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To Evaluate Abnormality In Serum Urea, Creatinine, Calcium, Phosphate And Vitamin D In CKD Patients

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Abstract

Aim & Objectives: The aim of this study is to estimate the levels of serum Urea, creatinine, calcium, phosphate and vitamin D in CKD patients and healthy controls.

Materials And Methods: In this study, 30 CKD patients and 30 healthy controls of both gender matching in age and sex were included. The analysis of biochemical parameters was done by using auto analyzer using diagnostic reagent kit.

Results: In the present study Mean of Serum Urea, Creatinine and phosphate was higher in CKD patients than controls ($P < 0.001$) and Calcium and Vitamin D was lower in CKD patients than controls ($P < 0.001$).

Conclusion: Significant changes were observed in of Serum Urea, Creatinine, Calcium, Phosphate and vitamin D. They are favorable biomarkers with high accuracy in patients with CKD..

Keywords: CKD,eGFR, PTH,Ca etc

Introduction

Renal failure refers to a condition where the kidneys lose their normal functionality, which may be due to various factors including infections, auto immune diseases, diabetes and other endocrine disorders, cancer, and toxic chemicals. It is characterized by the reduction in the excretory and regulatory functions of the kidney; it is the ninth leading cause of death in United States as well as most industrialized nation throughout the world [1,2].

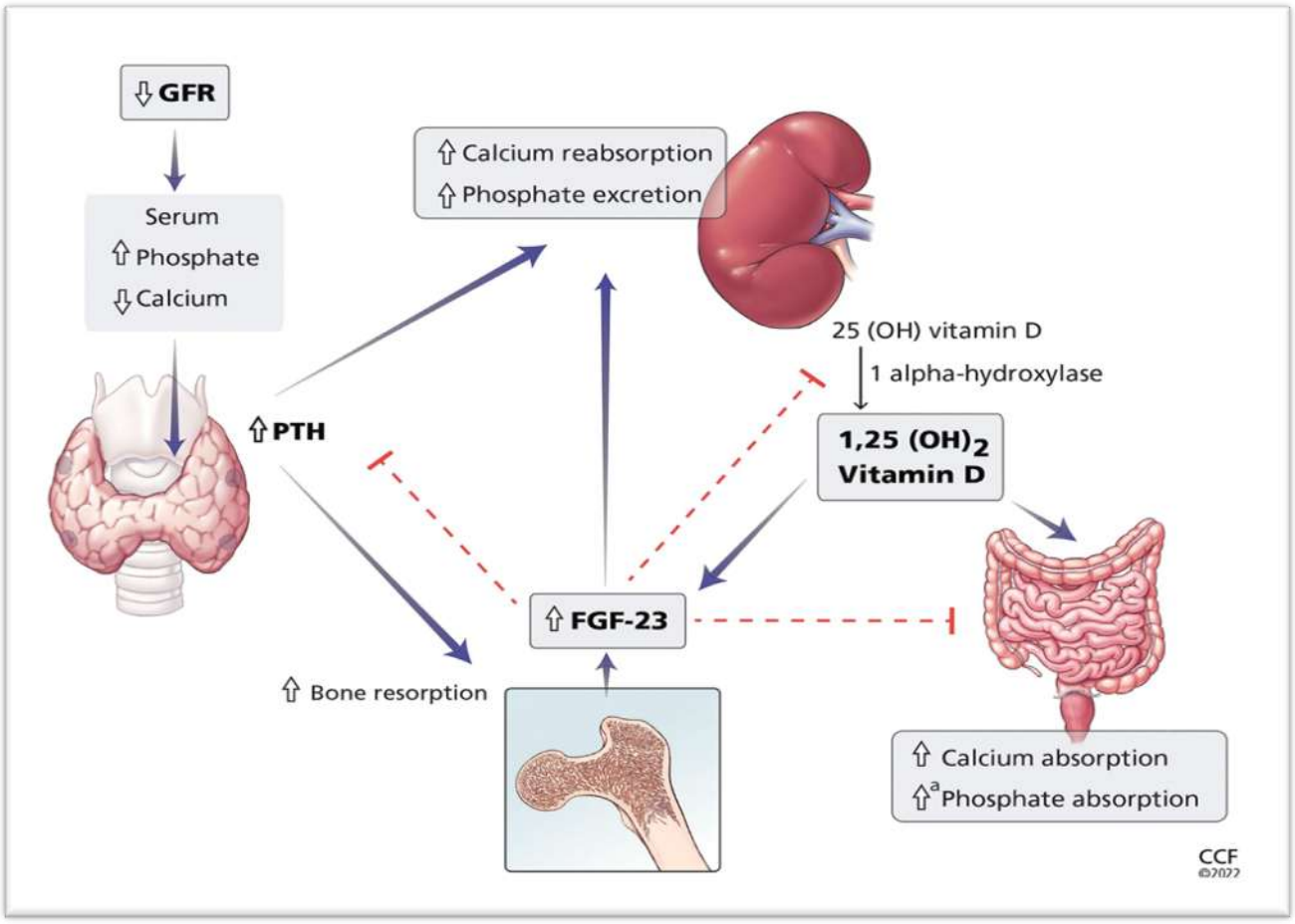

Figure 1. Calcium and phosphate metabolism in chronic kidney disease. Decreased glomerular filtration rate (GFR) leads to changes in serum calcium and phosphate, triggering release of parathyroid hormone (PTH) from the parathyroid glands and fibroblast growth factor 23 (FGF-23) from osteoblasts and osteocytes. These hormones have complex downstream effects on the kidney, gut, and bone, both from direct effects on the tissue and from indirect effects through modulation of enzyme activity in vitamin D conversion.

Serum calcium and phosphate levels are kept under tight control by regulatory hormones released by various organs, with complex feedback mechanisms (Figure 1). Interestingly, both calcium and phosphate are regulated by the same hormone, i.e, PTH. When serum calcium levels are low and serum phosphate levels are high, the parathyroid glands release more PTH, which acts in several organs to raise the calcium and, on the whole, to lower the phosphate levels. In the kidney, PTH directly increases calcium reabsorption in the distal tubule and loop of Henle and increases phosphate excretion by inhibiting its reabsorption in the proximal tubule. Also in the kidney, PTH upregulates production of 1 alpha-hydroxylase, leading to increased conversion of active vitamin D (1,25-dihydroxycholecalciferol) from its precursor, 25-hydroxycholecalciferol. In turn, in the intestine, active vitamin D increases the absorption of calcium and to a lesser degree phosphate, and in the bone, it has direct actions on both osteoblasts and osteocytes, promoting maturation, expression of skeletal hormones such as fibroblast growth factor 23 (FGF-23), and proper mineralization. FGF-23 is an important skeletal hormone that lowers phosphate levels by promoting its wasting (i.e., suppressing its reabsorption) in the kidney, suppressing its absorption in the intestine, and, in a negative feedback loop, lowering both PTH and 1,25-dihydroxycholecalciferol production. Klotho, a protein that has multiple effects in many tissues, facilitates binding of FGF-23 to FGF receptor 1 in the kidney, leading to fewer phosphate receptors in the proximal convoluted tubules, more phosphate excreted in the urine, and lower serum phosphate levels. The net effect of these interactions is

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homeostatic balance in serum calcium and phosphate levels. In chronic kidney disease, nephrons are progressively lost. Among the ill effects is a higher phosphate level, which in turn up regulates production of FGF-23 by the osteocytes and osteoblasts and leads to bone mineral disease (Figure 1). Bone mineral disease can begin early in the course of chronic kidney disease, when the eGFR may still be as high as 69 mL/ min/1.73 m2 . Meanwhile, klotho production is down regulated, so that less FGF-23 binds to its receptor in the kidney, less 1 alpha-hydroxylase and active vitamin D are produced, and more phosphate is reabsorbed in the proximal convoluted tubule. As chronic kidney disease progresses to its end stage, FGF-23 levels keep getting higher, and the elevation is accompanied by other calcium-phosphate axis derangements such as excess PTH release, decreased 1,25-dihydroxycholecalciferol, and increased sclerostin (an inhibitor of bone formation). Together, these derangements lead to the clinical manifestations.[3]

It is now accepted that the presence of chronic kidney disease (CKD) is associated with poor outcomes.[4-6] In particular, cardiovascular events and mortality increase as the estimated glomerular filtration rate (eGFR) declines below 60 ml/min.[7] In dialysis patients, cardiovascular disease is 10- to 20-fold higher than the general population, representing at least half of the 15–25% per year mortality rate.[8] The mechanisms associating CKD with mortality have not been determined, in part, owing to the lack of comprehensive clinical and biochemical analyses. Recently, increased attention has focused on endocrine abnormalities in patients with CKD as a way to explain some of these associations.[9,10] For example, 1,25-dihydroxyvitamin D (1,25 OH2 D3) deficiency is known to occur during the progression of CKD because the final hydroxylation step of 25-hydroxyvitamin D (25(OH)D3) to 1,25 OH2 D3 (calcitriol) is mediated by kidney 1a´-hydroxylase.[11] Calcitriol deficiency plays a major role in the development of secondary hyperparathyroidism (HPTH), as 1,25 OH2 D3 deficiency promotes parathyroid gland growth (hyperplasia) and increased parathyroid hormone (PTH) synthesis through loss of the ability to upregulate vitamin D receptor expression within parathyroid cells. The end result is elevated serum PTH and abnormal calcium (Ca) and phosphorus (P) balance. [12]

The control of Hypophosphatemia in advanced CRI is of utmost importance for 3 main reasons-

1. Hypophosphatemia contributes to the pathogenesis of [13] secondary hyperparathyroidism and its skeletal expression.

2. It promotes, together with calcium and vitamin D, the formation and deposition of calcium-phosphate crystals in [14] soft tissues, in particular in the vessel wall & in heart valves.

3. There is a direct, independent association between the degree of Hypophosphatemia and cardiovascular [15] morbidity and mortality in dialysis patients.

The objective of this study is to find out the biochemical changes (urea, creatinine, Calcium, phosphate and vitamin D) with chronic kidney disease patients and compare the obtained results with the results of healthy individuals as control groups.

Material And Methods

The study was done at Department of Biochemistry, Prakash Institute of medical Science and research, Urun-Islampur in collaboration with Department of Biochemistry Yogita Dental college and Hospital Khed.

Sample size: Blood samples for 30 patients suffering from CKD and 30 samples were collected as healthy volunteers.

Sample selection: During my study period diagnosed patients of Chronic Kidney Disease who attended Nephrology OPD or were admitted in Nephrology IPD of Prakash Institute of medical Science and research, Urun-Islampur were included in the study.

Blood samples were taken after overnight fasting. 5ml of blood sample were collected using aseptic measures. The samples were allowed to stand for 1hr and then centrifuged. The serum collected was analysed for serum urea, creatinine, calcium, phosphate, vitamin D. The samples were stored at -20°C for further use. Calcium, phosphate, vitamin D, urea, creatinine, sodium were tested by standardized reagent kits in the department of biochemistry.

1. Estimation of serum calcium by OCPC method.

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2. Estimation of serum phosphate by molybdate UV method.
3. Estimation of serum 25-Oh vitamin D by commercial ELISA kit.
4. Estimation of serum urea by Berthelot method.
5. Estimation of serum Creatinine by modified Jaffe Kinetic method

Distribution Of Study Subjects:

Group I	N = 30 CKD patients.
Group II	N= 30 Healthy controls

Results

Table no. 1: The mean value of means of Serum Urea, Creatinine, Calcium, Phosphate and vitamin D in CKD patients and controls.

Name Of the Parameters	**Malaria Patients (N=25)**		**Controls (N=25)**		**Significance**
	Mean ±SD	**Std. Error of Mean**	**Mean ±SD**	**Std. Error of Mean**	
UREA	149.9 ±13.8 ***	2.53	48.3 ±8.44	1.54	**P =< 0.001**
CREATININE	2.4±0.54 ***	0.09	0.86±0.2	0.03	**P = <0.001**
CALCIUM	5.98±0.44	0.08	8.27±0.77 ***	0.14	**P =< 0.001**
PHOSPHATE	6.05±0.44 ***	0.08	4.63±0.51	0.09	**P =< 0.001**
VITAMIN D	21.8±2.1 ***	0.38	31.2±3.2	0.58	**P =< 0.001**

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The statistical method used to compare data was unpaired' test

*P> 0.05……Not Significant

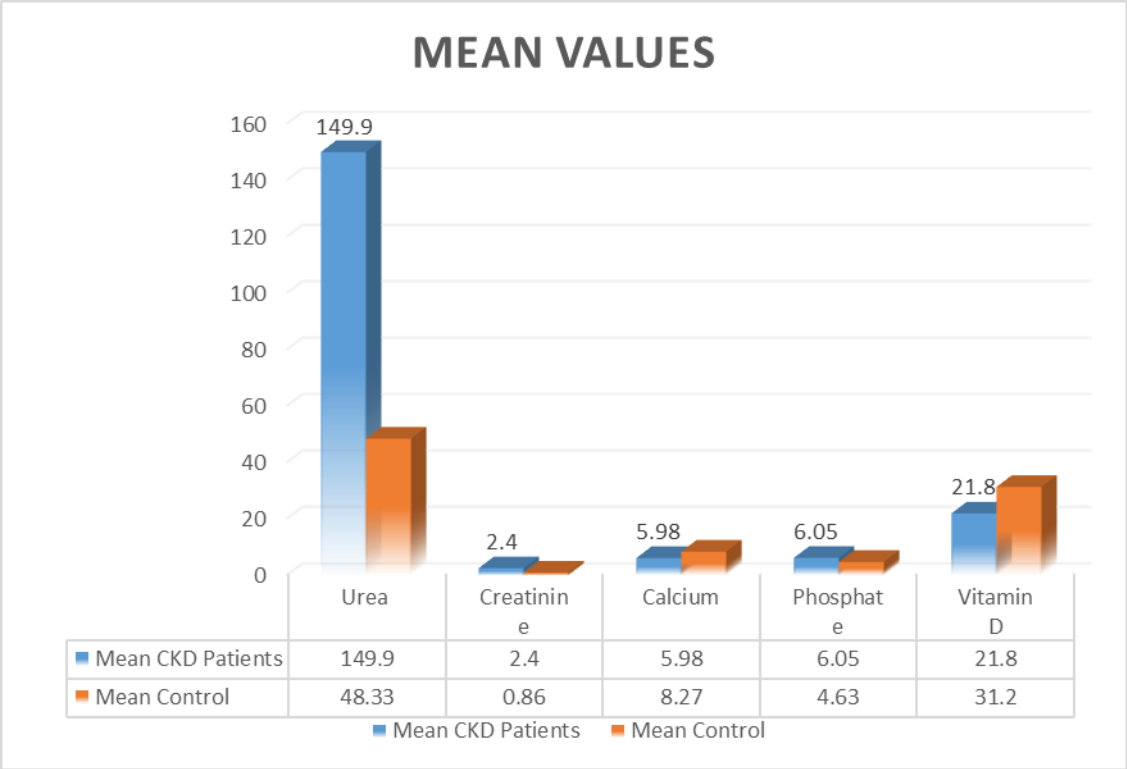
**P<0.05……...Significant

***P<0.001…...Highly Significant

There is highly statistically significant difference in means of Serum Urea, Creatinine, Calcium, Phosphate and vitamin D (P < 0.001) as compared to controls.

In the present study mean of Serum Urea, Creatinine and phosphate was higher in CKD patients than controls (P < 0.001) and Calcium and Vitamin D was lower in CKD patients than controls (P < 0.001).

Graph No.1: Comparison of Biochemical parameters in CKD patients with healthy controls



Discussion

Chronic kidney disease (CKD) is a term that refers to a variety of pathophysiologic processes that are linked to impaired kidney activity and a decrease in glomerular filtration (GFR). The leading cause of death is cardio-vascular disease (CVD), independent of age and race, and is mainly caused by cardiovascular and chronic renal disease risk factors. In the United States, the prevalence of CVD in CKD patients reaches 63%, in contrast with only 5.8% in people without CKD, and this prevalence is directly correlated with the severity of CKD. CVD accounts for 40% to 50% of deaths in dialysis patients. In dialysis patients, cardiovascular disease (CVD) is responsible for 40 percent to 50 percent of deaths. [16]

The abnormality in the regulation of Calcium and Phosphate metabolism in Chronic Renal Failure Patients is one of the most important complications of the conditions, which then leads to clinic pathological implications that affect the patient further.

In our study we found that Mean of Serum Urea, Creatinine and phosphate was higher in CKD patients than controls (P < 0.001) and Calcium and Vitamin D was lower in CKD patients than controls (P < 0.001).

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Our result is in accordance with similar studies done previously on different groups of population. Stevens L et al not only showed presence of abnormality in the calcium and phosphate levels, but also can predict mortality in these [17] patients . Block G et al also has shown in their study direct correlation of Calcium - Phosphate product also increases [18] mortality risk in CKD patients. The presence of elevated calcium - phosphate product and its long term negative effect [19] is also shown in the study of Egbuna et al and [20] Thongprayoon et al . The biochemical alterations of CKD include elevated fibroblast growth factor-23 (FGF23) and parathyroid hormone decreased , 2 5 - dihydroxyvitamin D (1,25D), elevated serum phosphate, and decreased serum calcium .[21]

The current study shows the similar changes in calcium-phosphate-Vitamin D levels in the CKD patients, in our population, and highlights the risk that these patients are under further complications of such dysregulation, and the importance of regularly monitoring these parameters in CKD patients.

Conclusion

The results of the present study underlines the importance of further studies to gather more data on the abnormality in calcium phosphate and vitamin D regulation in the Chronic Kidney Disease, especially in our population. The present study tries to bridge this gap to some extent but further studies including randomized controlled trial on any possible beneficial effect on Vitamin D supplementation in these patients are needed.

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