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Research article

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### Study the levels of specific biochemical markers and correlating the radiological findings in chronic kidney disease patients

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#### ABSTRACT

##### AIM

To study the changes in serum calcium, serum phosphorus, serum PTH levels and vitamin D levels in chronic renal failure patients. Study the bone changes on X-ray in cases of chronic renal failure. Find out the prevalence and nature of skeletal involvement in chronic renal failure and to associate the severity of skeletal involvement with the duration of chronic renal failure. Associate the biochemical profile changes and bone changes on x-rays and find their significance.

##### MATERIALS

50 Stage III chronic kidney disease patients who are under conservative management as well as Dialysis, meeting the Inclusion and Exclusion criteria are selected. Patients who are getting admitted as well as attending outpatient department in Rajah Muthiah Medical College & hospital. Patients with chronic kidney disease of stage 3 and above. Patients on both conservative management & on dialysis. Both male & female patients. Patients presenting with acute kidney injury. (serum creatinine rises by  $\geq 26\mu\text{mol/L}$  within 48 hours). No previous calcium, phosphate binder, vitamin D supplementation. Not more than 5 years on dialysis. Age  $>65$  years.

##### METHODOLOGY

50 patients of previously diagnosed chronic kidney disease of stage 3, stage 4 and stage 5 and patients on chronic dialysis who are meeting the inclusion and exclusion criteria are selected. Necessary investigations are performed and the proforma is filled with the values for each patient.

##### CONCLUSION

Out of 50 CKD patients, 35 (70%) patients had x-ray changes depicting skeletal abnormalities. Low calcium levels were found in majority of patients. High Phosphorous levels were found predominantly. High Parathyroid hormone levels were found predominantly. Low Vitamin D levels were found in majority of cases.

**KEY WORDS:** Chronic Kidney disease, Parathyroid hormone, Vitamin D, Serum Calcium, Serum Phosphorous.

#### INTRODUCTION

The presence of mineral 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<sup>1</sup> 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<sup>(1943)2</sup> 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)<sup>3</sup> and Later by Dent (1961)<sup>4</sup> which drew the attention of many and focused a new light on the subject. Stanbury (1957). 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) studied 14 cases of renal glomerular insufficiency to establish the theory of renal osteodystrophy. 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<sup>(1969)6</sup> 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 osteodystrophy is used to include two varieties of bone diseases.

- (a) Osteitis fibrosa - high bone turnover (a reflection of secondary hyperparathyroidism),
- (b) Osteomalacia - low bone turnover, often but not always related to aluminium toxicity.

## AIM

To study the levels of Serum Calcium, Serum Phosphorous, Serum Parathyroid Hormone and Vitamin D in Chronic Kidney disease patients and correlating the radiological findings of skeletal abnormalities.

## METHODOLOGY

### MATERIALS AND METHODS

#### STUDY POPULATION

50 Stage III chronic kidney disease patients who are under conservative management as well as Dialysis, meeting the Inclusion and Exclusion criteria are selected.

#### STUDY PLACE

Patients who are admitted as well as attending outpatient department in Rajah Muthiah Medical

College & hospital.

### PERIOD OF STUDY

September 2012 to October 2015

### INCLUSION CRITERIA

1. Patients with chronic kidney disease of stage 3 and above.
2. Patients on both conservative management & on dialysis
3. Both male & female patients.

### EXCLUSION CRITERIA

1. Patients presenting with acute kidney injury. (serum creatinine rises by  $\geq 26\mu\text{mol/L}$  within 48 hours)
2. No previous calcium, phosphate binder, vitamin D supplementation.
3. Not more than 5 years on dialysis.
4. Age > 65 years.

## METHODS

50 patients of previously diagnosed chronic kidney disease of stage 3, stage 4 and stage 5 and patients on chronic dialysis who are meeting the inclusion and exclusion criteria are selected. Necessary investigations are performed and the proforma is filled with the values for each patient. Purpose of the study will be carefully explained to the patients and consent will be taken. Institutional Ethical Committee Clearance will be taken. CKD is being diagnosed with following GFR values.

STAGE 3 – GFR 30 – 59 mL/min/1.73m<sup>2</sup>

STAGE 4 – GFR 15 – 29 mL/min/1.73m<sup>2</sup>

STAGE 5D – GFR < 15 mL/min/1.73m<sup>2</sup>

GFR is being calculated with the Cockcroft-Gault equation

$$\text{GFR} = \frac{(140 - \text{age}) \times \text{body weight (kg)}}{72 \times \text{Sr. Creatinine (mg/dL)}}$$

(Multiply by 0.85 for women)

X-rays of hand, wrist, skull, chest, pelvis and spine are taken. The changes of Osteitis Fibrosa and Osteomalacia are recorded. Radiologists opinion are obtained to confirm the x-ray changes and are confirmed with the findings. Sr. calcium, Sr. Phosphorous, Vitmain D levels and Sr. Parathyroid hormone levels are estimated. X-ray changes are correlated with every biochemical value. Findings are tabulated and their statistical significances are estimated using Chi -Square Tests. The association between X-ray changes and biochemical values are analyzed and discussed. Conclusion is written based upon the findings.

## RESULTS

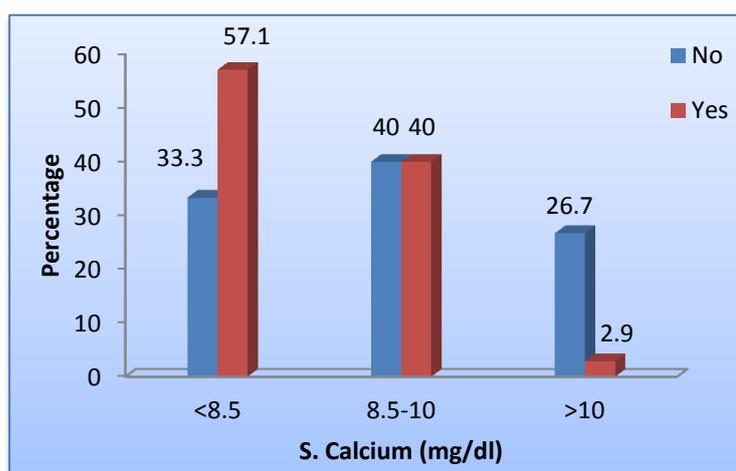
The following results were obtained with correlation:

- Among 35 patients who had bone changes, 20 (57.1%) patients had calcium levels less than 8.5 mg/dl, which was found to be statistically significant.
- Among 35 patients who had bone changes, 30 (85.7%) patients had vitamin D levels of <20, which was found to be statistically significant.
- Among 35 patients who had bone changes, 19 (54.3%) patients had Sr. Parathyroid hormone levels of more than 70, which were found to be statistically significant.
- Among 35 patients who had bone changes, 19 (54.3%) patients had bone changes with phosphorous levels between 2.5 – 4.5 mg/dl and 16 (45.7%) patients had levels more than 4.5 mg/dl, which was statistically found to be significant.

### SR. CALCIUM LEVELS

S. Calcium (mg/dl)	Bone changes				Total	
	No		Yes			
	No.	%	No.	%	No.	%
<8.5	5	33.3	20	57.1	25	50.0
8.5-10	6	40.0	14	40.0	20	40.0
>10	4	26.7	1	2.9	5	10.0
Total	15	100.0	35	100.0	50	100.0

P value 0.028

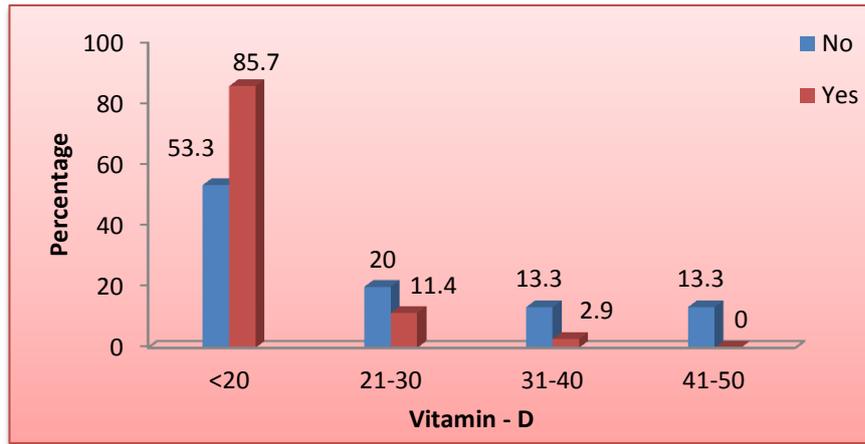


Among 35 patients who had bone changes, 20 (57.1%) patients had calcium levels less than 8.5 mg/dl, which was found to be statistically significant

### VITAMIN D LEVELS

Vitamin - D	Bone changes				Total	
	No		Yes			
	No.	%	No.	%	No.	%
<20	8	53.3	30	85.7	38	76.0
21-30	3	20.0	4	11.4	7	14.0
31-40	2	13.3	1	2.9	3	6.0
41-50	2	13.3	0	.0	2	4.0
Total	15	100.0	35	100.0	50	100.0

-P value 0.035

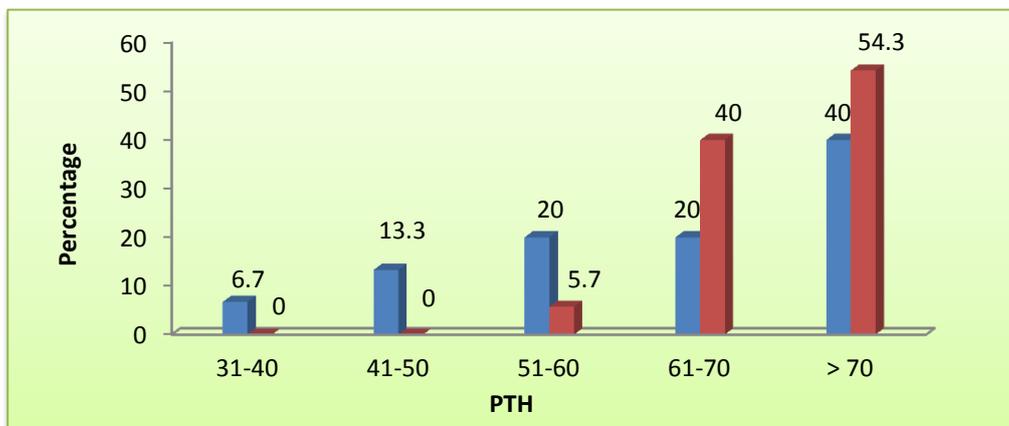


Among 35 patients who had bone changes, 30 was found to be statistically significant. (85.7%) patients had vitamin D levels of <20, which

**Sr. PARATHYROID HORMONE LEVELS**

	<u>PTH</u>		<u>Bone changes</u>		<u>Total</u>	
	No		Yes			
	No.	%	No.	%	No.	%
31-40	1	6.7	0	.0	1	2.0
41-50	2	13.3	0	.0	2	4.0
51-60	3	20.0	2	5.7	5	10.0
61-70	3	20.0	14	40.0	17	34.0
> 70	6	40.0	19	54.3	25	50.0
Total	15	100.0	35	100.0	50	100.0

-P value 0.029

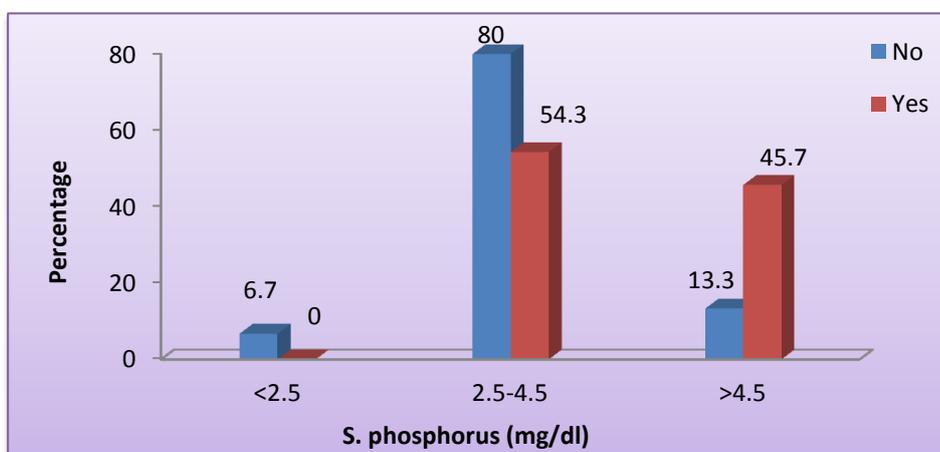


Among 35 patients who had bone changes, 19 of more than 70, which was found to be statistically significant. (54.3%) patients had Sr. Parathyroid hormone levels

**Sr. PHOSPHOROUS LEVELS**

S. phosphorus (mg/dl)	Bone changes				Total	
	No		Yes			
	No.	%	No.	%	No.	%
<2.5	1	6.7	0	.0	1	2.0
2.5-4.5	12	80.0	19	54.3	31	62.0
>4.5	2	13.3	16	45.7	18	36.0
Total	15	100.0	35	100.0	50	100.0

P value 0.039



Among 35 patients who had bone changes, 19 (54.3%) patients had bone changes with phosphorous levels between 2.5 – 4.5 mg/dl and 16 (45.7%) patients had levels more than 4.5 mg/dl, which was statistically found to be significant.

**DISCUSSION**

Chronic kidney disease has become a very common and progressive disease in the current scenario throughout the world. Due to various etiology, patients develop CKD and end up in End Stage Renal Disease and get dependent upon chronic dialysis or renal transplant. Chronic kidney disease has been known to be causing skeletal abnormalities due to alterations in the various biochemical process. Skeletal abnormalities have also been observed as a complication of chronic dialysis. The present study included patients of chronic kidney disease of Stage III, Stage IV and Stage V and

patients who were on dialysis. Biochemical values have been studied and associated with the skeletal abnormalities among them. X- ray changes with the help of radiologists, were confirmed of skeletal abnormalities. Patients showed X-ray changes as increased haziness or coarsening of trabecular and biconcavity of vertebral bodies with normal bone density ‘Cod Fish spine’, Bending deformities of long bones, Looser’s Lines or Pseudo fractures, Straight wide bands of radio lucency perpendicular to long axis of bone, Narrow area of sclerosis or small poorly mineralized callus, Medullary Trabeculae eroded, cortices narrowed, Sub – periosteal resorption of neck of humerus, ischium, pubis, Resorption in skull, Mottled luscent appearance, Patchy osteosclerosis ‘Rugger Jersey Appearance’ on lateral view of vertebrae, Salt and Pepper Appearance of Skull, Ground Glass appearance at vascular grooves.



Figure:1 Plain X-ray of hand AP view showing subperiosteal resorption of the phalange



Figure: 2 Plain X-ray of left hand AP view showing diffuse decrease in bone density with coarsening of trabecular pattern and tufting of the terminal phalanges indicating mixed osteomalacia – secondary hyperparathyroidism.

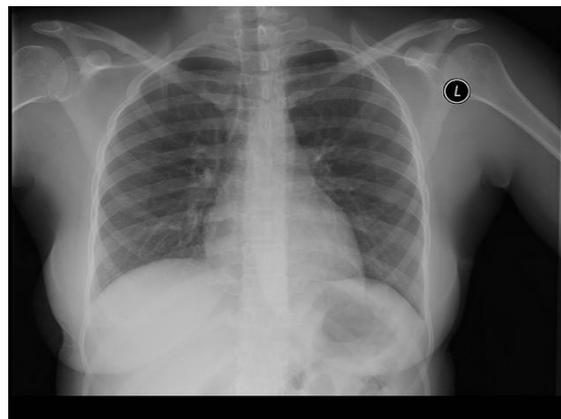


Figure 3: Chest X-ray PA view with Diabetic nephropathy who was on regular twice weekly hemodialysis since 1 year and 7 months. His creatinine clearance was just 4.9 ml/min. This X-

ray shows diffuse rarefaction with coarsening of trabecular pattern of the ribs (especially the lower ribs) and medial ends of both clavicles (right more than left). Also note the characteristic erosion and

sub-periosteal neostosis of medial and lateral ends of left clavicle, classical of mixed osteomalacia - osteitis fibrosis. In the present study, among 50

patients of CKD, 35 (70%) patients had bone changes in X-Ray and 15 (30%) patients did not have X-ray changes. Comparison with other studies

#### Comparison of X-Ray changes with other studies

X-ray changes	Rizvi et al.	Batila et al.	Meena et al.	Gupta et al.	Sahoo et al.	Present et al.
Number of cases	67	50	32	40	100	50
No bone changes on X-ray	19 (28.36%)	14 (28%)	17 (53.12%)	12 (30%)	60 (60%)	15 (30%)
Abnormal X-ray	48 (71.64%)	36 (72%)	15 (46.88%)	28 (70%)	40 (40%)	35 (70%)

In the present among the 35 patients who had X-ray findings of Bone changes, 20 (57.1%) patients had Serum Calcium levels of < 8.5 mg/dl. This was found to be statistically significant. This shows, 57.1% among bone changes group had low calcium levels. In the present study, among the 35 patients who had x-ray findings of bone changes, 30 (85.7%) patients had vitamin D levels of < 20 and 4 (11.4%) patients had Vitamin D levels between 21-30. This was found to be statistically significant. This shows 97.1% among bone changes group had low vitamin D levels. In the present study, among the 35 patients who had x-ray findings of the bone changes, 19 (54.3%) patients had Sr. PTH levels of > 70 and 14 (40%) patients had Sr. PTH levels of between 61 -

70. This was found to be statistically significant. This shows 94.3% among bone changes group had high Sr. PTH levels.

#### CONCLUSION

Out of 50 CKD patients, 35 (70%) patients had x-ray changes depicting skeletal abnormalities. Low calcium levels were found in majority of patients. High Phosphorous levels were found predominantly. High Parathyroid hormone levels were found predominantly. Low Vitamin D levels were found in majority of cases. Hence frequent screening of biochemical values are mandatory in chronic kidney changes patients to find out skeletal abnormalities.

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