage III to 19 in stage V. The prevalence of osteoporosis increased from 16% in Group A to 12% in Group B and 36% in Group C.

In our study, Mean hemoglobin level was 8.02 ± 1.98 gm/dl, Total leucocyte count was 8.93 ± 1.63 103/mm3 and mean platelets were 233 ± 81.23 103/mm3. Mean Alkaline phosphatase was 186.95 ± 110.86 IU/L and serum albumin was 3.25 ± 0.79 g/dL. Similarly Babak Hadian et al. (2020)29 in their study found that Serum alkaline phosphatase values were between 134 to 1578 mg/dL (with mean level 392.27 mg/dL). Fifty-five patients (50%) had normal levels of ALP
In our study, Mean Serum urea level was 130.3 ± 47.58 mg/dl, and serum creatinine was 6.8 ± 3.31 mg/dl. Mean Serum sodium level was 134.85 ± 7.24 IU/dl, serum potassium was 4.75 ± 0.86 IU/dl, and serum calcium was 7.73 ± 1.85 IU/dl. Similarly Babak Hadian et al. (2020)29 in their study found that patients' calcium values were between 5.86 to 11.06 mg/dL, with 41(37.3%) out of the normal range.

In our study, Mean HbA1c level was 8.4 ± 3.26 %, serum Vit D3 was 14.07 ± 2.70 ng/ml. similarly Babak Hadian et al. (2020)29 in their study found that 25(OH) vitamin D3 levels were within the target range in only 30 (27.3%) patients. Patients with low vitamin D values, 58 (52.8%) of the patients had deficient level (less than 50 nmol/l) and 20 (18.2%) of the patients had inadequate level (50-75 nmol/L).

Also H. K. Aggarwal et al. (2013)28 The mean vitamin D level of group A was 38.14 15.73, 31.16 17.91 in group B and 21.92 13.00 in group C. The mean level of vitamin D showed a trend of declination from group A to C (p50.05). mean corrected serum calcium and Vitamin D levels decreased progressively in group A, B and C.

In our study, mean value of BMD in CKD stage 1 was 0.91 ± 0.15 and 0.88 ± 0.10in stage 2, 0.84±0.10in stage 3, 0.82 ± 0.13in stage 4 and 0.80 ± 0.11 in stage 5cases. The mean BMD level decreases as the stage of CKD increases and was found statistically significant. (p<0.0001**). Similarly Sunil K. Patro et al. (2022)26 found that Mean BMD in our study was 0.506 ± 0.101 g/cm2 which was very lower as compared to other studies. Most of the above data from studies involved CKD patients not on haemodialysis30-31

In our study Mean Z score was 1.19 ± 0.17. Similarly H. K. Aggarwal et al. (2013)28 Bone densitometric analysis revealed progressive decline in the bone mineral density (BMD) with deterioration of renal function. Z-score decreased steadily as stage of CKD progressed. Z-score for group A, group B and group C was 1.11± 2.39, 0.87 ± 2.66 and 0.92 ± 1.59, respectively. There was statistically significant difference in the Z-score of group A, B and C.

In our study maximum 32.31% cases had osteopenia followed by osteoporosis (9.23%) whereas minimum 3.85% cases had sever osteoporosis. 54.62% were having normal BMD. Similarly Sunil K. Patro et al. (2022)26 found that DEXA scan showed that the prevalence of osteopenia and osteoporosis in the patients were 20% and 76%, respectively, with 4% normal BMD. Hassan et al (2022)32 found that as regard ESRD group according to BMD, there were 18 normal cases, [30%], 17 osteoporotic cases [28.3%] and 25 cases with osteopenia [41.6%].

Not enough Indian studies are available on prevalence of fracture risk in CKD patients not on haemodialysis. The prevalence of osteopenia in our study is similar to the study by Govindarajan et al.33 The results are not like other previous reports; prevalence of osteoporosis was much higher in our study population34-36. The cause for this difference may be different population characteristics, higher age group, malnutrition, and other confounding factors.

CONCLUSION

Our study found that osteoporosis was present in 9.23% of CKD patients, with a significant association to CKD stage rather than age or sex, indicating that mean bone mineral density decreases with advancing CKD. Notably, metabolic abnormalities such as hypocalcemia and hyperphosphatemia occur early, prior to overt osteoporosis. In resource-limited settings like India, simple and cost-effective methods, such as BMD measurements and biochemical assessments, can provide crucial insights into bone status, enabling timely interventions to reduce fracture risks.

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