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Original Research Article

Evaluation of changes in minerals like calcium, phosphorus and parathormone levels in ESRD patients on haemodialysis: A case control study

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is an international public health problem affecting about 5–10% of the population. KDOQI guidelines highlight the importance of measuring the parathyroid hormone levels annually once diagnosed with CKD. If the levels are maintained within the target range, then the various complications can be prevented by adequate treatment.

Objectives: 1. To measure the levels of Calcium, Phosphorus, Alkaline phosphatase and parathyroid hormone levels in patients with stage 4 kidney disease. 2. To compare these biochemical parameters with healthy controls.

Materials and Methods: 50 CKD patients visiting dialysis unit were included in the study. Patients with congenital renal disorders were excluded. A written informed consent was taken from all patients. The personal details of patients were documented. Clinical history, personal & family history was taken in detail from each patient. 50 Healthy individuals were included as controls in the study.

Results: Statistically significant increase in levels of Calcium, Phosphorus, Alkaline phosphatase, Uric acid and parathyroid hormones were seen in CKD patients as compared to controls.

Conclusion: The levels of parathormone, calcium & phosphorus are used as surrogate markers of disease progression. Alteration in minerals like calcium and Phosphorus occurs early in the course of disease and are responsible for various cardiovascular manifestations and bone osteodystrophy. The ultimate goals of treating secondary hyperparathyroidism are to normalize mineral metabolism, prevent bone disease and prevent extra skeletal manifestations of the altered biochemical processes.

1. Introduction

Chronic Kidney disease (CKD) is a progressive disease causing an irreversible damage in kidney function.[1] It is a major public health problem associated with premature mortality and decreased quality of life as well as high cost of health care. A trend towards increased incidence and prevalence is being reported worldwide with epidemic proportions in many countries.[2]

CKD is a state of imbalance of several important physiologic regulatory mechanisms, among them mineral balance, acid base balance, nutritional balance, and energy balance, resulting in accelerated cardiovascular disease (CVD) and mortality. Mineral disturbances and secondary hyperparathyroidism develop early in the course of disease, even when the GFR is 50–80 mL/minute/1.73 m2.[3]

ESRD is a progressive disorder for which there is no prospect of recovery, and for which patients receive regular haemodialysis. In ESRD the ability of the kidneys to excrete metabolic waste products and to regulate the composition of extracellular fluid is compromised. Symptoms of ESRD also include cardiovascular dysfunction, anaemia, malnutrition, muscle wasting, muscle weakness, glucose intolerance and reduced bone density.[4]

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In 2012, large-scale national survey from China found that the prevalence of CKD was 10.8%.[4] And it was found that 2% of patients with CKD would enter the stage of end-stage renal disease (ESRD), when dialysis or renal transplantation was needed to sustain life.[5]

Haemodialysis (HD) is a medical method that uses a special machine to filter waste products from the blood and to restore normal constituents to it when the kidneys are unable to do so. Haemodialysis is frequently done to treat patients with ESRD.[6]

The primary goal of haemodialysis is to restore the intracellular and extracellular fluid environment that is characteristic of normal kidney function. This is accomplished by the transport of solutes such as blood urea and bicarbonate take place down a concentration gradient from the circulation into the dialysate and in the reverse direction.[7]

2. Objectives

1. To measure the levels of Calcium, Phosphorus, Alkaline phosphatase and parathyroid hormone levels in patients with stage 4 kidney disease.
2. To compare these biochemical parameters with healthy controls.

3. Materials and Methods

50 CKD patients visiting dialysis unit were included in the study. Patients with congenital renal disorders were excluded. A written informed consent was taken from all patients. The clinical history, personal & family history was taken in detail from each patient. 50 Healthy individuals were included as controls in the study. Urea was measured by enzymatic urease method; Creatinine was measured by modified rate Jaffé method. Parathyroid hormone levels were analysed by CLIA. Calcium and Phosphorus were measured by ISE indirect method.[8–12]

3.1. Statistical analysis

Pearson correlation coefficients between continuous variables were used as a measure of association. The data obtained were statistically analyzed using SPSS version. The significance level for results was set as $P < 0.01$.[13,14]

4. Results

Samples are gender matched. Among cases-70% were Males and 30% were Females. Among the controls population included for study, 62% were Males and 38% were Females.

The mean age in Cases: 47.26 ±12.73 yrs. Controls: 43.83 ±15.12 yrs.

Co morbid conditions-66% had DM and 60% had Hypertension.

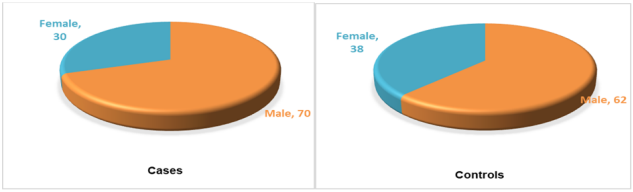
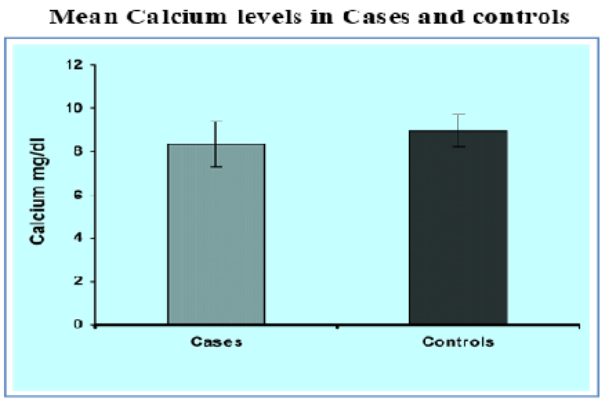


Fig. 1: Gender distribution in cases and controls



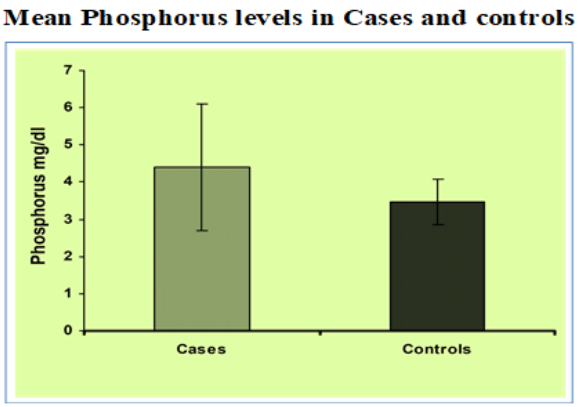


Fig. 2: Mean levels of calcium and phosphorus in cases and controls

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In our study, we found statistically significant increase in serum urea in cases with mean value 76.60 mg/dl, then controls with the mean value 23.54 mg/dl($p<0.001$). A statistically significant increase in serum creatinine in cases with mean value 4.11 mg/dl, then controls with the mean value 0.56 mg/dl ($p<0.001$).

There was a significant decrease in serum calcium in cases with mean value 8.38 mg/dl, then controls with the mean value 8.98 mg/dl ($p=0.001$). We found statistically significant increase in serum phosphorus in cases with mean value 4.66 mg/dl, then controls with the mean value 3.47 mg/dl ($p=0.001$). A significant increase in serum ALP in cases with mean value 90.92IU/L, then controls with the

Table 1: Mean values of all biochemical parameters in cases and controls

Biochemical parameters	Cases	Controls	P value
Urea mg/dl	76.60±69.77	23.54±7.46	<0.001**
Creatinine mg/dl	4.11±4.25	0.56±0.10	<0.001**
Calcium mg/dl	8.38±1.01	8.98±0.76	0.001**
Phosphorus mg/dl	4.66±2.07	3.47±0.62	0.001**
ALP IU/L	90.92±46.37	82.91±21.78	0.285
PTH pg/ml	211.13±88.0	52.47±16.34	<0.001**

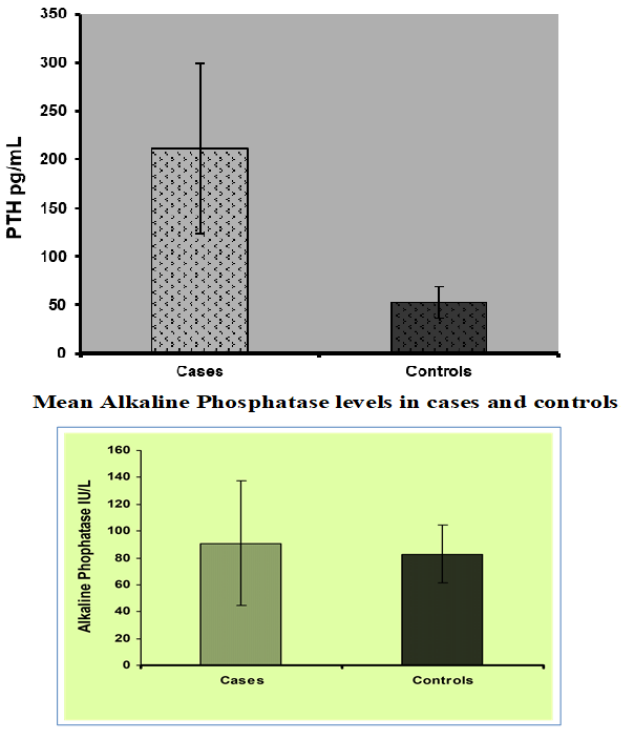

Fig. 3: Mean levels of parathyroid hormone & ALP in cases and controls

mean value 82.91 IU/L(p<0.001). We found statistically significant increase in serum PTH in cases with mean value 211.13 pg/ml, then controls with the mean value 52.47 pg/ml (p<0.001).

5. Discussion

The biochemical abnormalities of CKD-MBD may begin in CKD stage 3, the rate and severity of these changes are highly variable. Hence it is strongly recommended that monitoring serum levels of calcium, phosphorus, PTH, and alkaline phosphatase at CKD stage 3 will predict underlying bone turnover and reduce associated mortality.[15]

In ESRD, among mineral abnormalities, the most prevalent is hyperphosphatemia. Elevated serum phosphorus may aggravate the effects of coronary atherosclerosis through increased vascular calcification and smooth muscle proliferation resulting in cardiovascular morbidity.

Elevated phosphorus alters microcirculatory hemodynamics through increased extra vascular resistance and may compromise myocardial perfusion. Study done by Amman K et al found a significant increase in serum phosphorus levels in patients with CKD.[16]

These findings are similar to our study. In our study we observed a statistically significant increase in serum phosphorus levels in cases as compared to controls. Similar findings was also observed in a study done by J. Floege et al, Noordij et al. and Stevens, L. A et.al who reported a significant increase in phosphorus levels and concluded that high levels of phosphorus as a significant risk factor for mortality in CKD.[17–19]

Decrease in serum calcium during the course of CKD caused by phosphate retention leads to increased PTH mRNA levels and proliferation of parathyroid cells. The number of calcium-sensing receptors also may decrease in hypertrophied parathyroid tissue and lead to inadequate suppression of PTH secretion.[20] Elevated PTH stimulate bone demineralization leading to high- turnover, by accelerating rates of bone absorption and resorption with concurrent production of alkaline phosphatase from osteoblast cells contributing to its high levels in plasma as the renal function or GFR declines.[21]

In our study we observed a statistically significant increase in serum PTH levels and decrease in calcium levels in cases as compared to controls. Similar findings were found in study done by Freethi et al in CKD, where they observed, as glomerular filtration rate decreases, there is a decline in calcium and phosphorus homeostasis mechanisms, resulting in decreased calcium levels and increased phosphorus levels.[22]

ALP is produced by osteoblasts in bone tissue in response to decreased calcium levels, hence plays an important role in bone mineralization. ALP is a biochemical marker of bone turnover and is used to monitor the metabolic bone disease associated with renal insufficiency, resulting in renal osteodystrophy.[23] ALP has been shown to be associated with arterial calcification in the coronary, carotid, and aorta, and superficial femoral artery and therefore ALP has been suggested as a surrogate for arterial stiffening.[24]

In our study, we found a statistically significant increase in serum ALP levels in cases as compared to controls. Similar findings were observed in study done by Rhee et al., where higher ALP in patients on dialysis were associated with increased mortality.[25]

6. Conclusion

The levels of PTH, calcium & phosphorus are used as surrogate markers of disease progression. As the disorder begins early in the course of CKD, a proactive approach with intervention is important. Therapeutic strategies should be employed to prevent and correct these disturbances. Thus, aiming to improve cardiovascular outcomes and survival.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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