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SPECTRUM OF MINERAL BONE DISORDERS IN PATIENTS OF CKD AT TERTIARY CARE CENTRE OF UTTRAKHAND

Internal Medicine

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ABSTRACT

Introduction: Our bodies rely on two metabolic buffer systems, the kidneys, and bones, to maintain our internal environment. When one system is affected, it can have long-term effects on the other. Imbalances in minerals are increasingly important due to their correlation with cardiovascular disease and mortality. Chronic kidney disease (CKD) leads to mineral build-up in the kidneys, causing the parathyroid glands to overwork, resulting in mineral deposition in tissues. This compensatory response can lead to diseases when tissue function is affected. **Aim and Objectives:** Aim: To study the patterns of various mineral abnormalities in stage 3-5 CKD patients. **Objectives:** To evaluate the levels of S.CALCIUM, S.iPTH, S.ALKALINE PHOSPHATASE, SERUM PHOSPHOROUS, SERUM MAGNESIUM, and 25-Hydroxyvitamin D3 (25OHD) in CKD patients. **Materials and Methods**: This prospective observational study includes CKD patients in stage 3-5, aged over 18 years. Patients taking specific medications or with certain medical conditions are excluded. Data will be collected from 50 CKD patients, including demographic parameters, medical history, and various laboratory tests. Statistical analysis will be performed using SPSS Version 17 and Microsoft Excel 2010. **Results:** The baseline characteristics of the study population, including age and various mineral levels, are presented in Table 1. The study participants primarily had diabetes (46%) and hypertension (38%) as the etiology of CKD (Table 2). The majority of patients (74%) experienced symptoms related to CKD-MBD (Table 3). Various mineral levels were assessed, including S. calcium, iPTH, Vitamin D, magnesium, and phosphorus (Table 4). **Conclusion:** Hypocalcaemia is more common in early stages of CKD, while hyperphosphatemia is observed in all stages. Diabetes and hypertension are the main causes of CKD. High turnover bone disease is more prevalent than low turnover in CKD stages 3-5. Vascular calcification is also observed in CKD.

KEYWORDS

INTRODUCTION

Our bodies have two main metabolic buffer systems that help maintain our internal environment: the kidneys and bones. When one system is affected by pathology, it can have long-term effects on the other. Mineral imbalances are increasingly important due to their correlation with cardiovascular disease and mortality.

In chronic kidney disease (CKD), the glomerular filtration rate (GFR) declines, and minerals that need to be expelled are left behind. The parathyroid glands then overwork themselves to reduce the mineral burden on the kidneys by releasing calcium from bones and combining it with extra phosphate to produce adducts that deposit in tissues. However, this compensatory response can lead to disease when the deposition interferes with tissue function. Therefore, helping to reduce kidney mineral buildup is preferable to inhibiting the compensatory response.

CKD-MBD refers to metabolic and nutritional changes in CKD that affect mineral metabolism and bone health, leading to renal osteodystrophy, which contributes significantly to cardiovascular disease and mortality rates among CKD patients. Bone mineral density (BMD) is a well-established parameter used to monitor bone disease in CKD patients. However, other common factors, such as age, sex, and genetics, also affect BMD.(1)

While many circulating mineral mediators of CKD-MBD can be easily assessed, evaluating bone state requires more complicated techniques such as bone biopsy, which are not always available. Dual-energy X-ray absorptiometry (DEXA) is a practical method to evaluate bone mass and the risk of fractures. However, bone status is also influenced by dynamic processes, such as aberrant bone turnover and remodeling, which can lead to bone fragility and vascular calcification, contributing to cardiovascular disease and mortality.(2)

AIM AND OBJECTIVES:

AIM:

To study the patterns of various mineral abnormalities in stage 3-5 chronic kidney disease patients.

OBJECTIVES:

1)To evaluate S.Calcium, S.IPTH, S. Alkaline Phosphatase, Serum Phosphorous, Serum Magnesium and 25-Hydroxyvitamin D3(25OHD) indices in Chronic Kidney Disease patients.

MATERIALS AND METHODS

METHOD OLOGY

Study Design: This is a prospective observational study that aims to examine patients with chronic kidney disease (CKD) stage 3-5, who are over 18 years old. The inclusion criteria are patients with CKD stage 3-5, while patients taking calcimimetics, glucocorticoids, bisphosphonates, phenytoin, or warfarin, patients with primary parathyroid hormone (PTH) problems or rheumatologic diseases, patients with a history of bone fractures in the past six months, and patients with multiple myeloma will be excluded from the study.

Sampling: The study population will include all patients who present to the outpatient department or inpatient ward of SGRR&H DEHRADUN with clinical evidence of CKD-MBD. The sample size will be 50 subjects with CKD stage 3-5.

Study Procedure: All patients who are diagnosed with CKD-MBD based on clinical and laboratory evidence and present to the medicine OPD/ward will be recruited in the study. Using a data collection proforma, the demographic parameters, complete history and examination findings related to mineral bone diseases, detailed investigations such as serum creatinine, serum urea, serum calcium, serum phosphorous, serum magnesium, vitamin D levels, serum alkaline phosphatase levels, and serum iPTH levels in CKD-MBD patients, radiological investigation, etiology of kidney diseases, and medication history of CKD-MBD patients will be collected. An informed written consent from the patient and/or legal guardian will be obtained from all the patients included in the study.

Statistical Analysis: The information will be recorded in a pre-made study proforma. Frequency and percentage will be used to express qualitative data. Chi-Square test with Continuity Correction for all 2 X 2 tables and Fisher's exact test for all 2 X 2 tables will be used to analyze associations between qualitative variables. Mean, SD, and Median and IQR will be used to depict quantitative data. When comparing quantitative data from the two groups, an unpaired t-test

will be used if the data passed the "Normality test," and a Mann-Whitney test if it failed. The level of significance is defined as a p-value of 0.05 or less. Results will be graphically presented wherever needed, and SPSS Version 17 will be used for most analysis, and Microsoft Excel 2010 will be used for graphical representation.

Table 1 :baseline Characteristics Of Study Population (n=50)

	Age	Serum IPTH	Serum ALP	Serum Magnesium	25(OH) VIT D	serum phosphorous	serum creatinine	Hemoglobin	Corrected Calcium	eGFR
N	50	50	50	50	50	50	50	50	50	50
Mean	51.34	273.26	129.32	2.24	21.47	6.01	6.98	8.14	9.46	9.82
Std. Deviation	13.51	272.26	49.40	0.52	11.17	2.09	2.13	1.06	1.55	3.50

Table 2: Distribution Of Etiology Of Ckd In Study Participants (n=50)

	No. of cases	Percentage
DIABETIES	23	46.0%
HYPERTENSION	19	38.0%
OBSTRUCTIVE UROPATHY	5	10.0%
ADPKD	2	4.0%
TAKAYASU ARTIRITIS	1	2.0%

TABLE 2-Out of 50 patients 46% were diabetic, 38% were hypertensive, 10% had obstructive uropathy, 4% had ADPKD and 2% had Takayasu arteritis.

Table 3: Comparison Of Study Population Having Symptoms Or Not Having Symptoms

SYMPTOM	No. of cases	Percentage
N	13	26.0%
Y	37	74.0%
Total	50	100.0%

TABLE 3- Out of 50 patients 74% had symptoms whereas 26% had no symptoms.

Table 3: Aortic Knuckle Calcification:

		Aortic Knuckle Calcification				Total	Chi-square value	p-value
		NO	NO	YES	YES			
Diabetic	Non Diabetic	17	63.0%	10	43.5%	27	1.898	0.168
	Diabetic	10	37.0%	13	56.5%	23		
Total		27	100.0%	23	100.0%	50		

Difference in prevalence of aortic knuckle calcification in diabetic and non diabetic CKD is as follows:

The observed value of aortic knuckle calcification in non-diabetic and diabetic CKD stage 3-5 is 43% & 56.5 % respectively.

RESULTS

Table 1 summarizes the basic demographic factors of the population, which consisted of 50 CKD patients with a mean age of 51.33 +/- 13.51 years. Out of the 50 patients, 22 were female and 28 were male.

In table 4 Hypocalcaemia was observed in 64.7%, 25%, and 29.4% of patients in stages 3, 4, and 5 CKD, respectively. The overall observed value of hypoparathyroidism, normoparathyroidism & hyperparathyroidism in stage 3-5 CKD is 4%, 26% & 70% respectively. Vitamin D deficiency is seen in all the stages of CKD . Low magnesium levels are seen in early stages of CKD and as the CKD stage progresses hyperphosphatemia increases.

DISCUSSION

50 patients with CKD stage 3-5 were enrolled in our study. The CKD patients in our study have an average age of 51.3+/-13.5 years. The average age of the study population was similar across studies, at 50.5 years for Tapas R et al., 44 years for Agarwal SK et al., 46.2 years for Sakuja V et al., and 45.7 years for B. Ghosh et al. [3,4,5].

According to our study, 74% of participants had symptomatic CKD-MBD. The remaining 26% were symptom-free with regard to CKD-MBD. This demonstrates even more how subtle the clinical picture of MBD is in our situation. [6] A research by AT Valson et al. [7] found that 45% of patients had no symptoms associated with CKD-MBD, supporting the idea that the condition can be clinically silent.

In our study the etiology of CKD was diabetes mellitus (46% cases), hypertension (38% cases), obstructive uropathy in (10% cases) , ADPKD (4% cases) and Takayasu arteritis (2% cases) . Hypertension followed by diabetes mellitus is most frequently present co-morbidity. Majority of the patients developed hypertension as a sequale to CKD. In a study by *Ajay Singh et al* Diabetes and HTN were seen in 45.2% and 81.7% of patients respectively. The common etiology for kidney diseases in a study by *Ajay Singh et al* was diabetic kidney disease (39.7%),chronic glomerulonephritis (21.5%), hypertensive nephrosclerosis (15.0%), and chronic interstitial nephritis (11.83)%

According to our study, the prevalence of hypocalcaemia was 64.7%, 25%, and 29.4% in stages 3, 4, and 5, respectively.

Table 4: Showing frequency of S. calcium, iPTH, Vita D, Magnisum and Phosphorus.

		eGFR								
		Stage 3	Stage 3	Stage 4	Stage 4	Stage 5	Stage 5	Total	Chi-square value	P-value
S.Calcium Group	<8.4	11	64.7%	4	25.0%	5	29.4%	20	7.14	0.129
	8.4-10.2	5	29.4%	9	56.3%	8	47.1%	22		
	>10.2	1	5.9%	3	18.8%	4	23.5%	8		
Total Calcium group		17	100.0%	16	100.0%	17	100.0%	50		
SERUM IPTH GROUP	7.50-54	1	5.9%	3	18.1%	2	11.8%	6	1.294	0.524
	>54	166	94.1%	13	81.3%	15	88.2%	44		
Total SERUM IPTH GROUP		17	100.0%	16	100.0%	17	100.0%	50		
25(OH) Vit D group	<30	16	94.1%	13	81.3%	14	82.4%	43	1.418	0.492
	>30	1	5.9%	3	18.8%	3	17.6%	7		
Total 25(OH) Vit D group		17	100.0%	16	100.0%	17	100.0%	50		
S. Magnesium Group	<1.6	4	23.5%	0	0.0%	2	11.8%	6	4.355	0.360
	1.6-2.3	7	41.2%	9	56.3%	8	47.1%	24		
	>2.3	6	35.3%	7	43.8%	7	41.2%	20		
Total Magnisum group		17	100.0%	16	100.0%	17	100.0%	50		
S.Phosphorus group	<2.5	0	0.0%	0	0.0%	0	0.0%	0		0.811
	2.5-4.5	5	29.4%	4	25.0%	6	35.3%	15		
	>4.5	12	70.6%	12	75.0%	11	64.7%	35		
Total Phosphorus group		17	100.0%	16	100.0%	17	100.0%	50		

In stage 3-5 CKD, the prevalence of hypocalcemia, normocalcemia, and hypercalcemia is 40%, 44%, and 16%, respectively. Study by *Agarwal et al* revealed that 29.9% and 49.6% of hypocalcaemia is prevalent in stages 4 and 5. [8].

According to our study, the overall prevalence of hypoparathyroidism, normoparathyroidism, and hyperparathyroidism is 4%, 26%, and 70%, respectively, in stage 3-5 CKD. In a study by ***P Shankar et al***., the prevalence of hypoparathyroidism was found to be 6.02%, suggesting that low turnover bone disease may be present. In contrast, the prevalence of hyperparathyroidism, with a cutoff of iPTH >65 pg/ml, was found to be 65.06%.

Our study found elevated ALP in 41.2%,50% and 52.9% in CKD stage

3,4 and 5 respectively. ***Tapas Ranjan et al****[9]* found elevated ALP was present in 5.9% and 45.7% of patients of CKD stage 4 and 5, respectively.

The prevalence of hyperphosphatemia in stage 3, 4 & 5 CKD are 70%, 75% & 64.7% respectively. Our results are similar to other studies.

CONCLUSION

- Hypocalcaemia more common in early stages of CKD than advanced stages.
- Diabetes and hypertension main causes of CKD.
- Hyperphosphatemia observed in all stages of CKD.
- Low turnover bone disease less prevalent than high turnover in CKD 3-5.
- Vascular calcification observed in CKD 3-5 with severe mineral derangement.

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