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Internal Medicine

DEXA SCREENING IN CKD-MBD: A KEY TO PREVENTING OSTEOPOROSIS

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ABSTRACT **Introduction:** Many individuals afflicted with Chronic kidney disease (CKD), particularly those in stages 3 to 5, exhibit a substantial decline in bone mineral density, leading to an increased vulnerability to fractures and a notable surge in related morbidity and mortality. Moreover, Chronic kidney disease–mineral and bone disorder (CKD-MBD) remains inadequately investigated within this population. Thus, this study aimed to elucidate the metabolic bone profile of CKD patients utilizing DEXA (dual x-ray absorptiometry). **Material and Methods:** In this cross-sectional study, patients diagnosed with stages 3, 4, and 5 CKD were assessed. The serum concentrations of calcium, phosphorus, intact parathyroid hormone (iPTH), 25-hydroxy vitamin D, and total alkaline phosphatase were determined for all participants. Additionally, bone mineral density (BMD) was evaluated at the neck of the femur (NOF), lumbar spine (LS), and distal end of radius using dual-energy X-ray absorptiometry (DEXA) **Results:** The prevalence rates of various biochemical abnormalities were as follows: hypocalcemia (85%), hyperphosphatemia (74%), elevated alkaline phosphatase (89%), secondary hyperparathyroidism (68%), vitamin D deficiency (60%), and vitamin D insufficiency (26%). Osteoporosis, as determined by the femoral neck T-Score, was identified in 35 patients (35%), while 47 patients (47%) displayed osteoporosis at the lumbar spine (LS). Additionally, osteoporosis was detected in 40 patients at the radius. This data indicates a trend wherein as CKD advances to later stages, there is a notable increase in the prevalence of osteoporosis and osteopenia, with a particular emphasis on the lumbar spine. **Conclusion:** Hence, CKD represents a substantial risk factor for osteoporosis, independent of conventional risk factors. We emphasize the importance of early screening, identification, and management of osteoporosis to alleviate the related morbidity and mortality within this specific patient cohort.

KEYWORDS : CKD-MBD, DEXA, Osteoporosis

INTRODUCTION

Osteoporosis and fractures are frequently observed in individuals with advanced chronic kidney disease (CKD) who undergo maintenance dialysis.[1,2] Osteoporosis is a disease of the bones in which low bone mass and structural deterioration of bone tissue lead to an increase in bone fragility. Therefore it is very crucial to diagnose it early for timely prevention and treatment of osteoporotic fractures and their unfortunate consequences.[3]

The increased morbidity and mortality rates seen in advancing CKD are closely linked to the metabolic bone changes that occur. The MBD associated with CKD includes bone, biochemical, and cardiovascular abnormalities in the same entity since they share common pathophysiological mechanisms. Hypocalcemia is common in CKD patients and contributes to increased PTH secretion and abnormal bone remodeling.[4] The decrease in serum calcium concentration is sensed by a specific membrane calcium-sensing receptor (CaSR) on parathyroid glands and is a potent stimulus for PTH release.[5] Hypercalcemia lead to vascular calcification and cardiovascular events, while hypocalcemia may increase the risk of osteoporosis and fracture. The causes of increase in initiating and maintaining PTH included phosphate retention, decreased free ionized calcium level, decreased vitamin D level.[6] PTH levels are used as a surrogate to evaluate the status of bone turnover. Very high PTH levels (≥300 pg/mL) are usually associated with osteitis fibrosa, while very low PTH levels (<150 pg/mL) are associated with adynamic bone disease.[7] While biomarkers such as parathyroid hormone and alkaline phosphatase concentrations can assist in evaluating bone turnover. Individuals with CKD have a risk of fractures more than 2.5 times higher compared to those without CKD, while individuals undergoing dialysis face a risk exceeding 4 times that of the general population.[8,9]

In the general population, measurement of BMD by DEXA is used routinely in the diagnosis of osteoporosis and to assess fracture risk. Despite the challenges in diagnosing osteoporosis in this population, imaging techniques, particularly dual-energy x-ray absorptiometry (DEXA), prove beneficial in identifying those with CKD who are at the highest risk of fractures.[10,11] Bone biopsy remains the gold standard for the diagnosis of bone turnover abnormalities. However, it is an invasive method and repetitive assessment of bone status cannot be possible.[12] Several longitudinal studies confirmed that low BMD could predict fractures in patients with CKD.[13,14]

In patients with CKD G3–G5 with evidence of CKD-MBD and risk factors for osteoporosis, KDIGO in 2017 suggest BMD testing to assess fracture risk if results will impact treatment decisions.[15]

MATERIALS AND METHODS

Study Design and Setting It was a prospective cross sectional study conducted on patients of chronic kidney disease in Department of Medicine and Department of Nephrology IGMC Shimla, Himachal Pradesh.

Study Population and Study Period Study will be conducted for one year from 1st July 2021 to 30th july 2022 in patients with age 18 years or more with chronic kidney disease.

Inclusion Criteria

Patients 18yrs or more diagnosed with chronic kidney disease and who give consent to participate in the study

Exclusion Criteria

Previous history of chronic disorders associated with changes in mineral metabolism:

1. Thyroid disorders
2. Cushing's syndrome
3. Prolonged immobilization in the past
4. Liver disease
5. Primary hyperparathyroidism
6. Any medication which might influence bone metabolism (corticosteroids, hormone replacement therapy, calcitonin, bisphosphonates, cytotoxics, antimetabolites anticoagulants, anticonvulsants, thyroxine, interferon or lamivudine) was also excluded.

METHODOLOGY

All patients were subjected to detailed history and clinical examination. Only routine relevant lab investigations were done, so there was no extra burden on patients.

The definitions for hypocalcemia (Ca < 8.5 mg/dl), hypercalcemia (Ca >10.5 mg/dl), hyperphosphatemia (phosphorus >4.5 mg/dl), hypophosphatemia (phosphorus <2.5 mg/dl), elevated alkaline

phosphatase level (>120 IU/L), serum iPTH level (iPTH < 150pg/mL, 150–300pg/mL and >300pg/mL).[7,16,17,18]

Bone Mineral Density Measurement

Bone Mineral Density (BMD) was measured in g/cm2 in all patients at the lumbar spine, femoral neck and left radius by dual energy X-ray absorptiometry (DEXA) scan using Hologic osteoporosis assessment, Discovery QDR series, USA. Results were expressed in T-score {difference in Standard Deviation (SD) between the patient's measured BMD value and the maximum mean BMD of young adult of same gender. According to the World Health Organization (WHO) criteria: Normal BMD was being represented by a T score of more than -1. Osteopenia (low bone mass) was represented by a T score between-1 and -2.5. Osteoporosis was represented by a T score less than -2.5. Established osteoporosis was represented by a T score of less than -2.5 and a previous history of a fragility fracture.[19]

Statistical Analysis

Analysis was done using SPSS version 17.0 (IBM SPSS Statistics Inc., Chicago, Illinois, USA).Windows software program. Categorical variables were summarized as frequencies and percentages, and continuous variables as means and standard deviation. Significance of difference in mean in three groups was inferred by "ANOVA test" for parametric distribution of data and Kruskal-Wallis Test if the data were not normally distributed. Similarly, the significance of difference in proportion in the groups was inferred by "chi-square test". Statistical significance was assigned at p-value of less than 0.05.

RESULTS

Table-1 Demographic Characterstics

Gender	
Male	56 (56%)
Female	44 (44%)
Age	
Mean ± Std.55.76 ± 14.32	
Address	
Rural	68 (68%)
Urban	32 (32%)
Cause of CKD	
Diabetics Mellitus	41 (41%)
CGN	17 (17%)
HTN	14 (14%)
Obstructive uropathy	7 (7%)
CIN	6 (6%)
IgA nephropathy	6 (6%)
ADPKD	4 (4%)
LUPUS	3 (3%)
RSD	1 (1%)
FSGS	1 (1%)
CKD Stages	
3	15 (15%)
4	33 (33%)
5	52 (52%)

Table -2 Frequency Of Various Lab Parameters

	Stages of CKD					
n	Total	3	4	5	Total	p
Phosphorus	2.5-4.5 mg/dl (%)	10	14	2	26	<0.001
	>4.5 mg/dl	5	19	50	74	
Calcium	8.5-10.5 mg/dl	6	26	51	83	<0.001
	>10.5 mg/dl	9	7	1	17	
ALP	>120U/L	9	28	52	89	<0.001
	<120 U/L	6	5	0	11	
Vitamin D	<20 ng/dl	0	13	47	60	<0.001
	20-30 ng/dl	5	16	5	26	
	30-80 ng/dl	10	4	0	14	
	>80 ng/dl	0	0	0	0	
iPTH	<150 pg/dl	5	2	0	7	<0.001
	150-300 pg/dl	10	13	2	25	
	>300 pg/dl	0	18	50	68	

Table-3 Comparison Of Different Parameters With Different Stage Of Kidney

	Stages of CKD			p value
	3	4	5	
Phosphorus	3.83 ± 0.72	4.73 ± 0.91	6.31 ± 1.01	<0.001 One way ANOVA
Calcium	8.85 ±1.51	7.91 ±1.14	6.68± 0.93	<0.001 One way ANOVA
ALP	129.07 ±15.44	140.21 ±20.04	159.35 ±15.12	<0.001 One way ANOVA
Vitamin D	31.91 ±5.13	22.34 ±6.9	14.8 ±3.98	<0.001 Kruskal-Wallis Test
iPTH	265.87 ± 131.26	348.67 ± 151.58	531.5 ± 170.46	<0.001 Kruskal-Wallis Test

Table -4 Comparison Of Dexa With Stages Of Ckd

	Stages of CKD			Total	p
DEXA NOF	3	4	5		
osteoporosis	0	3	32	35	<0.001
osteopenia	3	21	18	42	
Normal density	12	9	2	23	
DEXA LS					
osteoporosis	0	9	38	47	<0.001
osteopenia	2	18	13	33	
Normal density	38	13	1	20	
DEXA Radius					<0.001
osteoporosis	0	4	11	40	
osteopenia	4	15	14	29	
Normal density	36	10	6	31	

Table -5 Comparison Of Dexa With Ipth

	iPTH				
DEXA NOF	Low bone turnover <150 pg/dl	150-300 pg/dl	High bone turnover >300 pg/dl	Total	P
osteoporosis	0	0	35	35	<0.001
osteopenia	1	10	31	42	
Normal density	6	15	2	23	
DEXA LS					<0.001
osteoporosis	0	3	44	47	
osteopenia	2	11	20	33	
Normal density	5	11	4	20	
DEXA Radius					<0.001
osteoporosis	0	2	38	40	
osteopenia	2	8	19	29	
Normal density	5	15	11	31	

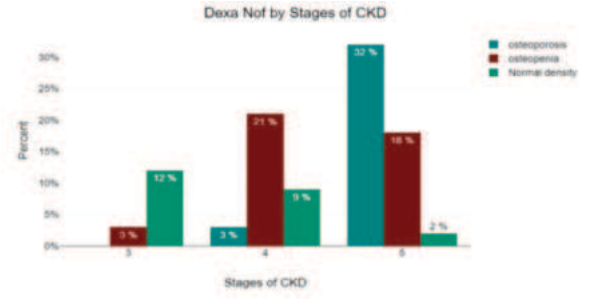

Figure-1

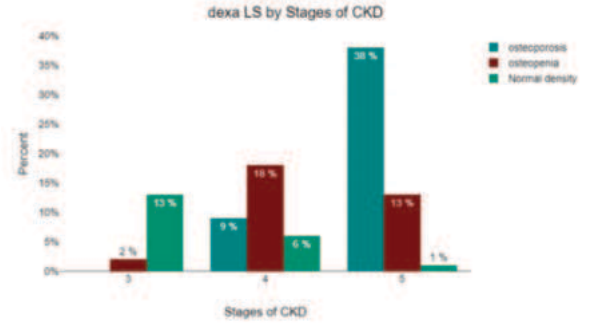

Figure -2

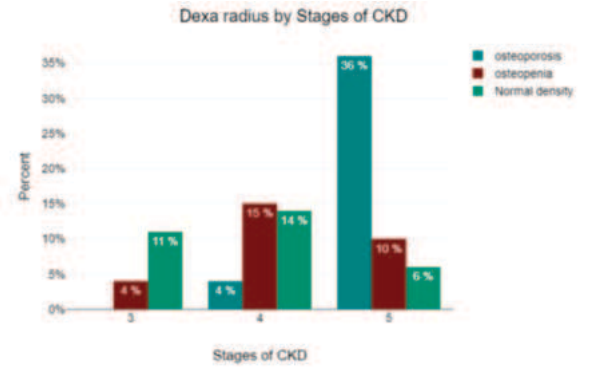

Figure- 4

Patient characteristics: Demographic characterstics has been shown in table:1. A total of 100 patients were included in this study. Mean age of the patients was Mean ± Std.55.76 ± 14.32 years. There was male predominance with 56 (56%) and 44 (44%) females. Most of patients 68 (68%) were from rural area and 32 (32%) were from urban area. Most common etiology for CKD among patients enrolled was Diabetics Mellitus 41 (41%), followed by Chronic Glomerulonephritis (CGN) and hypertension (HTN) 17 (17%), 14 (14%) respectively.

Biochemical Parameters

The distribution of the laboratory parameters in different stages of CKD has been compared with calcium and phosphorus, alkaline phosphatase (ALP) vitamin D and iPTH. On ANOVA and chi square test a significant difference was found of calcium, phosphorus, alkaline phosphatase, Vitamin D, serum iPTH in the various CKD stages (P = 0.001).

On comparison of biochemical profile among enrolled patients it was seen that 83% had calcium levels <8.5mg/dl and 17% had calcium levels between 8.5-10.5mg/dl. There were no patients who had calcium levels>10.5mg/dl. Similarly, Phosphorus levels in 76% patients were >4.5mg/dl and 2-4.5mg/dl in 26% patients. There were no patients who had phosphorus levels <2mg/dl. A total of 89% patients had ALP ≥120U/l and only 11% patients had ALP levels ≤120U/l.

A low proportion 14% of patients in various CKD stages had an adequate Vitamin D levels. Out of total 86% patients had inadequate 25OHD levels. The 25OHD levels were suggestive of vitamin D deficiency in 60% and Vitamin D insufficiency in 26% patients. There was a significant difference in the mean levels of 25OHD in the different CKD stages. Serum iPTH levels were <150pg/ml in 7% patients, 150-300pg/ml in 25% patients and >300pg/ml in 68% patient. The mean levels of iPTH in stages 3,4,5 were 165.87 ±66.77, 315.33±129.11 and 463.42±125.52 respectively. There was a significant difference in various stages of CKD and iPTH.

Tables -5 Comparison of laboratory parameters in different chronic kidney disease stages by one way ANOVA

On ANOVA, a significant difference was found in the mean values of, calcium, phosphorus, alkaline phosphatase, vitamin D, serum iPTH in the various CKD stages (P = 0.001).

When correlation of stages of CKD associated with bone mineral density observed using DEXA at neck of femur (NOF), it was observed that in stage 3, no patients had osteoporosis, 3 patients had osteopenia and 12 patients had normal BMD. Similarly in stage 4, 3 patients had osteoporosis and 21 patients had osteopenia and 9 had normal BMD. In stage 5, 32 patients had osteoporosis, 18 had osteopenia and 2 patients had normal BMD. Similarly, we have observed that BMD at lumbar spine (LS) it was seen that in stage 3, no patients had osteoporosis, 3 patients had osteopenia and 12 patients had normal BMD. Similarly in stage 4, 3 patients had osteoporosis and 21 patients had osteopenia and 9 had normal BMD. In stage 5, 35 patients had osteoporosis, 42 had osteopenia and 23 patients had normal BMD. When BMD observed at distal radius, it was seen that in stage 3, no patients had osteoporosis, 4 patients had osteopenia and 36 patients had normal BMD. Similarly in stage 4, 4 patients had osteoporosis and 15 patients had osteopenia and 10 had normal BMD. In stage 5, 40 patients had osteoporosis, 29 had osteopenia and 31 patients had normal BMD. The p-Value is <0.001 and there were a significant difference at NOF, LS and radius and different stages of CKD.

In our study, we have found that at NOF, in high turnover bone disease (iPTH≥300) 35 patients had osteoporosis, 31 patients had osteopenia and 2 patients had normal BMD. In low turnover bone disease 0 patients had osteoporosis, 1 patient had osteopenia and 6 had normal BMD. After statistical analysis, results were significant (p<0.0001).

At LS, in high turnover bone disease (iPTH≥300) 44 patients had osteoporosis, 20 patients had osteopenia and 4 patients had normal BMD. In low turnover bone disease 0 patient had osteoporosis, 2 patients had osteopenia and 5 had normal BMD. Results were showing statistical significant differenece with p<0.0001.

At radius, in high turnover bone disease (iPTH≥300) 38 patients had osteoporosis, 19 patients had osteopenia and 11 patients had normal BMD. In low turnover bone disease 0 patients had osteoporosis, 2 patients had osteopenia and 5 had normal BMD. After statistical analysis, results were significant (p<0.0001).

DISCUSSION

The mean age of the patients was 55.76 ± 14.32 years. There was a higher predominance of males compared to females [20] Most of the patients were from rural areas due to its geographical distribution. The most common etiology for CKD among the enrolled patients was Diabetes Mellitus, followed by Chronic Glomerulonephritis (CGN) and hypertension (HTN) respectively. This investigation, which involved patients across CKD Stage 3–5, revealed a notable prevalence of biochemical irregularities linked to CKD-MBD.[21]

In our study, 83% of the individuals showed calcium levels below 8.5 mg/dL, whereas 17% displayed levels ranging from 8.5 to 10.5 mg/dL. No patients had calcium levels surpassing 10.5 mg/dL. Similarly, phosphorus levels exceeded 4.5 mg/dL in 76% of patients and fell between 2 and 4.5 mg/dL in 26% of patients. None of the patients exhibited phosphorus levels below 2 mg/dL. Additionally, 89% of the patients had ALP levels exceeding 120 U/L, while only 11% had ALP levels below 120 U/L. Among the total patients, 86% had inadequate levels of 25OHD, with 60% indicating vitamin D deficiency and 26% showing vitamin D insufficiency. Significantly, there was considerable variation in the mean levels of 25OHD observed across different CKD stages. Within the patient cohort, serum intact parathyroid hormone (iPTH) levels were categorized as follows: below 150 pg/ml in 7% of patients, between 150-300 pg/ml in 25% of patients, and exceeding 300 pg/ml in 68% of patients. The mean iPTH levels exhibited variation across CKD stages, with values of 165.87 ± 66.77 in stage 3, 315.33 ± 129.11 in stage 4, and 463.42 ± 125.52 in stage 5. This observation underscores a notable difference in iPTH levels among the various stages of CKD. It is widely recognized that the primary cause of secondary hyperparathyroidism has been attributed to phosphate retention resulting from a decline in renal function. Moreover, the accumulation of phosphate leads to hyperphosphatemia, depletion of Vitamin D levels, and subsequent hypocalcemia. A similar study reported hypocalcemia, hyperphosphatemia, hyperparathyroidism, and hypovitaminosis D in 64.2%, 81.1%, 49.5%, and 89.5% of their patients, respectively.[22] Another study also demonstrated that secondary hyperparathyroidism, hyperphosphatemia, hypocalcemia, and vitamin D deficiency were prevalent among Indian CKD patients.[23]

DEXA is the predominant noninvasive method employed for assessing bone mineral content and evaluating bone mass. In 2017, the KDIGO Clinical Practice Guideline Update for Chronic Kidney Disease—Mineral and Bone Disorder Diagnosis, Evaluation, Prevention, and Treatment suggested employing DEXA for evaluating the risk of osteoporotic fractures in individuals with CKD in stages G3–G5D who exhibit risk factors for osteoporosis.[24]

In our investigation, utilizing DEXA scans at the Neck of Femur (NOF), we detected a rise in the severity of Mineral and Bone Disorder (MBD) alongside advancing stages of CKD. Comparable outcomes were identified at the Lumbar Spine (LS) and the distal end of the radius. Another research study observed diminished Bone Mineral Density (BMD) in the initial stages of CKD, as assessed by DEXA, with an escalating fracture risk that intensified with CKD advancement. There was an increased prevalence of osteoporosis with the progression of CKD.[20]

In the present study, the prevalence of osteoporosis was highest at the

LS, followed by NOF, and then the distal end of the radius. Our findings align with earlier studies, which similarly indicated a higher prevalence of osteoporosis in the LS region compared to the NOF region.[25,26]

When comparing high bone turnover and low bone turnover diseases, our study found a higher prevalence of osteoporosis and osteopenia in individuals with high bone turnover disease compared to those with low bone turnover disease. Elevated levels of PTH are known to have a catabolic effect on cortical bone. These biochemical changes may contribute to the deterioration of cortical architecture, leading to reduced cortical density and increased cortical porosity. 27

In our study, high bone turnover (iPTH>300 pg/dl) showed a significance difference at NOF, LS and radius. In patients with high PTH, the reduction of secondary hyperparathyroidism (SHPT) improved other biological parameters and the bone status. Another study discovered that the prevalence of MBD was greater in patients with SHPT (high bone turnover) compared to those with adynamic bone disease (low bone turnover), where MBD levels were closer to normal. These findings align closely with the observations made in our study.[28] Reduced BMD at the LS was found to be associated with both vertebral fractures and prevalent or self-reported peripheral fractures.[29]

Indeed, accounting for differences in baseline characteristics, multiple fractures, and/or events prompting discontinuation, oral cinacalcet efficiently reduced the rates of clinical fractures in elderly dialysis patients. These findings, considered together with the recent prospective study in CKD, and post hoc analyses of the pivotal fracture trials suggests that BMD may be clinically useful in assessing fracture risk in CKD. Clearly, our study confirms that low BMD is associated with osteoporosis and predicts fractures in CKD patients. Therefore, we recommend early screening, detection, and management of osteoporosis to reduce the burden of morbidity and mortality in this subset of patients

CONCLUSION

Despite the high prevalence of osteoporosis in people with CKD, to our knowledge, there is a lack of published research summarizing the prevalence estimates of osteoporosis in this population at the global level. However, these estimates serve as the basis for the development of preventative and management strategies, as well as providing useful data for health care planning decisions.

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