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STUDY OF BONE MINERAL DISORDERS IN CHRONIC KIDNEY PATIENTS

Nephrology

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ABSTRACT

Chronic Kidney Disease (CKD) often leads to mineral and bone disorders, manifesting as disturbances in calcium, phosphorus, parathyroid hormone (PTH), and alkaline phosphatase (ALP) levels. This study aimed to evaluate these biochemical markers in CKD patients across different stages and their interrelationships. A total of 108 CKD patients (72% male, 28% female) were analyzed, with the majority in stage 5 (63%). Biochemical analysis revealed a significant decrease in serum calcium levels and an increase in serum phosphorus and ALP levels as CKD progressed. Specifically, serum calcium decreased from 8.91 ± 1.88 mg/dL in stages 1-3 to 7.68 ± 1.22 mg/dL in stage 5, while serum phosphorus increased from 4.97 ± 1.71 mg/dL in stages 1-3 to 6.81 ± 2.95 mg/dL in stage 5. PTH levels rose significantly with advancing CKD stages. Notably, a significant negative correlation was found between serum calcium and PTH levels, while ALP showed a positive correlation with PTH. These findings underscore the importance of monitoring mineral and bone metabolism in CKD patients to manage and potentially mitigate associated complications.

KEYWORDS

Calcium, Phosphorus, Parathyroid Hormone (PTH), Alkaline Phosphatase (ALP)

INTRODUCTION

Disturbances of mineral and bone metabolism has become a major challenge to clinical nephrologists. Maintenance of calcium and phosphorous balance in the respectable range has led to the use of several new therapeutic options including Vitamin-D analogues and calci-mimetics. Prevention of bone disease in chronic kidney disease needs proper evaluation of mineral metabolism.

The presence of renal bone disease in patients with chronic renal failure has been known for years. The skeletal changes associated with chronic renal failure were described even before 1855. Virchow in 1855[1] described the skeletal changes that he noticed in his study of chronic renal failure patients.

Apart from its intrinsic clinical interest, renal osteodystrophy provides an opportunity to review various matters viz., (1) mineral deficiencies in man. (2) the sites and mode of action of Vitamin-D, (3) relation between crystal nucleation in bone and ionic concentrations of Calcium and Phosphorus in plasma, (4) Control of parathyroid activity and secretion.

The study of skeletal changes in renal diseases has been and continued to be neglected even though it is an interesting topic for clinical research. It was Liu and Chu (1943) [2]who coined the term "Renal osteodystrophy" to include all the bony diseases observed during the course of the renal disease. It is the excellent study of Stanbury (1957) [3] and later by Dent (1961) [4]which drew the attention of many and focused a new light on the subject.

Stanbury (1957) [3] putting forth the various proposed mechanisms of derangements in calcium metabolism, acquired vitamin-D resistance and parathyroid hyperfunction, discussed the causation of different skeletal changes occurring in chronic renal failure. Dent et al. (1961) [5] studied 14 cases of renal insufficiency to establish the theory of renal osteo-dystrophy. But, their study became inconclusive as it did not correlate the clinical features, the bio-chemical findings and the radiological changes they noticed in their study. Key et al (1969) [6]are of the opinion that the radiological criteria showed 25- 50% of the bony lesions even though clinically evident symptomatic bone disease were as less as 10%.

The Term Renal Osteo-dystrophy Is Used To Include,

(a) Osteitis fibrosa high bone turnover (a reflection of secondary hyperparathyroidism).

(b) Osteomalacia aluminium toxicity, low bone turnover, often but not always related to

(c) Adynamic bone disease (ABD) - low bone turnover. In children, rickets may be observed.

(d) Osteosclerosis is less common.

Stanbury (1957) [3] stated that more than one type of bone lesion in a given uremic patient is not uncommon, supported later by Pollock (1959)[7], Dent et al. (1961) [4] and Rizvi et al. (1974) .[8]

Chronic kidney disease - Mineral Bone disorder (CKD-MBD) is the term used to determine the patho-physiological changes that occur in the vascular and skeletal system in association with CKD. These changes can be diagnosed if a patient has evidence of one or more of the following-

1. Abnormalities of calcium, phosphorus, PTH or vitamin D metabolism.
2. Vascular and/or tissue calcification.
3. Abnormalities of bone turnover, metabolism, volume, linear growth or strength.

Kidney Disease Improving Global Outcome (KDIGO) CKD MBD guidelines have recommended monitoring serum calcium, phosphorus, PTH and alkaline phosphatase activity in CKD stage 3[9]

We studied abnormalities of calcium, phosphorus, PTH and alkaline phosphatase in CKD patients to evaluate CKD - MBD.

There are few studies available in Indian population from north Agrawal et al, (2005) [10]and in south India by Dr. Mani (2005)[11].

There are no published studies available in the region of Marathwada. There is regional difference in diet, exposure to sun; hence we have undertaken this study to find out mineral metabolism in chronic kidney disease patients in this region.

OBSERVATIONS

Table 1: Distribution Of Patients According To Gender

Sex	No. of patients	Percentage
Male	78	72%
Female	30	28%
Total	108	100%

In present study, 78(72%) patients were male and 30 (28%) were females; this suggests there was male preponderance with a male to

female ratio of 12:5.

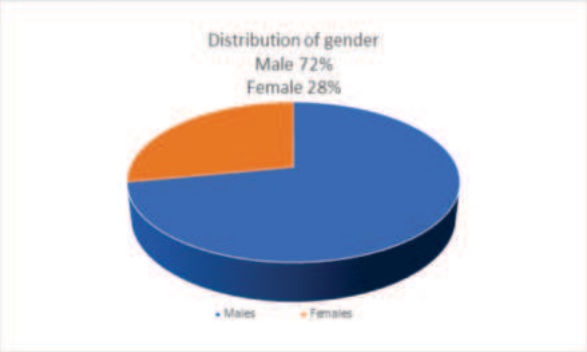
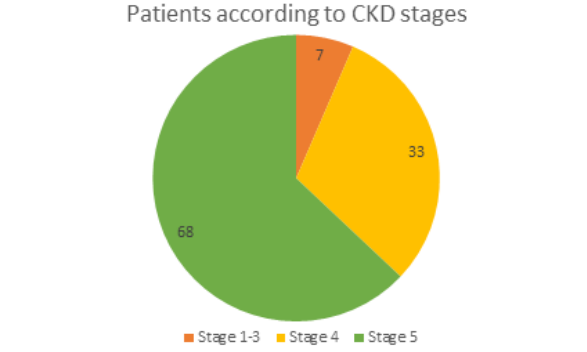


Table 2: Distribution Of Patients According To Stage Of CKD

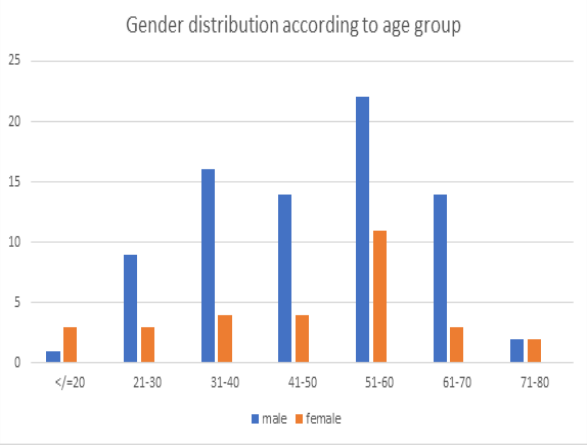
CKD Stage	GFR (ml/min)	No. of patients	Percentage
Stage 1-3	>29	07	06%
Stage 4	15-30	33	31%
Stage 5	<15	68	63%
Total		108	100%



It is observed that there are 68(63%) patients in stage 5, 33(31%) in stage 4 and 07(06%) in stages 1-3. Majority of patients are in CKD stage 5.

Table 3: Age And Gender Distribution

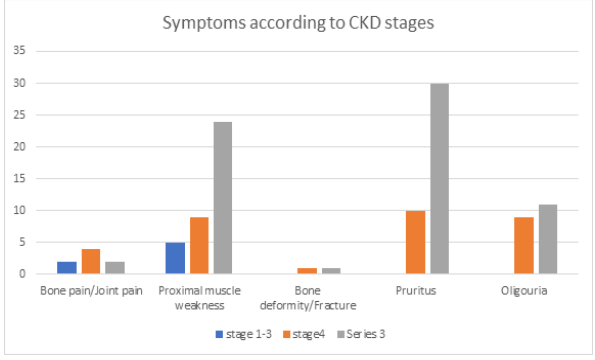
Age in years	Male NO. of patients	Female NO. of patients	Total NO. of patients	Percentage
< or =20	01	03	04	03%
21-30	09	03	12	11%
31-40	16	04	20	19%
41-50	14	04	18	17%
51-60	22	11	33	31%
61-70	14	03	17	16%
71-80	02	02	04	03%
Total	78	30	108	100%
Mean+/- SD	48.72+/-14.55	48.1+/-17.46	48.55+/-15.33	48.55+/-15.33



In this study, majority number of patients belonged to age group between 51-60 years (31%).

Table 4: Distribution Of Symptoms In CKD Stages

Symptoms	Stage 1-3	Stage 4	Stage 5	Total
Pruritus	0	10	30	40
Proximal muscle weakness	05	09	24	38
Oligouria	0	09	11	20
Body pain/joint pain	02	04	02	08
Bone deformity/Fracture	0	01	01	02
Total	07	33	68	108

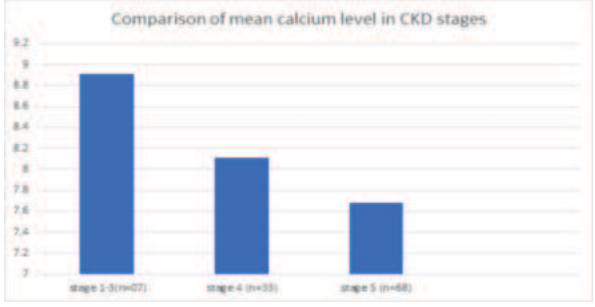


Pruritus was the most common symptom seen in 40(37%) patients followed by proximal muscle weakness seen in 38(35%) patients, whereas oligouria was seen in 20 (20%) patients which was statistically significant.

Table 5: Comparison Of Serum Calcium Level According To CKD Stages 1-5: (ANOVA)

Stages	N	Mean+/-SD	F-value	P-value
Stage 1-3	07	8.91+/-1.88	3.97	P=0.046 S
Stage 4	33	8.11+/-1.12	3.97	P=0.046 S
Stage 5	68	7.68+/-1.22	3.97	P=0.046 S
overall	108	7.90+/-0.95	3.97	P=0.046 S

(p<0.05 Significant)

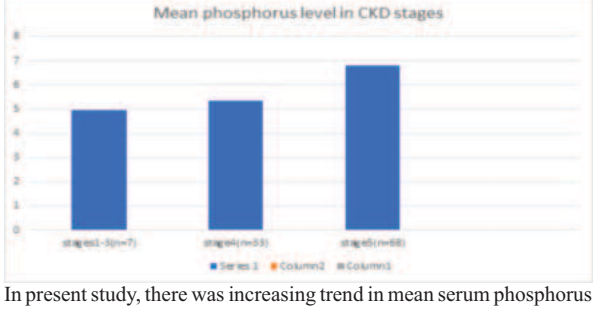


The mean serum calcium level was low in stage 5 as compared to stage 1-3, which is statistically significant with P value (P=0.046).

Table 6: Comparison Of Serum Phosphorus Level According To CKD stages 1-5: (ANOVA)

Stages	N	Mean+/-SD	F-value	P-value
Stages1-3	07	4.97+/-1.71	4.32	P= 0.016 S
Stage4	33	5.34+/-1.98	4.32	P= 0.016 S
Stage5	68	6.81+/-2.95	4.32	P= 0.016 S
overall	108	6.21+/-2.69		

(p<0.05 Significant)

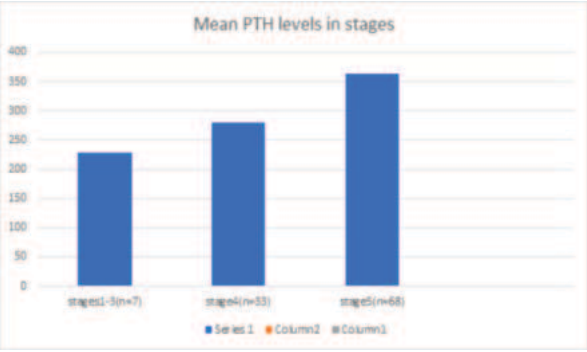


In present study, there was increasing trend in mean serum phosphorus level. In CKD stage 5, serum phosphorus level was more as compared to stage1-3 with P value of 0.016 which is statistically significant.

Table 7: Comparison Of PTH Level According To CKD Stages: (ANOVA)

Stages	N	Mean+/-SD	F-value	P-value
Stages1-3	07	227.73+/-50.98	7.05	P=0.001 S
Stage4	33	279.12+/-125.52		
Stage5	68	363.15+/-121.99		
overall	108	328.46+/-126.33		

(p<0.05 Significant)

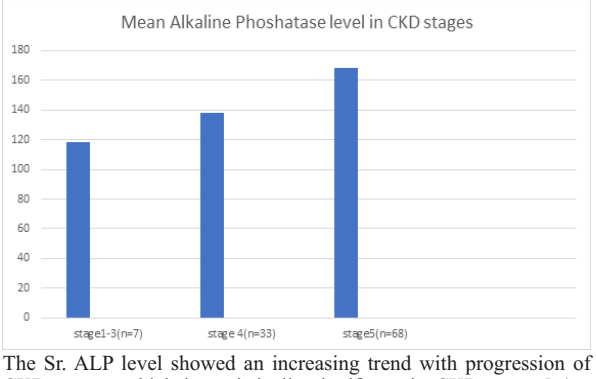


In present study, there is an increasing trend in serum PTH levels with progression of CKD stages, which is statistically significant (p=0.001).

Table 8: Comparison Of Alkaline Phosphatase Level (ALP) According To CKD Stages1-5 (ANOVA)

Stages	N	Mean+/-SD	F-value	P-value
Stages1-3	07	118.06+/-47.88	3.29	P=0.038S
Stage4	33	138.14+/-45.30		
Stage5	68	168.22+/-57.34		
overall	108	157.08+/-52.47		

(p<0.05 Significant)

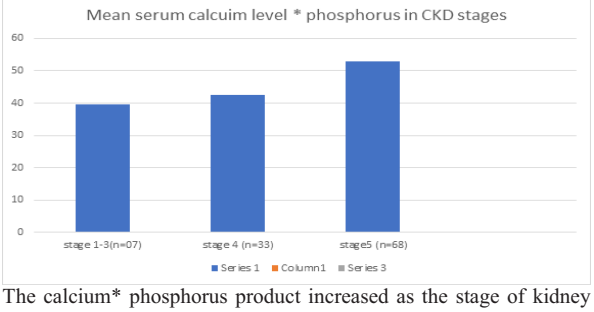


The Sr. ALP level showed an increasing trend with progression of CKD stages, which is statistically significant in CKD stage 5 (p= 0.038).

Table 9: Comparison Of Serum Calcium * Phosphorus According To CKD stages 1-5 (ANOVA)

Stages	N	Mean+/-SD	F-value	P-value
Stages1-3	07	39.56+/-14.23	3.83	P= 0.025 S
Stage4	33	42.54+/-13.23		
Stage5	68	52.99+/-23.04		
overall	108	48.93+/-20.61		

(p<0.05 Significant)

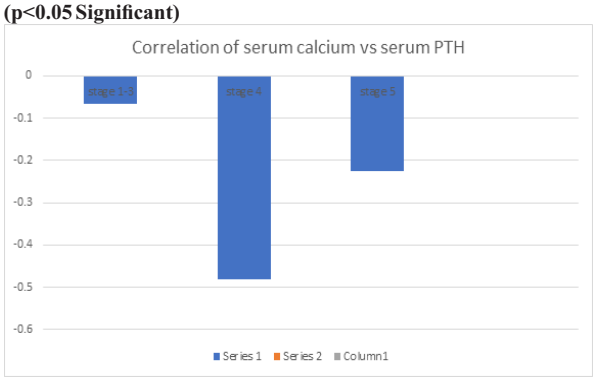


The calcium* phosphorus product increased as the stage of kidney disease progressed. The increasing trend was significant between CKD stage5 and CKD stage 1-3, which is statistically significant (p=0.025).

Table 10: Correlation Between Serum Calcium Level And PTH According To CKD Stages

CKD stage	Sr. Ca	Sr. PTH	r value	P value
Stages1-3	8.91+/-1.88	227.73+/-50.98	-0.065	0.890 NS
Stage 4	8.11+/-1.12	279.12+/-125.52	-0.481	0.005 S
Stage 5	7.68+/-1.22	363.15+/-121.91	-0.226	0.048 S
overall	7.90+/-0.95	328.46+/-126.33	328.46+/-126.33	

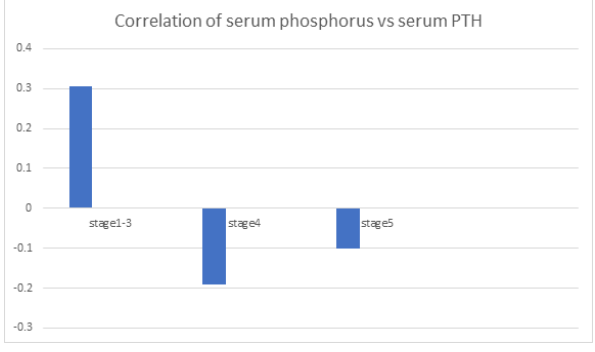
(p<0.05 Significant)



The present study shows sigmificant negative correlation between serum calcium and serum PTH in stage 4 and CKD stage 5 as compared to CKD stage 3 with P value 0.048.

Table 11: Correlation Between Serum Phosphorus Level And PTH According To CKD stages

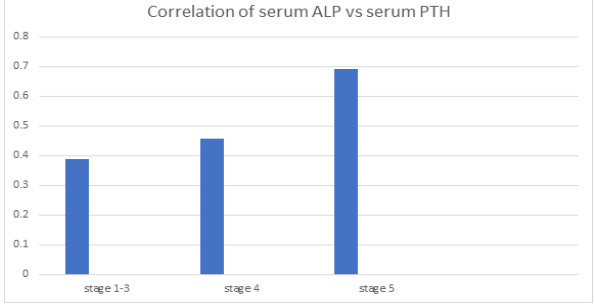
CKD stage	Sr. Ca	Sr. PTH	r value	P value
Stages1-3	4.97+/-1.71	227.73+/-50.98	0.307	0.504 NS
Stage 4	5.34+/-1.98	279.12+/-125.52	-0.190	0.101 NS
Stage 5	6.81+/-2.95	363.15+/-121.99	-0.10	0.634 NS
overall	6.21+/-2.69	328.46+/-126.33		



The present study shows no significant correlation between Serum phosphorus and serum PTH in all stages of CKD.

Table 12: Correlation Between Serum Alkaline Phosphatase Level And PTH According To CKD Stages

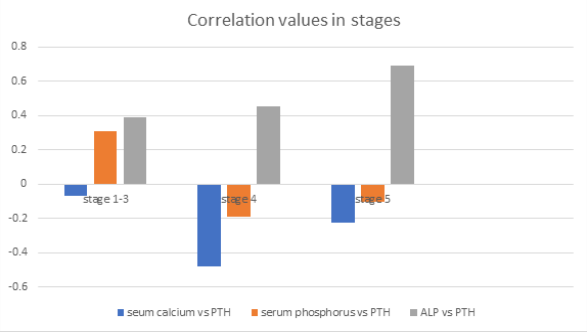
CKD stage	Sr. Ca	Sr. PTH	r value	P value
Stages1-3	118.06+/-47.88	227.73+/-50.98	0.389	0.437 NS
Stage 4	138.14+/-45.30	279.12+/-152.52	0.456	0.008 NS
Stage 5	168.22+/-57.34	363.15+/-121.99	0.691	0.047 NS
overall	157.08+/-52.47	328.46+/-126.33		



In present study shows positive correlation between serum ALP with serum PTH with statistically significant p value (p= 0.047) with increasing trend in all CKD stages.

Table 13: Correlation Between Serum Calcium Level, Serum Phosphorus Level And Alkaline Phosphatase (ALP) Levels With PTH According To CKD Stages

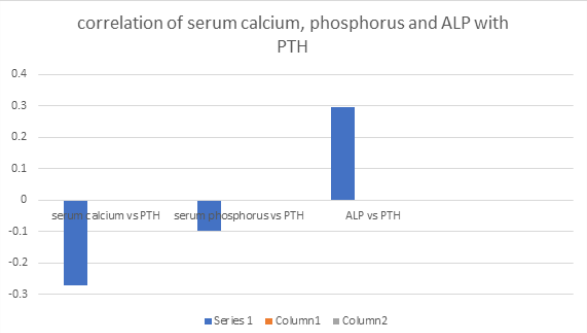
correlation	Stage1-3		Stage4		Stage 5	
	r-value	p-value	r-value	p-value	r-value	p-value
Serum calcium vs PTH	-0.065	P= 0.890 NS	-0.481	P= 0.005 NS	-0.226	P= 0.048 NS
Serum phosphorus level vs PTH	0.307	P= 0.504 NS	-0.190	P= 0.101 NS	-0.10	P= 0.634 NS
Alkaline phosphatase level (ALP) vs PTH	0.389	P= 0.437 NS	0.456	P=0.008 NS	0.691	P=0.047 NS



In CKD stage 1-3 there is negative significant correlation between serum calcium and serum PTH, while its significantly negative correlated between CKD stage 4 and CKD stage 5. Serum ALP is positively correlated with PTH in all CKD stages with increasing trend, while there is no significant correlation between serum phosphorus and serum PTH.

Table 14: Correlation Between Serum Calcium Level, Serum Phosphorus Level And Alkaline Phosphatase Level (ALP) with PTH

Correlation	r-value	p-value
Serum calcium level vs PTHs	-0.271	P=0.004S
Serum phosphorus level vs PTH	-0.098	P=0.311S
Alkaline phosphatase level vs PTH	0.295	P=0.002S



The present study shows a negative correlation of serum calcium, serum phosphorus and alkaline phosphatase. There is significant negative correlation between serum calcium and serum PTH with significant p-value (p=0.004) and with serum ALP and serum PTH with p value (p=0.002), while correlation of serum phosphorus and serum PTH is not significant.

CONCLUSION

This study highlights the progressive changes in mineral metabolism and bone health in CKD patients. As CKD advances, disturbances in calcium and phosphorus metabolism, along with increasing PTH and ALP levels, are evident. Monitoring these parameters is essential for managing CKD and preventing complications such as renal osteodystrophy. Further research with larger and more diverse populations is needed to validate these findings and explore regional variations in mineral metabolism.

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