Research article

Imbalances in parathyroid hormones and few electrolytes in patients with renal failure

Aseel Ibrahim Suhael[1], Lana Nazar Abdul-Razzaq[2], Majid M. Mahmood[3]

[1]Ministry of Education, Second Rusafa Directorate, Baghdad, Iraq
[2]Ministry of Education, Educational Rusafa Directorate 1, Baghdad, Iraq
[3]Department of Biology, College of Science, Mustansiriyah University, Baghdad, Iraq

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Corresponding author: **Majid M. Mahmood.** Email: majidmahmood93@yahoo.com

ABSTRACT

Introduction and Aim: Chronic kidney disease also referred as chronic renal disease is a condition in which there is a gradual loss of kidney function. End-stage renal failure (ESRD) is the final stage of the disease in which the kidneys cease to function, and the patient continues to depend on long-term dialysis. In this study we aimed to analyze the relationship between parathyroid hormone (PTH), electrolyte disturbances and vitamin D3 in ESRD patients and compare it to healthy individuals.

Materials and Methods: 100 outpatients (ages 30-70 years) from Al-Diwaniyah General Hospital and 49 healthy participants (ages 35-65 years) were investigated between July and October 2022.

Results: A significant increase in PTH concentrations was observed in the ESRD group 275.16 ± 224.03 pg/ml) when compared to the healthy group (44.42 ± 19.26 pg/ml). Similarly, phosphate concentrations differed significantly between ESRD patients and the healthy group (1.52 ± 0.53 vs. 1.04 ± 0.15 mmol/L, respectively).
A non-significant positive correlation was noticed between PTH and phosphate levels (p value = 0.068; r = 0.253). There was a significant (p-value 0.001) decrease in calcium levels between patients and healthy samples (2.06 ± 0.28 mmol/L vs. 2.36 ± 0.11, respectively), and a negative correlation (r = -0.536) between PTH and calcium levels. The vitamin D3 values showed no significant differences (p > 0.01), between ESRD patients and healthy subjects.

Conclusion: A positive correlation existed between serum PTH and phosphate levels in patients with ESRD. Hence these parameters could be monitored on a regular basis to ensure appropriate dietary and medical treatments.

Keywords: Electrolytes; parathyroid hormones; renal failure; vitamin D3.

INTRODUCTION

Chronic kidney disease (CKD) is a relatively common condition, in which the kidneys are damaged or lost its function. Worldwide, CKD has become more common and a leading cause of death (1,2). Electrolyte balance is necessary for homeostasis and is controlled by renal function (3). Magnesium, sodium, potassium, calcium, and phosphates are among the electrolytes whose metabolism is disrupted by CKD. Secondary hyperparathyroidism (SPTH), a rise in blood levels of parathyroid hormone (PTH), and poor calcium/ phosphorus balance are among the many side effects associated with CKD (4). SPTH results from hypocalcemia caused by phosphate retention and a lack of 1,25-dihydroxycholecalciferol production. PTH secretion increases as 1,25-dihydroxy cholecalciferol production declines due to increased serum phosphate levels (5).

PTH is a fundamental regulator of the homeostasis of a number of electrolytes. PTH regulates bone resorption to release calcium and compensate for a calcium deficiency in the blood (6). The PTH protein receptors are members of the G-protein-coupled receptor (GPCR) family found associated with bone, kidney, and cartilage. Calcium has a significant role in the biosynthesis of PTH. Studies on mice have indicated a significant reduction in blood calcium levels, leading to an increased transcription of the hormone within one hour (7). As for the rise in calcium level in the blood, the role of the enzyme may be diminished or absent during the process of the hormonal gene transcription. As a result, the parathyroid gland is in a condition of readiness and responds much more quickly to this fall in calcium than it does to a high amount of calcium (8). Vitamin D3 does not directly affect the secretion of PTH; rather, it inhibits the process of gene transcription for the hormone (9). Vitamin D3 entering the bloodstream through the skin or food is transformed to 25(OH)D3 by the enzyme 25-hydroxylase (25-OHase) in the liver. The 25(OH)D3 is released to the bloodstream and transported to the kidney, where the enzyme 25(OH)D31-hydroxylase (1-OHase) converts 25(OH) D3 to 1,25(OH)2D3 cholecalciferol (10). In this study, we aimed to find the relationship between blood PTH, serum vitamin D3, and several types of electrolytes in end-stage renal failure (ESRD) patients.

MATERIALS AND METHODS

Study population

The study conducted between July and October 2022, included 100 patients (60 men and 40 women) suffering from renal failure and on regular haemodialysis at the Department of Kidney Diseases, Al-Diwaniyah General Hospital, Baghdad. The study also included 49 healthy patients (30 men and 19 women) aged 35-65

years, who did not have signs of renal failure, diabetes, or a parathyroid disorder.

Clinical and laboratory parameters

The variables in this research were selected using a simple non-random selection procedure, and they were as follows: age, sex, weight, systolic blood pressure, diastolic blood pressure. Venous blood (5 mL) drawn from each participant was transferred to sterile tubes and kept at room temperature for 30 mins. This was followed by centrifugation at 3000 rpm for 10 mins to separate out the serum. The serum obtained was checked for PTH, phosphate, calcium, and vitamin D3 concentrations. The serum PTH was measured by the chemiluminescence immunoassay (CLIA) assay using the TOSOH AIA-360 instrument (Roche Diagnostics, Germany). Phosphorus and calcium levels were measured using the COBAS INTEGRAL analyzer (Roche Diagnostics, Germany). Quantitative determination of 25-OH Vitamin D was measured in all patients by enzyme-linked immunosorbent assay (ELISA) using a commercial kit (Vitamin D Enzyme Immunoassay Kit, Monocent, Inc., USA).

Statistical analysis

Data collected was subjected to statistical analysis using the SPSS software, version 20. The least significant difference (LSD) was also employed to evaluate differences. The ANOVA was used in finding the significant differences between the samples. The linear correlation coefficient was calculated, and correlation strength was measured by calculating Person's moment correlation.

RESULTS

In this study a significant correlation was observed between parathyroid hormone (PTH) levels with serum electrolyte levels in the end-stage renal failure (ESRD) patients (Table 1).

As seen from Table 1, there was a significant increase ((P < 0.001) in PTH concentration among ESRD patients (275.16 ±224.03pg/ml) in comparison to the healthy group (44.42±19.26 pg/ml). As for calcium levels, the tests revealed a drop in calcium levels in the patients relative to the healthy group; the healthy had 2.36 ± 0.11 mmol/L, and those with ESRD had 2.06 ± 0.28 mmol/L (Table 1). An association for serum PTH and vitamin D3 levels in ESRD patients showed no significant difference in their levels between ESRD patients and healthy subjects (33.08 ±11.87 ng/ml vs. 34.32 ± 4.05 ng/ml) (Table 1).

Table 1: Laboratory parameters tested in ESRD patients and healthy controls

Parameters	**ESRD patients (N=100)**	**Healthy controls (N=49)**
PTH (pg/ml)	275.16 ± 224.03***	44.42 ±19.26
Vitamin D3 (ng/ml)	34.32 ±4.05	33.08 ±11.87
Phosphate (mmol/L)	1.52± 0.53***	1.04±0.15
Calcium (mmol/L)	2.06 ±0.28***	2.36± 0.11

*** significant at p<0.001

Correlation studies for each of the parameters in this study, showed PTH and phosphate levels to be positively correlated in ESRD patients (r = 0.253, Fig.1). Similarly, a negative correlation (r = -0.537, Fig.2) was observed between PTH and calcium levels in the serum of ESRD patients. While drawing the relationship between vitamin D3 to and phosphate calcium levels in ESRD patients, it is noted that there is a non-significant positive correlation between Vitamin D3 and phosphate levels (r = 0.163, Fig.3), as well as Vitamin D3 and calcium levels (r = 0.205, Fig.4). Vitamin D3 on the other hand was seen to be negatively correlated to PTH (r=-0.058, Fig.5) in ESRD patients.

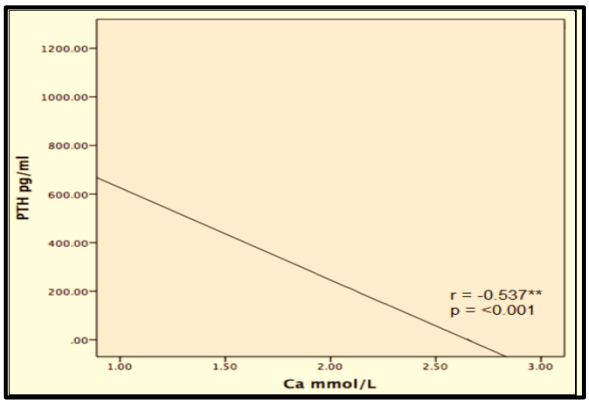

Fig. 2: The relationship between PTH and calcium

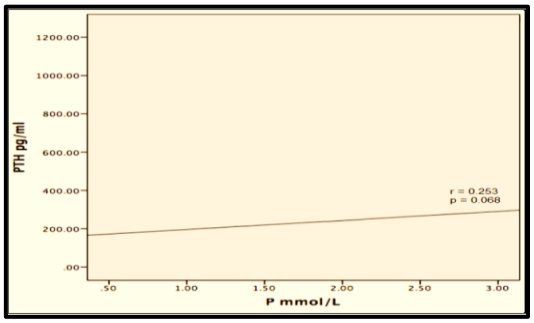

Fig. 1: The relationship between PTH and phosphate levels

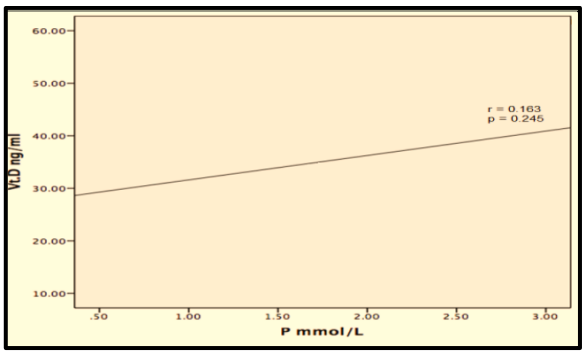

Fig. 3: The relationship between vitamin D3 and phosphate

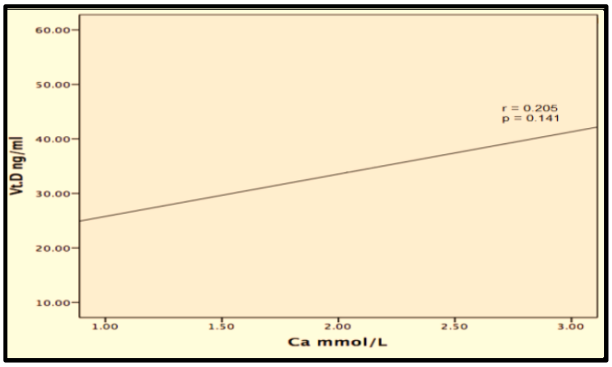

Fig. 4: The relationship between vitamin D3 and calcium

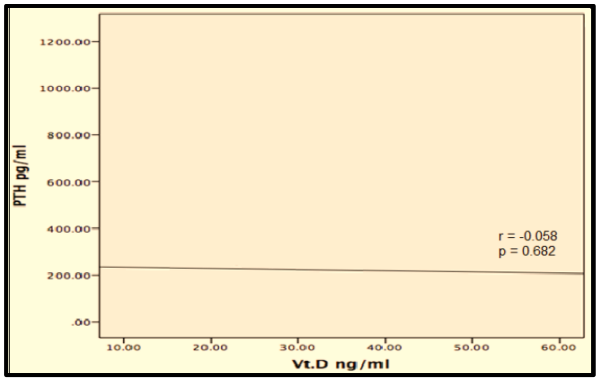

Fig. 5: The relationship between vitamin D3 and PTH

DISCUSSION

In this study we investigated the association between PTH, vitamin D3, and few electrolytes in end-stage renal failure (ESRD) patients and compared it to healthy individuals. Serum phosphate levels were raised in ESRD patients, supporting the theory that hyperphosphatemia causes parathyroid gland hypertrophy, which increases parathyroid hormone release, resulting in high phosphate concentrations in the blood (11). On the other hand, the study revealed a decrease for calcium levels in the ESRD patients relative to the healthy group which is consistent with previously published findings (12). It has been shown that the considerable decrease in calcium in ESRD patients is caused by a decrease in renal synthesis of 1,25-dihydroxycholecalciferol, which causes a decrease in calcium absorption in the gut, resulting in hypocalcaemia (13).

The imbalance in serum calcium and phosphate levels concerning PTH, renal, skeletal atrophy, and renal bone atrophy, as well as decreased renal production of vitamin D3, may be attributed to hypocalcemia (14). Moreover, reducing serum calcium caused by phosphate retention in the circulation and creating a complex with retained phosphorus stimulates PTH production (15). The persistence of low extracellular calcium for several weeks or months promotes hyperplasia of the parathyroid gland, a characteristic of excessive PTH (16).

Although all average values for vitamin 25 hydroxy vitamin D3 in both study groups were within the limits of vitamin sufficiency, a significant decrease was observed in patients with ESRD. This decrease can be attributed to malnutrition and lack of exposure to sunlight, which has a major role in the production of the vitamin (17). Since the kidneys are the main site of 1,25-dihydroxy vitamin D3 production from dihydroxy vitamin D through the enzyme 1α-Hydroxylase, the significant decrease of active vitamin D3 seen in ESRD patients could be due to loss of the enzyme (18).

Patients with ESRD exhibited a clear association between vitamin D3 and phosphate. The high level of phosphate in the blood serum stimulates FGF-23, which leads to severe inhibition of the enzyme 1-Hydroxylase, which in turn leads to a decrease in vitamin D3 (19). The development of hyperthyroidism is caused by a decrease in the glomerular filtration rate (GFR) to less than 30 ml/min, which inhibits the activity of the enzyme 1-Hydroxylase and, as a result, drastically reduces calcium absorption in the gut and blood calcium levels (20).

Vitamin D3 has several direct and indirect effects on the parathyroid gland. As in the case of chronic renal failure, the regulatory ability of the vitamin D3 receptors present in the parathyroid gland decreases as a result of low levels of vitamin D3 or a high level of phosphate, which leads to gland resistance to the vitamin and loss of the feedback mechanism (21). The opposite effect of the vitamin is on the parathyroid gland, so through this direct mechanism, PTH gene expression is stimulated, resulting in increased PTH secretion (22).

CONCLUSION

Patients with end-stage renal disease (ESRD) had lower blood calcium levels and higher PTH and phosphate levels when compared to healthy adults. These vital components are important aspects of ESRD; hence it must be addressed methodically.

CONFLICT OF INTEREST

Authors have no conflicts of interest.

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