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A study of the Variation in the Levels of Parathyroid Hormone, Calcium and Phosphorus among Patients at the Kidney Services Center - Al-Khums

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الملخص

الكلى ضرورية لصحة الجسم. وهي مسؤولة بشكل كبير عن تصفية النفايات والمياه الزائدة والشوائب الأخرى من الدم. يتم تخزين هذه السموم و المواد الزائدة في المثانة ثم يتم إزالتها أثناء التبول. يمكن أن يؤدي مرض الكلى إلى مشاكل صحية أخرى خطيرة ، بما في ذلك وتلف الأعصاب و ضعف العظام وسوء التغذية. ومع مرور الوقت، قد تتوقف الكلى عن العمل بشكل كامل، أجريت الدراسة على 70 مريض لغسيل الكلي في مركز خدمات الكلى – الخمس، ورصد التغيرات التي تحدث على مستويات هرمون الباراثيرويد و الكالسيوم و الفسفور ، و جاءت النتائج موضحة ان هرمون الباراثيرويد كان مرتفعا عند الاناث اكثر من الذكور مقارنة مع المجموعة الضابطة أما الفوسفات فكان مرتفعا في الذكور عنه في الاناث في حين لم يكن هناك اي اختلاف معنوي يذكر في معدل الكالسيوم مقارنة مع المجموعة الضابطة .

الكلمات المفتاحية / الغسيل الكلوي – هرمون البارثيرويد – الفوسفور – الكالسيوم .

Abstract

Kidneys are essential for a healthy body. It is largely responsible for filtering waste, excess water and other impurities from the blood. These toxins and excess materials are stored in the bladder and then removed during urination. Kidney disease can lead to other serious health problems, including nerve damage, weak bones, and malnutrition. Over time, the kidneys may stop working completely .The study was conducted on 70 dialysis patients at the Kidney Services Center - Al-Khums and monitored the changes that occur in the levels of the parathyroid hormone) PTH ,(calcium and phosphorus. The results revealed that the PTH was higher in females than in males compared to the control group, and phosphate was higher in males than in females, while there was no significant difference in calcium levels.

Keywords: dialysis - parathyroid hormone - phosphorus - calcium.

Introduction

Chronic kidney disease is a progressive disease with no cure and high morbidity and mortality that occurs commonly in the general adult population, especially in people with diabetes and hypertension) **William *et al*** .(**2011**). The doctor always advises to maintain and improve kidney function, non-pharmacological planning (for example, regulating dietary pattern), pharmacological interventions targeting chronic kidney disease, and kidney disease-specific pharmacological interventions are used (**Panel et al 2015)**. Additional studies on diet and pharmacological interventions and the development of innovative strategies are necessary

to ensure the care required to preserve the kidneys and achieve a longer lifespan (**Kamyar 2020)**.

Some observational studies in cases of secondary hyperparathyroidism have demonstrated the association of PTH with renal anemia or immunodeficiency **(Trunzo *et al* 2008).** In addition, it has been recently founded that PTH increases consumption by changing adipocytes to brown adipocytes, leading to cachexia-like pathology seen in patients with malignancy **(Kir *et al* 2016**). Furthermore, PTH can induce various effects by encouraging the secretion of fibroblast growth factor 23 (FGF23). FGF23 is a humoral factor produced by osteocytes and has been known as a significant predictor of life prognosis in patients undergoing dialysis in other that it can induce cardiac hypertrophy, renal anemia, immunodeficiency, and chronic inflammation (**Meir *et al* 2014**). Additionally, both PTH and FGF23 increase pathological fibrosis in chronic kidney disease (CKD) **(Rossaint *et al* 2016; Singh *et al* 2016).**

Early reports recorded that substantial amount of calcium were absorbed from the gastrointestinal tract and that total body calcium balance became positive when calcium carbonate was used exclusively as a phosphate binding medication in kidney failure patients **(Jansz *et al* 2018).**

Increases in serum calcium concentrations were common during calcium carbonate therapy. The relative frequency led to overall reductions in the calcium concentration of hemodialysis and peritoneal dialysis solutions from earlier standard concentrations of 3.0–3.5 mEq/l to the concentration of 2.5 mEq/l that is being used most widely nowadays **(Peter *et al* 2017).**

Hyperphosphatasemia promotes the development of parathyroid gland hyperplasia, and high ambient phosphorus concentrations facilitate PTH synthesis by stabilizing PTH mRNA and facilitating message translation (**Goyal and Ishwarlal 2019**). Persistent hyperphosphatasemia may further diminish the effectiveness of treatment with calcitriol in patients with established secondary hyperparathyroidism (**Cunningham *et al.* 2011).** Adequate control of serum phosphorus concentrations is important, therefore, in the prevention and management of excess PTH secretion **(Takeda *et al* 2014).**

The parathyroid gland plays a central role in regulating mineral metabolism in patients with chronic kidney disease (CKD), preventing levels of parathyroid hormone (PTH) gradually increase with decreased renal function, as a result of phosphate retention, hypocalcemia, and decreased production of 1 ,25 dihydroxy Vitamin D **(Plit and Kendrick 2014)**. There are a lot of endogenous changes within the parathyroid gland, and skeletal resistance to the actions of PTH **(Mishaela et al 2002).** The body cannot produce vitamin D. It can be taken from food and by exposing our skin to sunlight (**Michael 2016**). Healthy kidneys can take the vitamin D, the body we absorb and change it into the active form. Without enough active vitamin D, the body absorbs less calcium from the food, and so it becomes low in the blood (**Hitesh *et al*2020**). Also, excess phosphorous in the blood of people with chronic kidney disease may be associated with calcium in the blood (**Michael 2016**). This can then lower the serum calcium level, stimulating the cell surface calcium sensing receptor (CaR) by high concentrations of extracellular calcium in serum PTH (**Ramanaiah *et al*2008**). This study analyzes and evaluates the relationship of parathyroid hormone (PTH), calcium (Ca) and phosphorus (P) in patients with renal failure within the Al-Khums Dialysis Center .

Material and Methods

Scope of the research:

The scope of the research includes the PTH, Calcium and phosphorus at the Kidney Services Center - Al Khums. This study period ranging was from June to August 2022. It is a field study that focuses on the extent of the change in PTH, calcium and phosphate. The number of people from whom samples were taken are 35 healthy adults comparing with (70) dialysis patients. They are classified into: 40 males and 30 Females, and their ages ranged from 12 to 80 years.

Research tools and Materials:

The blood sample was transferred from the syringe to the collection tube, and left for 10 to 15 minutes at a temperature no higher than 37 (or at room temperature), being careful not to shake the blood tube vigorously so that it does not break. Serum sample were separated by centrifugation at 3000 g for 5 minutes.

The data were collected after testing the patients through a structured questionnaire administered to each patient. These questionnaires included (age, gender) and the test to be measured was (PTH, Ca and P).

Biochemical parameters test:

The basis of testing the samples is by blood samples for PTH, Ca and P measurement should be taken into plain tube, ideally between 10:00 and 16:00. Serum samples were stored at 4°C and analyzed within 72 h of venipuncture, reading these samples.

Statistics analysis:

XLSTAT program was used herein for descriptive statistics, graphing data and comparative statistics. The results were analyzed using one-way analysis of variance (ANOVA) followed by T test to compare groups with each other and Dennett two-sided test for comparisons with the control group.

RESULTS AND DISCUSSION

1. Results and Discussion:

This study was conducted to compare the change that occurs to each of the parathyroid hormone (PTH), calcium (Ca) and phosphorus (P) for dialysis patients in the Kidney Services Center - Al Khums, who were 35 healthy adults, males (Group 1), females (Group 2), and compared it with (70) dialysis patients, males (Group 3), females (Group 4) in the period from June to August 2022.

The study revealed that about 65% of the patients were between 30 and 60 years old. The results further showed that there were significant differences in the majority of the studied parameters, which were as follows:

Table (1) PTH, Ca and P for healthy adults, males (Group 1), females (Group 2) compared with patients, males (Group 3), females (Group 4).

P. Value	Means ± S.E.M FEMALE		P. Value	Means ± S.E.M MALE		*Parameter*
	Group 4	Group 2		Group 3	Group 1	
0.000	862.5 ± 128.01	32.14 ± 3.93	0.000	1224.3 ± 263.5	36.40 ± 4.56	PTH
0.949	8.78 ± 0.16	9.03 ± 0.136	0.527	8.94 ± 0.12	8.86 ± 0.09	Ca
0.000	5.21 ± 0.22	3.90 ± 0.20	0.000	8.94 ± 0.12	3.22 ± 0.18	P

Values are mean ± S.E.M. The values with different heights within each row are very different (analysis of variance, $P < 0.05$).

1.1. Change in parathyroid hormone (PTH) activity in hemodialysis patients:

Table (1) summarizes the parathyroid hormone activity for healthy male (group1) compared to male patients (group 3), and healthy female (group 2) compared to female patients (group 4). PTH activity was significantly higher in male groups (1,3) and in female groups (2,4). PTH activity was **36.40 ± 4.56, 1224.3 ± 263.5** in groups (1, 3), respectively, and **32.14 ± 3.93, 862.5 ± 128.01** in groups (2, 4), respectively. The same results are also represented in figures (1) and (2).

Measuring parathyroid hormone (PTH) is very important to reach a treatment decision in patients with bone disorder resulting from chronic kidney disease (CKD). Accordingly, second-generation thyroid hormone tests, known as the "intact PTH" test, are the standard and most widespread tests in clinical medicine. In addition, normal thyroid hormone tests measure both active and inactive thyroid hormone fractions in the blood, giving sometimes unclear value when evaluating thyroid hormone in patients with chronic kidney disease Variation in PTH assays, sample errors that occur during analysis, and the phenomenon of target organ PTH hyperresponsiveness. Current CKD-MBD guidelines recommend a wide range of serum PTH targets (2-9 upper normal limit for a proper PTH assay) in hemodialysis patients to reduce the risk of morbidity, Clinical orthopedics. However, a significant proportion of CKD patients continue to suffer from renal osteodystrophy despite having blood PTH levels within the recommended range. The main reason for this inconsistency is the analytical interference of different PTH forms and oxidized forms of PTH that accumulate significantly in CKD patients. Therefore, a new test based on mass spectrometry has been improved, which is able to measure the entire PTH spectra and specifically the fragments in the circulation. Studies have shown that it is likely to improve the accuracy of the diagnosis of renal osteodystrophy and give clear and definite indicators of the condition of patients. In addition, the effects of different parts of thyroid hormone on bone metabolism, vascular calcification, and mortality in patients with chronic kidney disease require further research and study due to the importance of the

repercussions of a deficiency or increase in the level of the hormone in general **(Kritmetapak and Chatlert 2019) .**

Our findings on parathyroid hormone elevation were consistent with several studies that demonstrated that chronic kidney disease, which leads to dialysis, causes many disturbances in PTH, calcium, phosphorus, and vitamin D levels. **Ivena *et al* 20019** explained in their study that the complications of kidney disease appear clearly on men and women, with the presence of some other influences that increase the severity of the infection, such as hormonal differences, menopause, or age.

Bahena and Jessica 2023 in their results found that CKD led to changes in experimental rat parathyroid level proteome and phosphoproteome profiles. Furthermore, both acute and chronic kidney failure led to increased PTH expression ex vivo in parathyroid glands in culture and in transfected cells through the PTH mRNA-protein interaction element and phosphorylation.

Moawad 2022 mentioned in their study that High PTH activity is likely to increase intracoronary calcification, and cause inadequate stent expansion, which may be related with rise risk of future adverse events in dialysis patients.

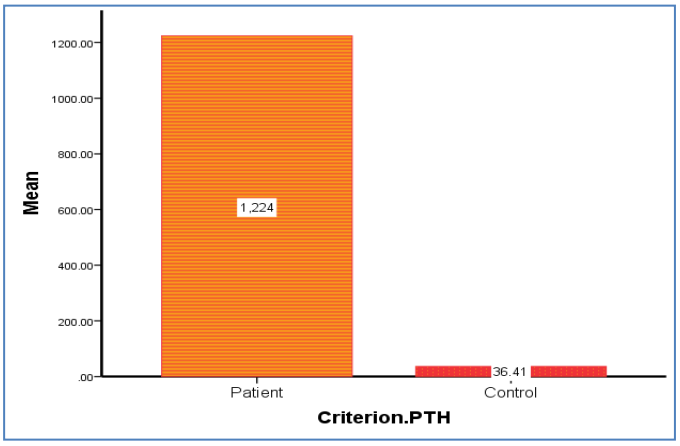

Figure (1): Shows the statistical differences in PTH in male with hemodialysis

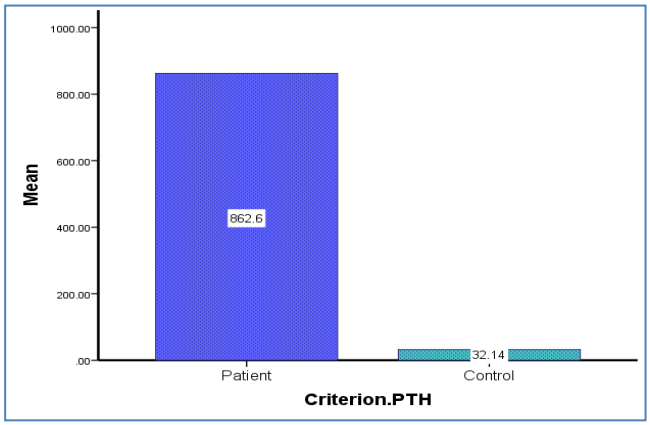

Figure (2): Shows the statistical differences in PTH in female with hemodialysis

1.2. Change in calcium (Ca) concentration in hemodialysis patients:

Table (1) summarizes the calcium concentration (Ca) for healthy male (group1) comparing with male patients (group 3), and healthy female (group 2) comparing with female patients (group 4), no significant effects were found in Ca concentration in male groups (1,3) and female groups (2,4). Ca concentration was **8.86 ± 0.09, 8.94 ± 0.12** in groups (1, 3), respectively, and **9.03 ± 0.136, 8.78 ± 0.16** in groups (2, 4), respectively. The same results are also represented in figures (3) and (4).

Calcium is an integrated element that is necessary and important for the health of the human body and performing its functions to the fullest. Calcium intake has been proven to be beneficial in preventing and treating osteoporosis, which has become one of the most serious public health problems around the world because of its medical repercussions on patients (**Akiyama *et al* 2020**).

In our study, the level of calcium in kidney patients was given in the current study a balance between the control groups and the patients, and this matter appeared naturally as a result of giving the patients nutritional supplements, including calcium doses.

Patients with chronic kidney disease (CKD) suffer from a marked disturbance in bone and mineral metabolism leading to a complex disorder called CKD. Disturbances begin in the early stages of CKD and increase with progressive kidney disease **(Isakova et al. (2011).** Biochemical changes of CKD include elevated and increased fibroblast growth factor and parathyroid hormone (PTH) levels, and decreased 1,25-dihydroxyvitamin D (1, 25) 25D), high serum phosphate, low blood calcium. Negative balance may increase the risk of osteoporosis and fractures, and positive balance may increase the risk of extra skeletal calcification and cardiovascular disease (**Mirani 2023)**. However, it is unlikely that negative or positive calcium balance alone is an initiating factor, and it has not been proven, although clinically plausible, that negative or positive calcium balance contributes to the development of CKD-MBD in adult patients (**Moorthi and Moa 2011**).

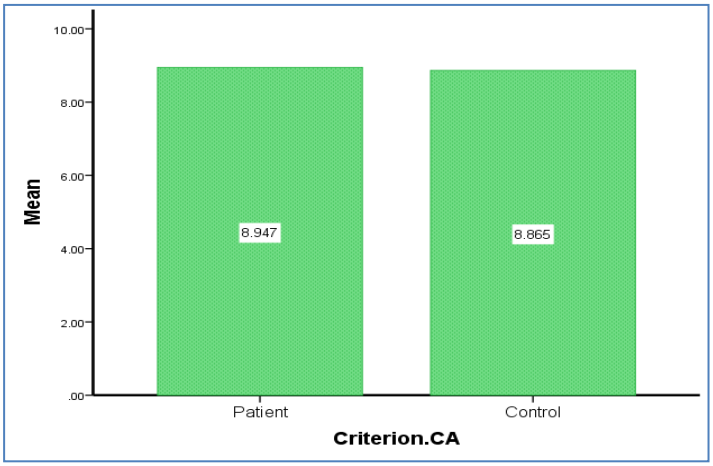

Figure (3): Shows the statistical differences in Ca in male with hemodialysis

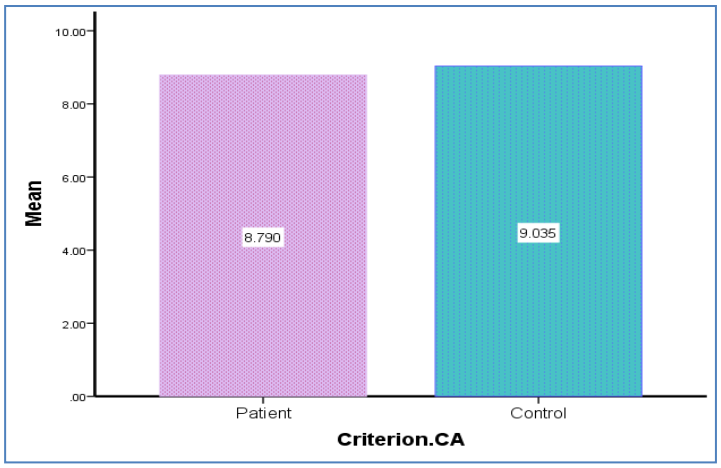

Figure (4): Shows the statistical differences in Ca in female with hemodialysis

1.3. Change in phosphorus (P) concentration in hemodialysis patients:

Table (1) summarizes the phosphorus concentration (P) concentration for healthy male (group1) comparing with male patients (group 3), and healthy female (group 2) comparing with female patients (group 4), P concentration was significantly higher in male groups (1,3) and female groups (2,4). P concentration was **3.22 ± 0.18**, **8.94 ± 0.12**in groups (1, 3), respectively, and **3.90 ± 0.20**, **5.21 ± 0.22**in groups (2, 4), respectively. The same results are also represented in figures (5) and (6).

Serum phosphate (P) is used to monitor the retention of P, which is the result of a decrease in the glomerular filtration rate (GFR), which gives clear and direct indicators of the extent of the efficiency of the kidneys. Therefore, any decrease in this rate gives data regarding patients regarding the possibility of any severe complications in the bones and in the kidneys. Cardiovascular system of patients with renal failure **(NKF 2002). (Maciel et al 2022).**

It should be noted that death rates are still alarmingly high despite their decline in the past two decades. Hyperphosphatemia (elevated blood phosphate levels) is seen in almost all patients with advanced CKD and is by far the largest remaining modifiable contributor to mortality in CKD patients. Studies have shown that phosphate retention leads to multiple physiological mechanisms associated with an increased risk of cardiovascular disease and diseases of the circulatory system in general, and increases fibroblast growth factor 23 and parathyroid hormone (PTH) levels, both of which are suggested to have internal effects that have a direct impact on Many diseases appear later, as a kind of pathological effect and the occurrence of phosphate retention in the dialysis patient)**Moawad 2022.(**Phosphate, calcium, and PTH levels are associated in a progressively worsening cycle with increasing washout intervals. Maladaptive upregulation of phosphate absorption is also likely to occur, leading to progressive hyperphosphatemia. It is worth noting that high phosphate levels within the normal range may be a risk factor for calcification of blood vessels, and thus, diseases of the blood vessels, the heart ,and the circulatory system in general, and deaths, and this is what doctors try to avoid by giving the patient the nutritional supplements or treatments necessary for the dialysis patient) .**McCullough 2021** .(Our study is completely consistent with **(Liu et**

al)2019 who proved that adult dialysis patients had elevated levels of creatinine and phosphate compared with the control group.

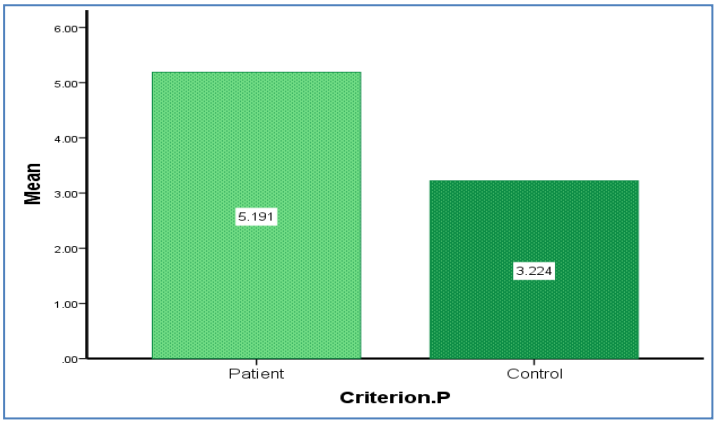

Figure (5): Shows the statistical differences in p in male with hemodialysis

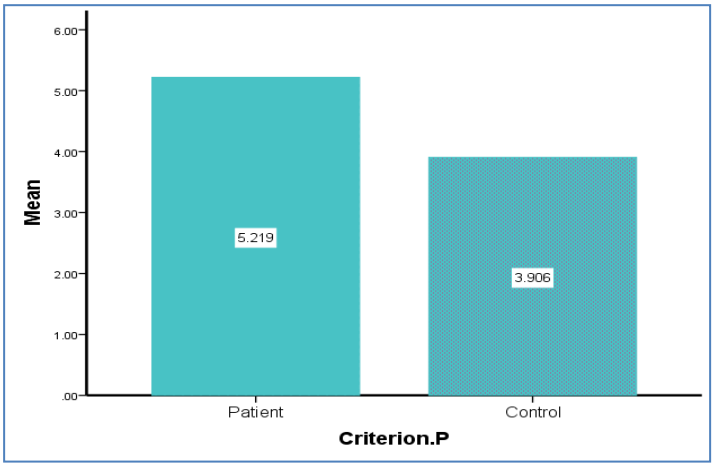

Figure (6): Shows the statistical differences in p in female with hemodialysis.

Conclusion:

PTH is one of the key hormones in regulating multiple organs and systems and calcium and phosphorus metabolism for whole body homeostasis due to altered or secreted PTH in a wide range of abnormalities in which calcium and phosphorus metabolism play an important role. Studies examining changes associated with dialysis vary from person to person depending on their health condition and medical history. What emerges from the studies reviewed here is that dialysis patients experience varying increases in the PTH hormone, especially in the late stage of long-term dialysis, as many studies have shown that an increase in PTH occurs in both sexes, with some differences between males and females. Females are interconnected and compatible with the physiological effect of some other stimuli, depending on the sexes. The current study showed that an increase in the PTH hormone and a difference in the levels of

phosphorus and calcium during illness is a dangerous indicator if the patients are not followed up and other causes are not linked to the dialysis patient.

Recommendations:

Kidney disease affects millions of people around the world, and often no symptoms appear in the initial stages and the disorder is not discovered until it reaches an advanced stage. A person with kidney disease or undergoing a transplant must take extra care to avoid additional pressure on the kidneys. The patient must also follow a specialized diet because like these patients, the body cannot digest everything properly and excrete it easily. Doctors also advise kidney patients to lose excess weight, exercise regularly, and quit smoking. If the patient suffers from diabetes or high blood pressure, he must undergo additional care to maintain blood pressure and blood sugar at normal levels, educate patients about the dangers of dialysis, and conduct educational programs to explain the seriousness of the disease in the event that patients do not follow the doctor's instructions. Continue Conducting research and studies that clarify and demonstrate the risk of high or low biochemical parameters or hormones associated with dialysis.

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