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ASSOCIATION OF PARATHYROID HORMONE, CALCIUM AND PHOSPHORUS WITH HEMODIALYSIS PATIENTS

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ABSTRACT

This study included 65 hemodialysis patients (HD) and 25 healthy volunteers as normal control group. High level of iPTH is associated with low level of calcium (hypocalcemia) and high level of phosphorus (hyperphosphatemia) leads to development of secondary hyperparathyroidism (sHPT). This study estimated that the levels of calcium were significantly lower; on the other hand, the levels of serum phosphorus and iPTH were significantly higher in comparison with those in the control group. It was observed that there was a significant negative correlation between serum calcium and phosphorus levels in chronic renal failure patients. On the other hand, there was a significant positive correlation between serum iPTH and phosphorus levels in chronic renal failure patients.

KEYWORDS: Hemodialysis, intact parathyroid hormone, Secondary hyperparathyroidism.

INTRODUCTION

Parathyroid hormone (PTH) is secreted by the chief cells of the parathyroid glands as a polypeptide containing 84 amino acids. PTH controls the level of ionized calcium (Ca+2) in the blood and extracellular fluid by acting upon the 1_receptor"parathyroid hormone 1 receptor (high levels in bone and kidney) and the 2 _ receptor" parathyroid hormone 2 receptor (high levels in the central nervous system, pancreas, testis, and placenta).[1] The

primary physiologic function of PTH is to maintain the concentration of ionized calcium in the extracellular fluid, which is achieved by the following mechanisms.

(1) Stimulation of osteoclastic bone resorption and release of calcium and phosphate from bone; (2) stimulation of calcium reabsorption and inhibition of phosphate reabsorption from the renal tubules; and (3) stimulation of renal production of 1, 25-(OH) 2D3, which increases intestinal absorption of calcium and phosphate.[2]

Chronic kidney disease (CKD) is characterized by a gradual reduction in the number of functional nephrons[3] and associated with multiple metabolic disturbances of calcium and phosphorus.[4] Alterations in the control mechanisms for calcium and phosphorus homeostasis occur early in the course of CKD and progress as kidney function decreases; if left untreated and then alterations can result in significant consequences.[4] Mortality is markedly elevated in patients with CRF. Hemodialysis (HD) remains the most common technique for treatment of CRF patients.[5]

The development of secondary hyperparathyroidism results from many factors, including retention of phosphorus, a decrease in the activation of the calcium-sensing receptor (CaR) in the parathyroid gland and skeletal resistance to the calcemic effect of PTH. As kidney function declines, so does phosphorus excretion, thus causing plasma phosphorus levels to rise while plasma calcium levels decrease.[6]

In this study, we evaluated intact parathyroid hormone (iPTH) in patients with chronic renal failure also, estimated the potential link between serum iPTH, calcium and phosphorus concentration, in order to know if the elevation of intact parathyroid hormone can be used as predisposing risk factors and morbidity indicator among hemodialysis patients.

SUBJECTS AND METHODS

This study included 90 subjects; 65 patients with mean age 45.16 ± 14.01 years they were 39 (60%) males and 26 (40%) females. All patients were undergoing dialysis treatment following diagnosis of chronic renal failure disease (CRF) by nephrologists in the Urology and Nephrology Center, Mansoura University; each patient was dialyzed 3 times per week. Twenty five healthy volunteers as normal control group were collected from donner blood bank, Mansoura University, with mean age 39.30 ±10.20 years; they were 13(52%) males and 12 (48%) females. Serum creatinine, uric acid, blood urea nitrogen (BUN) and liver

function parameters as serum albumin, total bilirubin, liver enzymes ALT, AST and ALP were tested. The control subjects had normal kidney function and normal level of intact parathyroid hormone (iPTH), they were free from any kidney diseases. The studied subjects (patients and controls) were in the same socioeconomic class and had similar nutritional habits.

Blood sample collection and examination

Five milliliters venous blood was collected using a disposable plastic syringe from each patient and healthy individuals. All samples of patients were collected before the dialysis. One milliliter from 5 ml was collected on ethylene diamine tetraacetic acid (EDTA) for measuring hemoglobin level. The rest of blood (4ml) were collected on free tubes without addition anticoagulants, were centrifuged at 3000 rpm for 5 minutes to obtain serum and measured serum intact parathyroid hormone (iPTH) by Electrochemilumenecence immunoassay; Elecsys 2010[7], also serum calcium and phosphorus levels were measured by colorimetric end point method according to the method of.[8]

Statistical analysis

Data were obtained using Statistical package for social Sciences (SPSS) version 19.0 software. Data were expressed as mean ± standard deviation (M±SD). Results of CRF patients and control subjects were performed using chi- square analysis, independent t-test. Correlation between parameters was determined by pearson's correlation coefficient (r). Chi square and odds ratio were calculated with 95% confidence interval .A probability value less than 0.05 was considered statistically significant.

RESULTS

As observed in table (1), there was no significant difference of age and body mass index (BMI) in CRF patients when compared with control subjects. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in CRF patients than in control subjects, ($p < 0.001$).On the other hand, the level of hemoglobin was significantly lower in CRF patients as compared to control subjects ($P<0.001$).

Table (1): Demographic and clinical data of studied subjects.

Parameters	Control Subjects (n=25)	CRF patients (n=65)
Age(years) (Mean ± SD) *P*	39.30 ±10.20	45.16 ± 14.01 >0.05
BMI(kg/cm²) (Mean ± SD) *P*	31.01 ± 5.20	28.60 ± 4.80 >0.05
SBP(mmHg)/ 24h (Mean ± SD) *P*	122.10 ± 6.80	158.80 ± 13.10 < 0.001**
DBP(mmHg)/ 24h (Mean ± SD) *P*	78.01 ± 4.20	96.20 ± 5.10 < 0.001**
Hemoglobin (mg /dl) (Mean ± SD) *P*	13.20 ± 1.10	8.90± 2.30 < 0.001**

*Significant value (p<0.05). Data were expressed as mean ± SD. Results were obtained using independent t-test. Body mass index (BMI). Systolic blood pressure (SBP). Diastolic blood pressure (DBP).

In the present study, clinical parameters such as creatinine, blood urea nitrogen (BUN) and uric acid were tested for chronic renal failure (CRF) patients, (n=65), as well as control subjects (n=25). Table (2 and 3) show the levels of creatinine, BUN, uric acid and alkaline phosphatase were significantly increased in CRF patients when compared with control subjects (p<0.001) figure (1 and 2). On the other hand, there was lower significant in the level of albumin in chronic renal failure patients than in control subjects, also as observed there were no significant in the levels of alanine aminotransferase (ALT) enzyme, aspartate aminotransferase (AST) enzyme, and total bilirubin (TB).

Table (2): Renal function parameters in chronic renal failure (CRF) patients and control subjects.

Parameters	Control Subjects (n=25)	CRF patients (n=65)
Creatinine (mg/dl) (Mean ± SD) *P*	0.50 ± 0.10	8.80 ± 0.30 < 0.001**
BUN (mg/dl) (Mean ± SD) *P*	7.40 ± 0.40	86.60 ± 7.90 < 0.001**
Uric acid (mg/dl) (Mean ± SD) *P*	4.20 ± 0.30	6.60± 0.20 < 0.001**

*Significant value (p<0.05).Data were expressed as mean ± SD. Results were obtained using independent t-test. Blood urea nitrogen (BUN).

Table (3): Liver function parameters in chronic renal failure (CRF) patients and control subjects.

Parameters	Control Subjects (n=25)	CRF patients (n=65)
Albumin(g/dl) (Mean ± SD) *P*	4.55 ± 0.14	3.26 ± 0.19 < 0.001**
ALT(Iu/l) (Mean ± SD) *P*	17.10 ± 0.41	18.30± 0.33 >0.05
AST(Iu/l) (Mean ± SD) *P*	19.90 ± 0.26	21.10 ± 0.22 >0.05
ALP(Iu/l) (Mean ± SD) *P*	81.20 ± 4.20	139.50 ± 61.10 < 0.001**
TB(mg/dl) (Mean ± SD) *P*	0.71 ± 0.03	0.74 ± 0.08 > 0.05

*Significant value (p<0.05).Data were expressed as mean ± SD. Results were obtained using independent t-test. Alanine aminotransferase (ALT) enzyme. Aspartate aminotransferase (AST) enzyme. Alkaline phosphatase (ALP) enzyme. Total bilirubin (TB).

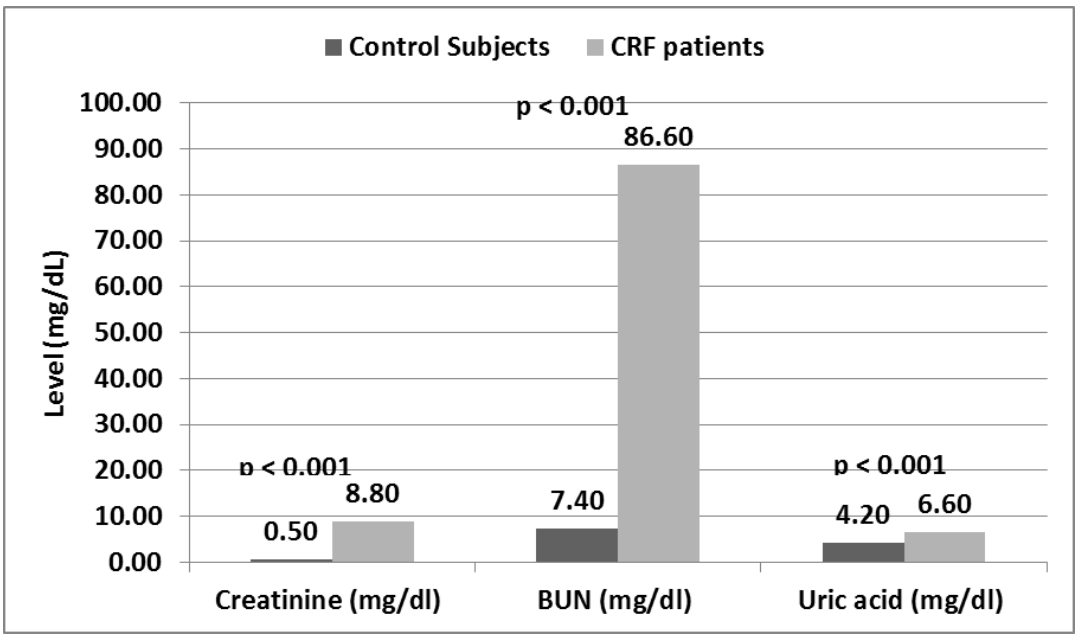

Figure (1): Renal function parameters in chronic renal failure patients and control subject.

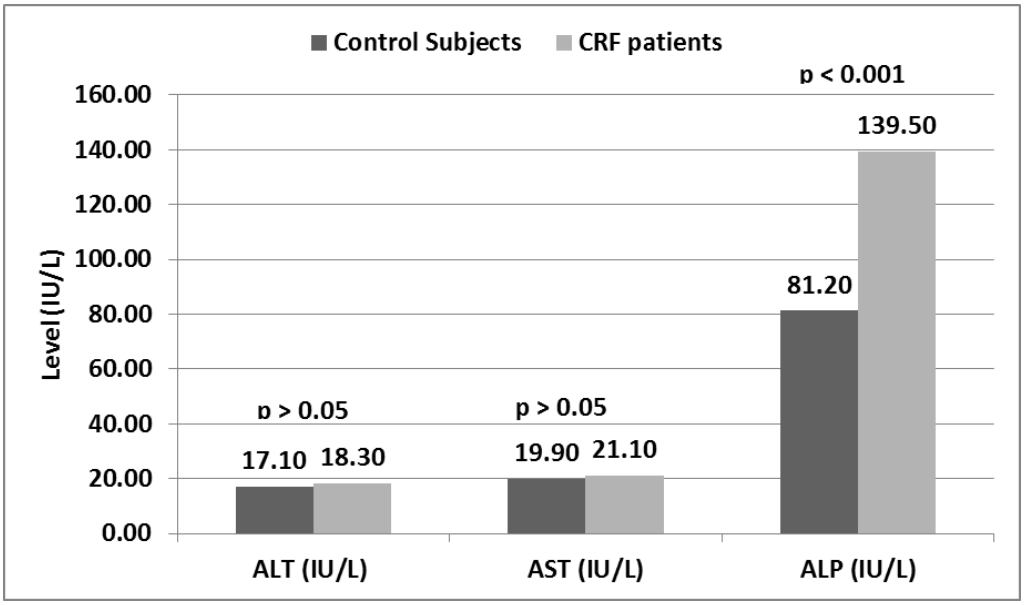

Figure (2): Liver function parameters in chronic renal failure patients and control subjects.

As observed in table (4) there were highly significant in the levels of serum intact parathyroid hormone (iPTH) and phosphorus in CRF patients when compared with control subjects but there were lower significant in the levels of serum calcium than control subject figure(3,4 and 5).

Table (4): Biochemical Features of studied subjects with control subjects.

Parameters	Control Subjects (n=25)	CRF patients (n=65)
iPTH (pg/ml)	39.30 ±10.20	246.11 ± 34.21
P		< 0.001**
Calcium (mg/dl)	10.15 ± 0.10	8.01 ± 0.20
P		< 0.001**
Phosphorus (mg/dl)	3.20± 0.09	5.40 ± 0.18
P		< 0.001**

*Significant value (p<0.05). Data were expressed as mean ± SD. Results were obtained using independent t-test. Intact parathyroid hormone (iPTH).

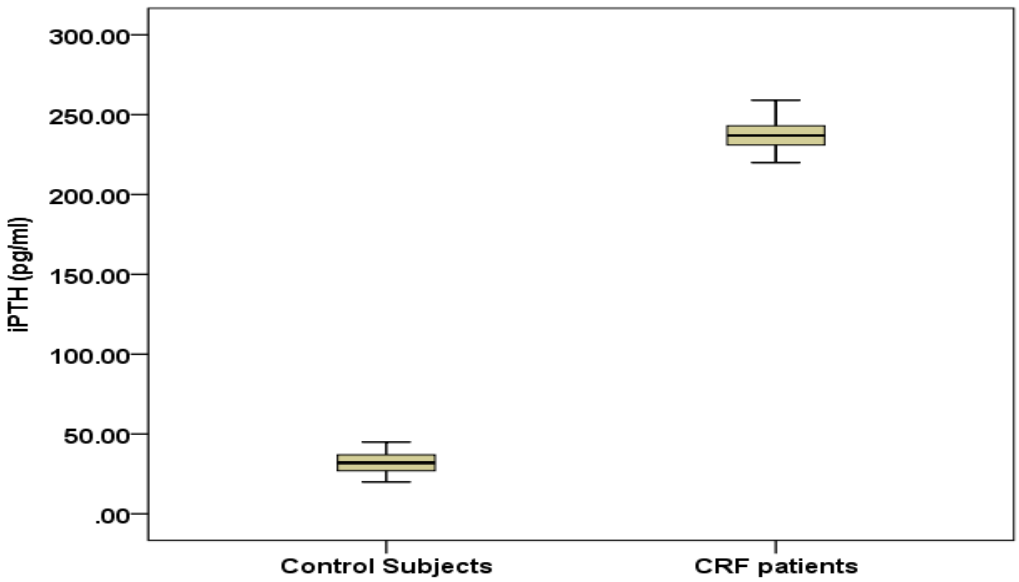

Figure (3): Boxplot of iPTH (pg/ml) in CRF patients against control subjects. The box represents the interquartile range. The whiskers indicate the highest and lowest values, and the line across the box indicates the median value. Overall significance difference was $p < 0.001$.

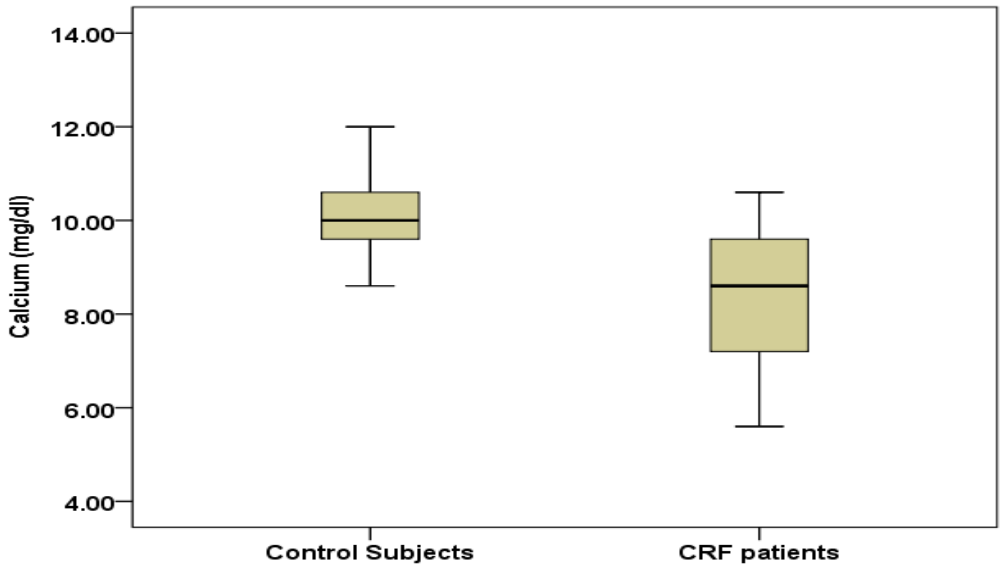

Figure (4): Boxplot of Calcium (mg/dl) in CRF patients against control subjects. The box represents the interquartile range. The whiskers indicate the highest and lowest values, and the line across the box indicates the median value. Overall significance difference was $p < 0.001$.

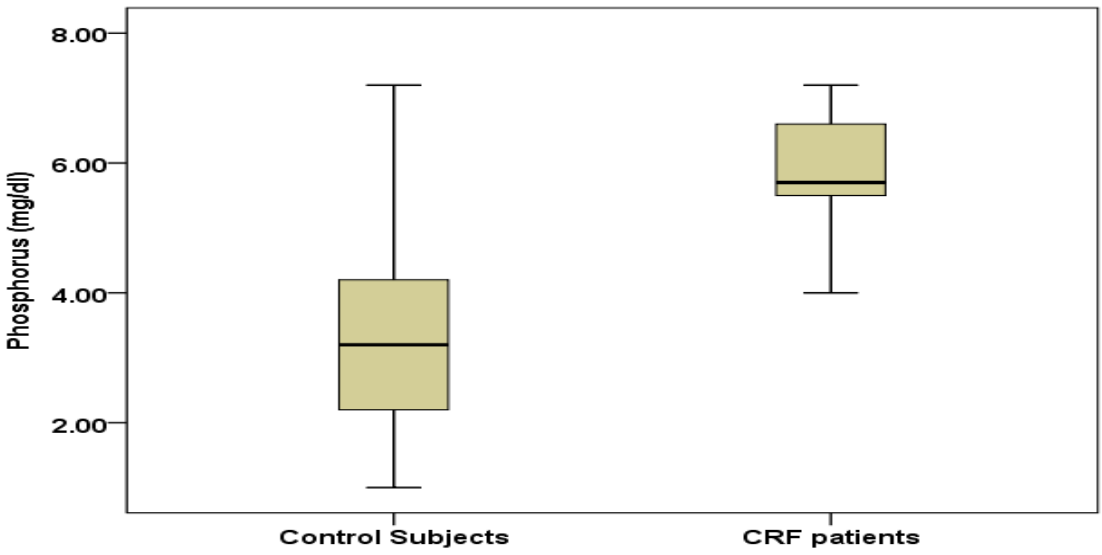

Figure (5): Boxplot of phosphorus (mg/dl) in CRF patients against control subjects. The box represents the interquartile range. The whiskers indicate the highest and lowest values, and the line across the box indicates the median value. Overall significance difference was p < 0.001.

As shown in table (5) there was a significant negative correlation between serum calcium and phosphorus levels figure (6). On the other hand, there was a significant positive correlation between serum iPTH and phosphorus levels figure (7).

Table 5: Correlation between studied parameters in chronic renal failure patients.

Parameters	Calcium		phosphorus		iPTH	
	r	p	r	p	r	p
Calcium	NS		-0.5	0.001	NS	0.090
Phosphorus	-0.5	0.001	NS		0.4	0.001
iPTH	NS	0.090	0.4	0.001	NS	

Not significant (NS), p< 0.05; Significant**.**

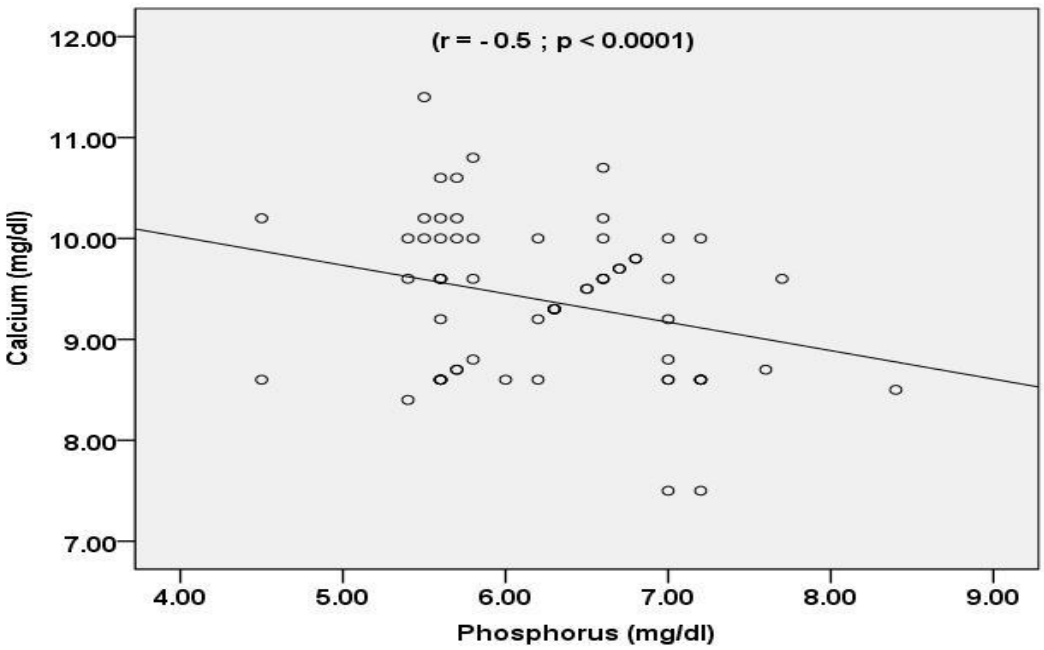

Figure (6): Linear Correlation between calcium level and phosphorus level in chronic renal failure patients.

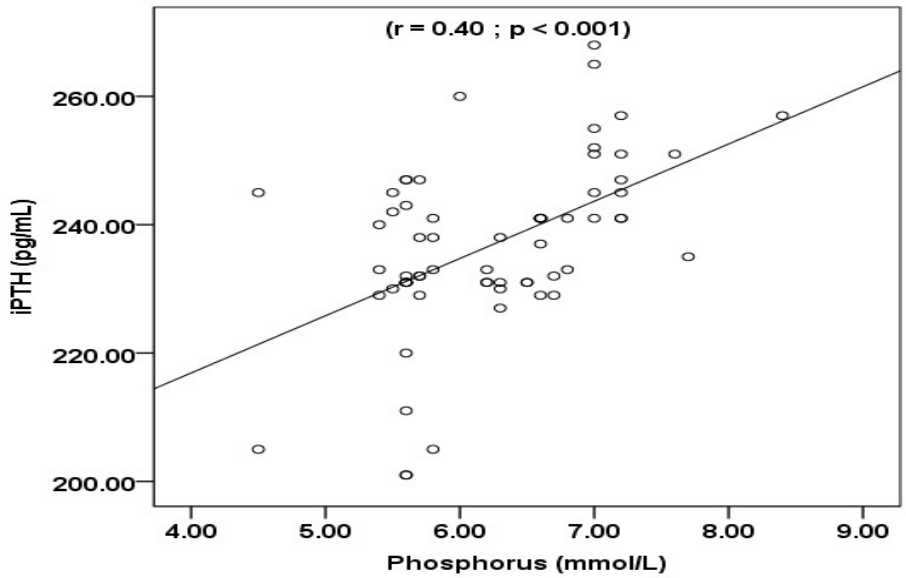

Figure (7): Linear Correlation between iPTH level and phosphorus level in chronic renal failure patients.

DISCUSSION

In normal humans, it has been shown that an oral phosphorus load results in an increase in serum phosphorus, a decline in the level of ionized calcium and an increase in the levels of PTH in blood.[9] Phosphorus also seems to have major effects on parathyroid growth by increasing the concentration of TGF- 23 which interacts with the EGF receptor and lead to

activation of the mitogen- activated protein kinase and the induction of cyclin-1 to drive the cell into a proliferation cycle.[10] Secondary hyperparathyroidism is a common complication of chronic kidney disease (CKD) and is part of a broad spectrum of disorders of mineral metabolism that occur in this clinical setting. Alterations in the control mechanisms for calcium and phosphorus homeostasis occur early in the course of CKD and progress as kidney function decreases.[4]

Secondary hyperparathyroidism is one of the main complications in patients with chronic renal failure.[11] Most patients with chronic renal failure have secondary hyperparathyroidism (sHPT), stimulation of parathyroid function is caused by insufficient production of calcitriol by the kidney, calcium deficiency and increased phosphorus.[12] The progression of renal disease is related to the development of calcium and phosphorus metabolism disorders, it has been well established that reduction of phosphate excretion and production of calcitriol stimulate the activity of the parathyroid gland.[13] The major role of phosphate retention in the pathogenesis of secondary hyperparathyroidism is the regulation of calcitriol production, such that phosphorus retention could lead to a decrease in the levels of calcitriol in blood.[14]

Many studies have demonstrated that elevation of iPTH level is associated with increased chronic kidney disease mortality. This study shows Low calcium levels are associated with high levels of iPTH and phosphorus, there was a significant positive correlation between phosphorus and iPTH levels (r 0.4 p 0.001) and a significant negative correlation between phosphorus and calcium levels (r -0.5 p 0.001), these results were in accordance with studies reported by[15,16] that show higher levels of iPTH are correlates of hyperphosphatemia in CRF patients and in contrast with studies reported that lower levels of iPTH and normal levels of calcium which reported by.[17]

CONCLUSION

This study shows that elevation of iPTH (hyperparathyroidism) in chronic renal failure patients is associated with high level of phosphorus (hyperphosphatemia) and low level of calcium (hypocalcemia), so high level of iPTH may be used as morbidity indicator and risk factors as useful for identification of the development of sHPT in CRF patients. Finally this study recommends further hormones and minerals study about the role of parathyroid hormone in chronic renal failure patients.

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