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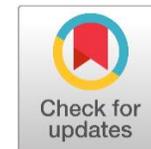
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# Iraqi Journal of Pharmacy

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Research Article:

## Evaluate the Fluctuation in the Level of PTH, and Assess the Relationship Between PTH and Some Biochemical Parameter in Chronic Kidney Disease Patients Undergoing Hemodialysis

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### Article Information

#### Article history:

Received on: 12 December 2023

Revised on: 17 January 2024

Accepted on: 10 February 2023

Published on: 01 March 2024

#### Keywords:

Parathyroid hormone,  
Chronic kidney disease,  
Renal function tests.

### Abstract

**Background:** As a key regulator of bone metabolism, parathyroid hormone (PTH) also modulates the homeostatic response to changes in plasma calcium concentrations. PTH values are often used in patients with "chronic kidney disease (CKD)" as a surrogate for assessing bone and mineral disease associated with CKD. **Objectives:** The present study sought to evaluate the PTH level alongside measured serum electrolytes and renal function in CKD patients. **Method:** This study was based on a cross-sectional comparative study which considered the sample size of 120 individuals who were divided into two groups, the control group (n=30) which had apparently healthy individuals, and the second group which consisted of (n=90) patients diagnosed with CKD, and associated medical conditions including hypertension and diabetes. Parathyroid hormone, calcium, phosphate, fasting blood sugar, creatinine, blood urea, serum sodium were measured. **Results:** The results summarize that the levels of PTH, FBS, phosphate, urea, and creatinine were significantly increased in the patients with CKD as compared to the healthy individuals. However, no marked differences were found in the values of Na, K, and Ca. **Conclusion:** PTH should be considered as a marker for CKD and outlined in the investigation and follow-up of the prognosis of these patients.

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## 1. Introduction

The chronic kidney diseases (CKD) is kidney chronic pathological conditions associated with a continuous renal function declining resulting in reduced glomerular filtration rate (GFR), reaching to down to GFR <15 ml/min/1.73 m<sup>2</sup>, at which renal dialysis or replacement ensued (1-3). Hypertension and diabetes seem to be the central causative underlying risk factor for kidney damage and hence CKD(1,4,5). These associated condition worsen the pathology of CKD overtime resulting in dysregulation of serum electrolyte with subsequent multiple impacts on vital organs (1,5-7).

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#### How to cite:

Alsarraf, Z., H., Saber, N., A., (2024). Evaluate the Fluctuation in the Level of PTH, and Assess the Relationship Between PTH and Some Biochemical Parameter in Chronic Kidney Disease Patients Undergoing Hemodialysis. *Iraqi J. Pharm.* 21), 15-19.

DOI: <https://doi.org/10.33899/iraqij.p.2024.145254.1076>

The CKD is associated with bone and systemic mineral dysregulation (2,8). This mineral dysregulation include calcium, phosphate, potassium, sodium, and chloride dysregulation, resulting in bone metabolic derangement's (1,5-7). Collectively, this coexistence of CKD with alteration in bone mineralization as chronic kidney disease-mineral and bone disorder (CKD-MBD) (8-10). Hence, bone health status should be monitored regularly through important measured biomarkers; for which the gold-standard is transiliac crest bone biopsy draw backed by being an invasive technique (11), therefore, measuring PTH and profiling the serum electrolytes could give a clue about bone health status. The following research aimed to evaluate the fluctuation in the level of PTH, and assess the relationship of PTH with systemically important biochemical markers in patients with chronic kidney disease.

## 2. Methods

This study was carried out at IBN-SINA Teaching Hospital in Mosul city. The study design is a cross-sectional comparative study consisting of sample size of 120 individuals who were divided into two groups, the control group (30 individuals) which were apparently healthy individuals, and the second group (90 patients) which consisted of the patients diagnosed with CKD, undergoing hemodialysis treatment with stage 4 (GFR = 15-29 mL/min) of both genders aged (20-69 year), and associated medical conditions including hypertension, diabetes and immunologic diseases. Patients were informed about their sample collection for the present study before their inclusion alongside blood pressure measurement.

A consent form of participation in the study was taken from both groups. The study was registered in College of Pharmacy/Ninevah University and approved by Ethical Committee of the College of Medicine at Ninevah University (Approval Letter no. 149 on 15.09.2022). The patients and control group were matched for demographic parameters. Cancer patients, patients with autoimmune diseases, and pregnant women were excluded from the study. Inclusion criteria included CKD patient with commonly coexisted diseases, such as, hypertension and diabetes.

The number of dialyses which were recorded for each patient per month was between six to eight sessions. The methods of measurement of studied parameters include creatinine (Jaffé reaction colourimetric method), calcium (colourimetric method), phosphate (blood gas analyzer), fasting serum glucose (colourimetric method), blood urea (colourimetric method), serum sodium (blood gas analyzer), and parathyroid hormone (VIDAS® PTH (1-84) were measured according to the instruction supplied by the manufacturer. The results of measured parameters were compared to control group. Data expressed as mean±SD. The statistical analysis of the data was done using SPSS version 24. Student t-test and correlation analysis were done for the secondary statistical analysis. A p-value of less than 0.05 was accepted as being significant in all types of statistical tests.

## 3. Results

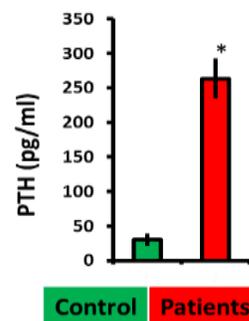
The demographic data of the studied groups are outlined in (Table 1). The patient's groups were matched regarding age, sex and BMI with no significant differences existing between groups.

**Table 1.** Demographic characteristics of the studied groups.

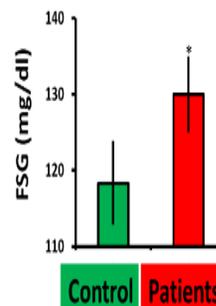
Demographic parameters	Control (n=30)	Patients (n=90)
Age (Years)±SD (range)	49±16 <sup>a</sup> (20-69) <sup>a</sup>	51±13 <sup>a</sup> (16-71) <sup>a</sup>
Sex (M/F)	14/16	15/15
BMI±SD	26.7±8 <sup>a</sup>	27±7 <sup>a</sup>
Duration of chronic diseases (Years)±SD (range)	-----	17±5.1 (1-20)
Duration of CKD (Years)±SD (range)	----	3±0.5 (0.5-5)

<sup>a</sup> Indicates a non-significant changes at p value > 0.05

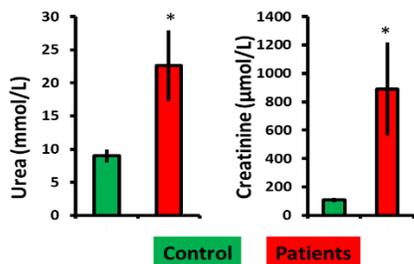
The results of the following research showed that the level of PTH was  $30 \pm 9.1$ pg/ml in the control group which was found to be significantly higher in the CKD group ( $263.4 \pm 28.71$  pg/ml) (Figure 1). The level of blood sugar was significantly ( $p < 0.05$ ) higher in the patients ( $131.1 \pm 5.3$ mg/dl) as compared to the control group ( $118 \pm 5$  mg/dl) (Figure 2). Urea and creatinine were significantly ( $p < 0.05$ ) higher in patients (Urea  $22.6 \pm 5.3$  mmol/l, Creatinine  $891.3 \pm 326.8$   $\mu$ mol/L) compared to control group (Urea  $9 \pm 1$  mmol/l, Creatinine  $110 \pm 15$   $\mu$ mol/l) (Figure 3). However, there was no marked difference ( $p > 0.05$ ) found in the values of Na (mmol/l), K( mmol/l), and Ca (mg/dL), which were 140, 4, and 4 in the control group, and 139.8, 4.75, and 3.57, in the patient group respectively (Figure 4). Phosphate (mmol/l) has significantly ( $p < 0.05$ ) elevated in patients  $1.7 \pm 0.5$  compared to the control group ( $1 \pm 0.35$ ), (Figure 4).



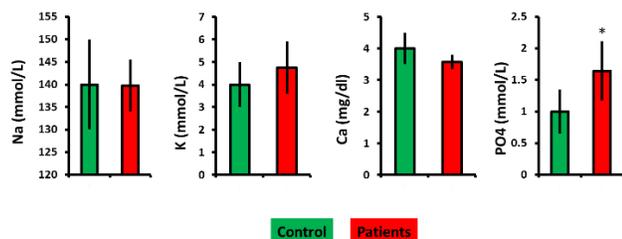
**Figure 1.** PTH level in patients with CKD on dialysis. Data expressed as mean ± SD. \* $p < 0.05$  as compared to another group.



**Figure 2.** FBS level in patients with CKD on dialysis. Data expressed as mean±SD. \* $p < 0.05$  as compared to another group.



**Figure 3.** Renal function tests in patients with CKD on dialysis. Data expressed as mean±SD. \*p<0.05 as compared to another group.



**Figure 4.** Electrolytes levels in patients with CKD on dialysis. Data expressed as mean±SD. \*p<0.05 as compared to another group.

The correlation test between PTH and measured parameters has shown a positive correlation between Calcium, Phosphate, Creatinine, and urea, whereas a weak or no correlation has been found between sodium, potassium, FBS and PTH (Table 2).

**Table 2.** Pearson correlation between PTH and measured parameters

Parameters compared to PTH	Correlation coefficient (r)
Ca	0.56
PO <sub>4</sub>	0.61
Na	0.04
Potassium	0.1
Creatinine	0.6
Urea	0.8
FBS	0.03

#### 4. Discussion

The present study result showed that PTH secretion greatly increased in patients with CKD when compared with health participant. Measurement of PTH concentrations in blood or plasma is frequently used as a noninvasive biochemical method to assess bone turnover in patients with CKD. These changes have also coexisted with elevated levels of electrolytes in particular phosphate significantly elevated.

Due to the kidney's critical role in managing bodily fluid, electrolytes, acid-base balance, and iron metabolism, electrolyte and mineral abnormalities are frequently seen in patients with decreased kidney function (12). However, the concentration of Na, K, and Ca in the present study has not changed compared to a healthy individual, these outcomes were similar to the study conducted by Hsiao et al.(2020), who reported that the serum sodium, potassium, and calcium levels have only significantly elevated in patients with end-stage CKD despite significantly positive correlation with parathyroid hormone (Table 2). Moreover, Hsiao et al.(2020), have reported that the progression of the disease further elevated these electrolytes regardless of the presence of other systemic diseases (such as diabetes or hypertension) (6). Osmotic diuresis, tube damage, and an inability to acutely shut off natriuretic pressures are the mechanisms hypothesized to be implicated in additional urine Na<sup>+</sup> loss in CKD(13). Aldosterone activity, which arises from sufficient sodium transport to the distal tubule and the cortical collecting duct, is necessary for urine K<sup>+</sup> excretion. A decrease in tubular Na<sup>+</sup> reabsorption causes the urine flow in remaining nephrons to increase dynamically; this adaptive process may also help to maintain urine K<sup>+</sup> excretion by causing a large drop in urine K<sup>+</sup> level. In contrast to our findings, some studies have reported that PTH elevation leads to increased serum calcium levels due to increased retention, however, these studies have enrolled patients with end-stage renal diseases (14,15). In agreement with earlier studies (13-15), the present study has reported only a slightly correlation with Na and K.

It has been reported that increased phosphate levels were associated with late-stage CKD patients due to reduced kidney excretion of phosphate (16, 17). Increased phosphate level has been reported to be a causative hallmark of vascular calcification and pathological bone mineralization and defective bone turnover (18). These pathological abnormalities associated with hyperphosphatemia have a direct influence on the heart with increased morbidity and

mortality in patients with CKD alongside other chronic diseases, such as diabetes mellitus (19). In the present study, hyperglycemia coexisted with hyperphosphatemia and there has been reported to further increase the chance of vasculopathy, especially calcification of the aorta when compared to either condition alone (either hyperglycemia or hyperphosphatemia) (19).

The present study has also confirmed that there is an elevation in the level of urea and creatinine. A combined elevation of phosphorous and uric acid leads to tissue toxicities with higher levels of polyamines (18). This study provides insight to the valuable diagnostic role of PTH on bone health status, however, the limitation of the present study includes small sample size which might not be representative of the general populations. Patients with associated diseases should be separately studied in term of hypertensive and diabetic groups. Finally, vitamin D should have been measured as a complementary factor to support the overall representative picture of the patients enrolled in the study.

## 5. Conclusion

The study concludes that the increased levels of PTH and creatinine were indicators of chronic kidney disease and their association with bone deficit. PTH monitoring could be used as a non-invasive marker for follow-up of bone mineralization in CKD patients to avoid using a more invasive diagnostic method.

## 6. Acknowledgment

The authors thanks IBN-SINA Teaching Hospital in Mosul city for the facilities in conducting this research .

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### تقييم مستوى هرمون الغدة الجار الدرقية وارتباطه ببعض المتغيرات البيوكيميائية لدى مرضى غسيل الكلى المزمن

#### الملخص

**المقدمة:** كمنظم رئيسي لعملية التمثيل الغذائي للعظام ، يقوم هرمون جار الغدة الدرقية أيضا بتعديل الاستجابة التمثالية للتغيرات في تركيزات الكالسيوم في البلازما. غالبا ما تستخدم قيم هرمون جار الغدة الدرقية في المرضى الذين يعانون من مرض الكلى المزمن كبديل لتقييم أمراض العظام والمعادن المرتبطة بمرض الكلى المزمن. الأهداف: سعت الدراسة الحالية إلى تقييم مستوى هرمون جار الغدة الدرقية جنبا إلى جنب مع قياس شوارد الدم ووظائف الكلى في مرضى الكلية المزمن.

**الطريقة:** استندت هذه الدراسة إلى دراسة مقارنة مقطعية أخذت في الاعتبار حجم العينة من 120 فردا تم تقسيمهم إلى مجموعتين ، المجموعة الضابطة (ن = 30) التي كان لديها أفراد أصحاء ظاهريا ، والمجموعة الثانية التي تألفت من (ن = 90) مريضا تم تشخيص إصابتهم بمرض الكلى المزمن ، والحالات الطبية المرتبطة بها بما في ذلك ارتفاع ضغط الدم والسكري. تم قياس هرمون الغدة الدرقية والكالسيوم والفوسفات وسكر الدم الصائم والكرياتينين واليوريا في الدم وصيديوم المصل. **النتائج:** تلخص النتائج أن مستويات هرمون جار الغدة الدرقية و مستوى السكر والفوسفات واليوريا والكرياتينين قد زادت بشكل ملحوظ في المرضى الذين يعانون من مرض الكلى المزمن مقارنة بالأفراد الأصحاء. ومع ذلك ، لم يتم العثور على اختلافات ملحوظة في قيم الصوديوم والبوتاسيوم والكالسيوم. **الاستنتاج:** يجب اعتبار هرمون جار الغدة الدرقية علامة على مرض الكلى المزمن وتحديدتها في التحقيق ومتابعة تشخيص هؤلاء المرضى.

**الكلمات المفتاحية :** هورمون الغدة الرقية ، امراض الكلى المزمنة ، اختبارات وظائف الكلى