Section: Nephrology

Original Research Article

SPECTRUM OF MINERAL AND BONE DISEASE IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT

Background: Decline in kidney function causes progressive deterioration in mineral homeostasis leading to mineral bone disorder (MBD). The present study is an attempt to determine the prevalence and evaluate the different biochemical parameters of MBDs in different stages of chronic kidney disease (CKD).

Materials and Methods: This cross-sectional study was conducted on 150 CKD patients of all stages and sex. Patients were classified based on different parameters. Evaluated parameters include complete blood count, kidney and liver function tests, serum calcium and phosphate, intact parathyroid hormone (iPTH), alkaline phosphatase (ALP), Vitamin-D and Bone Mineral Density (BMD).

Results: Hypocalcemia (21.2%), hyperphosphatemia (54.5%) and hyperparathyroidism (87.9%) were found to be most common in stage 5 CKD. Serum iPTH was found to be elevated CKD stage 3 onwards while serum ALP was high in all stages of CKD. Vitamin D deficiency was seen across all stages of CKD. Hypocalcemia (78.37%) and vitamin D deficiency (74.7%) were more common in females. High iPTH was seen in 53.3% of males, 30.3% of females and 69.1% of non-diabetic patients. Osteoporosis was predominant in stage 5 CKD (86.67%) and females (45.16%).

Conclusion: CKD-MBD is very common among CKD patients in this part of India. Regular follow-up of CKD patients for any changes in CKD-MBD status is recommended.

Keywords: chronic kidney disease, mineral bone disorder, DEXA scan, iPTH.

INTRODUCTION

Chronic kidney disease (CKD) is a global public health problem affecting 5–10% of world population.[1] Kidney function declination causes progressive deterioration in mineral homeostasis and changes in circulating levels of hormones which are critically important in the regulation of bone formation, its structure and function resulting in bone abnormalities as found in most patients with CKD requiring dialysis (stage 5D), and in the patients with CKD stages 3–5.[2,3]

Chronic Kidney Disease-Mineral Bone Disorder (CKD-MBD) is characterized by the following: (i) Abnormal metabolism of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D (ii) Abnormalities in bone turnover, mineralization, volume linear growth or strength (iii) Soft-tissue calcifications, either vascular or extra-osseous.[4]

Many attempts have been made in the past to determine and define the mineral bone disorders (MBDs) in CKD and the pathophysiology causing this spectrum.[5] PTH, which is believed to be a key factor causing loss of bone mass have been traditionally measured by different biochemical methods with variable interpretation probabilities.[6,7] Several attempts have been made to address the issues regarding variability of results and interpretation of key biochemical parameters of MBDs in CKD.[8] Regarding the association between hyperparathyroidism and MBD in CKD, parathyroidectomy studies have shown beneficial results.[9] Similarly, normalization of PTH level and restoration of vitamin D with interventions have

proven to decrease cardiac events and death in CKD patients.[10]

The present study is an attempt to determine the prevalence of MBDs in different stages of CKD and to correlate the different biochemical parameters of MBDs in different sex and stages of CKD in this part of the world. A comparison of the biochemical parameters of MBDs amongst different etiologies causing CKD has also been done.

MATERIALS AND METHODS

This cross-sectional study was conducted on CKD patients of all stages irrespective of sex, in the Department of Nephrology, RIMS for the period of 2 years from 2021 to 2023.

Exclusion criteria include patients taking calcium supplement, phosphate binder, vitamin D or its active metabolites and analogues, calcimimetic agents, glucocorticoid, bisphosphonate, NSAIDs, phenytoin, or warfarin. Patients having rheumatologic diseases, liver disease or history of bone fracture in preceding 6 months were also excluded.

Patients were classified based on the stage of CKD, native aetiology of CKD, sex and age. All baseline routine investigations including CBC, KFT, LFT, Calcium, Phosphate, iPTH, ALP, Vitamin-D and Electrolytes were evaluated. iPTH and Vitamin D were measured by chemiluminescence using Vitros ECiQ equipment and Bone Mineral Density (BMD) was measured by DEXA scan.

Statistical Analysis

Systematic analysis was done using SPSS version 23. Various parameters of the whole group were analyzed and compared between the groups belonging to different stages of CKD. Non-parametric variables were compared using Chi-square test. Pearson correlation test was applied to find out correlation of the different parameters. P value of <0.05 was taken as significant.

RESULTS

One hundred fifty patients (male=76, female=74) were enrolled in the study with mean age of 55.8 ± 14.67 years. There were total of 33 males and 39 females in the higher stage of CKD (stage 4 and stage 5) [Figure 1]. Diabetes was found to be the most common etiology of CKD comprising 54% of the cases followed by hypertension (22.66%). Other causes were obstructive uropathy (10%), glomerular diseases (6.67%) and miscellaneous (6.67%) [Figure 2].

[Table 1] shows different biochemical parameters in the study population. Hypocalcemia was predominantly found in stage 4 and stage 5 CKD with highest occurrence in stage 5 CKD (21.2%). Hyperphosphatemia was found to be most common in stage 5 CKD, where 54.5% of the patients had hyperphosphatemia. Serum iPTH was found to be elevated from stage 3 onwards with maximum incidence in stage 5 CKD, where 87.9% of the patients had hyperparathyroidism. Serum alkaline phosphatase was found to be high in all the stages of CKD without any statistically significant difference.

[Table 2] shows Vitamin-D deficiency was found across various stages of CKD i.e. 75.0%, 85.7%, 92.3% and 84.8% cases in stage 3a, stage 3b, stage 4 and stage 5 patients respectively.

While comparing the gender differences, it was found that hypocalcemia and viamin-D deficiency was much more common in females than males (78.37 vs 25%; 74.7 vs 58.7%). There was no significant difference between males and females in terms of hyperphosphatemia (18.7 vs 25.3%). No significant difference was found between males and females in terms of alkaline phosphatase status with elevated ALP found in 76% and 70.7% of males and females respectively. iPTH was found elevated in 53.3% of the males and 30.3% of the females.

On comparing the variables between diabetics and non-diabetics, no significant difference in calcium, ALP and phosphorus status between the two groups were seen. High iPTH was found to be more common in non-diabetic patients with 69.1% of the cases having high iPTH level where diabetics (52.2%).

[Table 3] shows the relation between BMD and CKD stage. Osteoporosis was most commonly seen in the patients with stage 5 CKD where 86.67% of the cases were found to have a T score for LS spine below -2.5. The prevalence of osteopenia was highest in stage-4 CKD with 66.67% of cases. Osteoporosis was more common in females with 45.16% whereas it was 27.9% in males.

Table 1: Relation between serum calcium, phosphorus, iPTH and CKD stage (n=150)

Serum Calcium	CKD Stage						p- value
	1 n(%)	2 n(%)	3a n(%)	3b n(%)	4 n(%)	5 n(%)	
Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (12.8)	7 (21.2)	Value=13.2 p-0.215
Normal	11 (100.0)	33 (97.1)	12 (100.0)	21 (100.0)	32 (82.1)	26 (78.8)	
High	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	2 (5.1)	0 (0.0)	
Total	11 (100.0)	34 (100.0)	12 (100.0)	21 (100.0)	39 (100.0)	33 (100.0)	
Serum phosphorus	**CKD Stage**						**p- value**
	1 n(%)	**2 n(%)**	**3a n(%)**	**3b n(%)**	**4 n(%)**	**5 n(%)**	
Low	0 (0.0)	2 (5.9)	6 (50.0)	0 (0.0)	3 (7.7)	0 (0.0)	Value=62.9 p-<0.001
Normal	8 (72.7)	28 (82.3)	6 (50.0)	19 (90.5)	30 (76.9)	15 (45.5)	
High	3 (27.3)	4 (11.8)	0 (0.0)	2 (9.5)	6 (15.4)	33 (54.5)	
Total	11 (100.0)	34 (100.0)	12 (100.0)	21 (100.0)	39 (100.0)	33 (100.0)	
Serum iPTH	**CKD Stage**						**p- value**
	1 n(%)	**2 n(%)**	**3a n(%)**	**3b n(%)**	**4 n(%)**	**5 n(%)**	
Low	1 (9.1)	2 (5.9)	2 (16.7)	4 (19.0)	2 (5.1)	1 (3.0)	Value=28.2 p-0.002
Normal	10 (90.9)	32 (94.1)	7 (58.3)	4 (19.0)	15 (38.5)	3 (9.1)	
High	0 (0.0)	0 (0.0)	3 (25.0)	13 (62.0)	22 (56.4)	29 (87.9)	
Total	11 (100.0)	34 (100.0)	12 (100.0)	21 (100.0)	39 (100.0)	33 (100.0)	

Table 2: Relation between Serum Vitamin D and CKD stage (n=150)

Vitamin D	CKD Stage						Chi-square test p- value
	1 n(%)	2 n(%)	3a n(%)	3b n(%)	4 n(%)	5 n(%)	
Deficiency	3 (27.3)	19 (55.9)	9 (75.0)	18 (85.7)	36 (92.3)	28 (84.8)	Value=19.8 p-0.001
Not deficient	8 (72.7)	15 (44.1)	3 (25.0)	3 (14.3)	3 (7.7)	5 (15.2)	

Table 3: Relation between BMD status reflected by DEXA scan and CKD stage (n=150)

BMD status	Stage 1 n(%)	Stage 2 n(%)	Stage 3a n(%)	Stage 3b n(%)	Stage 4 n(%)	Stage5 n(%)
Normal	11 (91.67)	5 (100)	6 (100)	7 (70)	1 (8.33)	0 (0)
Osteopenia	1 (8.33)	0 (0)	0 (0)	2 (20)	3 (25)	2 (13.33)
Osteoporosis	0 (0)	0 (0)	0 (0)	1 (10)	8 (66.67)	13 (86.67)
Total	12	5	6	10	12	15

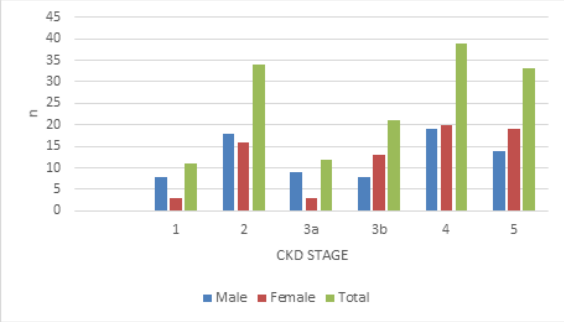

Figure 1: Sex distribution according to stages of CKD (n=150)

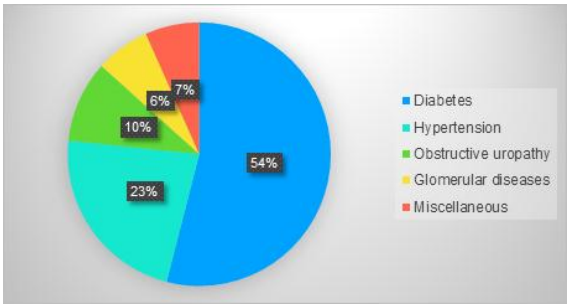

Figure 2: Number of cases according to etiology of CKD (n=150).

DISCUSSION

A total of 150 CKD patients were enrolled in this study with mean age of 51.8 ± 14.67 years which was comparable to other studies.[3,11-13] The male: female ratio was 1.03 in comparison to Valson et al. in Christian Medical College, Vellore, where the male to female ratio was 2.7:1. This may be due to the higher incidence of ESRD among male. This reflects a combination of physiological and socio-structural risk factors that modulate kidney disease and its progression.

Diabetes was the most common etiology of CKD comprising 54% of cases followed by hypertension (22.66%), obstructive uropathy (10%), glomerular diseases (6.67%) and miscellaneous causes (6.67%). Similar findings were seen in the study conducted by Valson et al. where diabetic nephropathy was found to be the most common etiology of CKD (52.2%), followed by hypertension (22%).[11]

Hypocalcemia was progressively seen in stage 4 and 5 CKD with highest prevalence in stage 5 CKD (21.2%) and predominantly affecting female patients (78.37%). This finding is consistent with the findings of previous studies.[11-14] Hypocalcemia may be because of hormonal changes which is common in females during this age group.

Hyperphosphatemia was most prevalent in stage 5 CKD (54.5%) which was similar to observations by Valson et al., Agarwal et al. and Valencia et al.[11,12,14] But the fact that hyperphosphatemia was found in all stages of CKD warrant its evaluation in all cases of CKD irrespective of stage.

Patients with stage CKD-3 onward had high prevalence of elevated iPTH level with highest prevalence in stage 5 CKD (87.9%) similar to other studies.[11-14] Serum iPTH was found elevated in 52.2% of diabetics as opposed to 69.1% in non-

diabetics suggesting high turnover disease to be more common in non-diabetics. We should conduct more studies with larger sample size to validate this finding. Serum ALP which serves as a crucial marker of bone resorption was found to be high across all the stages of CKD similar to Valencia et al.[14]

Deficiency of vitamin D was found in 85.7%, 92.3% and 84.8% of the patients in stage 3b, 4 and 5 of CKD respectively. The high prevalence of vitamin D deficiency across all the stages of CKD in this study was similar to the Indian population scenario.3 This explains the gradual loss of physiological function of kidney.

Serum calcium, phosphorus, ALP and Vitamin D level showed no statistically significant difference between diabetics and non-diabetics. Higher prevalence of hyperphosphatemia was seen in the non-diabetic group similar to Vavanikunnel et al.[15] This probably reflected the fact that diabetic patients are more prone to develop adynamic bone diasease.[16]

Amongst 150 patients, it was found that prevalence of hypocalcemia, hyperphosphatemia and vitamin D deficiency was higher in females compared to males. ALP level did not differ between males and females significantly.

BMD was analyzed using the T-score of lumbo-sacral spine using DEXA scan on 60 patients. As expected, Osteoporosis was more common in female patients and as the CKD stage advances. Osteopenia was also equally more common in females (16.13%) compared to males (10.35%). Males had more numbers of normal BMD findings than females, 62.06% vs 38.71%. Haseltine et al. have also mentioned that women were twice as commonly affected as men by osteoporosis which is consistent with the findings in our study.[17]

CONCLUSION

MBD is a common and important complication associated with CKD. High prevalence is seen in the CKD population of this topographical population as well. It is recommended that routine screening and management of the same should be included in the management plan of all diagnosed CKD patients.

The limitations of the study include small sample size from a single center and the exclusion of FGF-23 as a study parameter.

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