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Full length research paper

# Relationship between parathyroid hormone and electrolytes in chronic kidney disease

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**Parathyroid hormone (PTH) has been identified as the main regulator of some electrolytes homeostasis. This study evaluated the relationship between PTH and these electrolytes as well as their ratios. The study population included 146 individuals with mean age of 50.18 ± 1.14 with various chronic kidney diseases and who were undialysed. 80 healthy subjects without kidney pathology but of similar age and sex distribution were used as controls. Estimated glomerular filtration rate (eGFR) was calculated using the 4v-MDRD and CKD was defined as eGFR <60 ml/min/1.73 $m^2$. For every mmol/l increase in the serum concentration of phosphate ($PO_4^{3-}$) ($r^2$ = 0.78, p < 0.0001), potassium ($K^+$) ($r^2$ = 0.00366, p < 0.0211) and magnesium ($Mg^{2+}$) ($r^2$ = 0.2861, p < 0.0001) there was a corresponding increase in serum concentration of PTH with beta values of 0.005, 0.0007, 0.001 respectively. However, there was no linear relationship between sodium ($Na^+$) and PTH ($r^2$ = 0.0013, p = 0.6687). The serum concentration of PTH decreased, for every mmol/l increase in the serum concentrations of calcium ($Ca^{2+}$) ($r^2$ = 0.33, p < 0.0001). Excess PTH is linked with derangements in the metabolism of electrolytes like calcium, magnesium, phosphorus and potassium in subjects presenting with CKD and contributes to a plethora of complications.**

**Keywords:** Parathyroid hormone; electrolytes; metabolism; hypocalcaemia; chronic kidney disease.

## Introduction

The occurrence of chronic kidney disease (CKD), a highly prevalent condition, has been escalating in recent years. High mortality and morbidity rates have been observed in CKD patients, compared with a matched general population (Foley *et al*., 1998; Yeo *et al*., 2004). Electrolytes are the key to homeostasis and furthermore, their regulation is dependent upon renal function. CKD is associated with aberrations in the metabolism of electrolytes such as calcium, phosphates, magnesium,sodium and potassium.Among the numerous complications associated with CKD is secondary hyperparathyroidism (SPTH), which is characterized by an increase in the serum concentration of parathyroid hormone (PTH) and deranged homeostasis of calcium and phosphorus (Slatopolsky *et al*., 1999). Secondary hyperparathyroidism arises due to hypocalcaemia, consequent to phosphate retention and deficient synthesis of 1, 25dihydroxycholecalciferol (Salusky *et al*., 1987). As a result of elevated serum phosphate concentration, secretion of PTH is increased as

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production of 1, 25 dihydroxycholecalciferol decreases. This results in increased urinary excretion of serum phosphate and thus maintenance of normal serum levels of calcium and phosphate. The target organs of PTH are the kidneys and the skeleton (Juppner *et al*., 1991; Hruska and Khan, 2000). An elevated serum PTH level occurs early in the course of the disease and plays an essential role in the development of renal osteodystrophy (Malluche *et al*., 1976; Slatopolsky *et al*.,1999). Various studies have identified PTH as the main regulator of calcium (Hamann and Lane, 2006) phosphate (Slatopolsky *et al*., 1996), magnesium (Mountokalakis, 1990; Navarro *et al*., 1997) and potassium (Sugarman and Kahn, 1988; Soliman *et al*., 1989) homeostasis.

Therefore this study was conducted to evaluate the relationship between PTH and the afore-mentioned electrolytes and their ratios among CKD patients in Ghana.

## Materials and Methods.

### Study area and subjects

This study was carried out at the Komfo Anokye Teaching Hospital (KATH), Kumasi and Tamale Teaching Hospital (TTH) between August 2007 and September 2009. One hundred and forty six (146) patients comprising of eighty (80) females and sixty-six (66) males within age range 20-80 years were signed on as cases. Patients with clinically diagnosed CKD including those yet to start dialysis were randomly selected for the study. Patients on any form of dialysis were excluded from the study. The aetiology of the CKD ranged from diabetic nephropathy, 90(61.6%) patients; chronic glomerulonephritis, 12(8.2%) patients; adult polycystic kidney disease, 1(0.7%) patient; hypertensive nephropathy, 10(6.8%) patients and chronic kidney disease of unknown aetiology, 33(22.6%) patients. Eighty (80) healthy volunteers of similar age and sex distribution were studied as controls. The participation of the respondents who are all indigenes of Ghana was voluntary and informed consent was obtained from each of them. The study was approved by the School of Medical Sciences and KATH Committee on Human Research, Publication and Ethics (SMS/KATH/CHRPE).

### Sample collection

Venous blood samples were drawn from each study participant after an overnight fast (12 – 14 hours), between 7am and 10am. About 5 ml of venous blood was collected out of which three (3) ml was dispensed into vacutainer® plain tubes and 2 ml into fluoride oxalate tubes. After centrifugation at 500 g for 5 minutes, the serum and plasma were stored at - 80°C until assayed.

### Biochemical assays

Serum biochemistry was performed with ATAC® 8000 Random Access Chemistry System (Elan Diagnostics, Smithfield, RI, USA). Parameters that were determined included; sodium ($Na^+$), potassium ($K^+$), magnesium ($Mg^{2+}$), calcium ($Ca^{2+}$), phosphate ($PO_4^{3-}$), albumin, fasting blood glucose (FBG) and creatinine (CRT). The following were also calculated; adjusted calcium was calculated from the formula: Adjusted calcium (mmol/l) = total calcium (mmol/l) + 0.02 × [40 – serum albumin (g/dl)]. The methods adopted by the automated instrument for the determination of the above parameters were predetermined by the reagent manufacturer - JAS™ diagnostics, Inc. (JAS Diagnostics, Inc. Miami Florida, USA).

### Hormonal assays

Serum intact PTH was measured by an immunoenzymatic assay, a solid phase Enzyme Amplified Sensitivity immunoassay performed on microtiter plates (Genway Biotech Incorporated, USA. Cat. No.: 40-056-205022).

### Estimation of GFR

The 4-variable modification of diet in renal disease (4v-MDRD) equation was used to calculate the estimated GFR (eGFR) of both subjects and controls using serum creatinine.

$$4v-MDRD = 186 \times SCr^{-1.154} \times age^{-0.203} \times (1.212\ if\ black) \times (0.742\ if\ female)$$

This equation has been found to be the most accurate among the renal function equations in CKD applicable to Ghanaians (Owiredu *et al*., 2008).

### Staging of CKD

The GFR results from the equations was used to divide the study population into five categories corresponding with the five stages of CKD in the kidney disease outcome quality initiative (K/DOQI) CKD classification (National Kidney Foundation, 2002). The staging classified GFR ≥ 90 ml/min/1.73 $m^2$ as stage 1; 60-89 ml/min/1.73 $m^2$ as stage 2; 30-59 ml/min/1.73 $m^2$ as stage 3; 15-29 ml/min/1.73 $m^2$ as stage 4; and < 15 ml/min/1.73 $m^2$ as stage 5.

### Blood pressure (Krotkoff 1 and 5)

Blood pressure was measured by trained personnel using a mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after

subjects had been sitting for >5 min in accordance with the recommendation of the American Heart Association (Kirkendall *et al*., 1967). Duplicate measurements were taken with a 5-minute rest interval between measurements and the mean value was recorded to the nearest 2.0 mmHg.

### Statistical analysis

GraphPad Prism version 5.00 for windows was used for statistical analysis (GraphPad software, San Diego California USA, www.graphpad.com).The results are expressed as Means ± SEM. Unpaired t-test was used to compare mean values of continuous variables and $\chi^2$ was used to compare discontinuous variables. Relationship between the various electrolytes, electrolyte ratios and parathyroid hormone was assessed by linear regression. Odds ratio (OR, s) (with 95% CI) of CKD and controls with high or low electrolytes was calculated using chi-square. A level of $p<0.05$ was considered as statistically significant.

## Results

### Electrolytes and electrolyte ratios in CKD patients

Table 1 shows the demographic, electrolyte and electrolyte ratios of CKD test subjects compared to controls. From this study, the mean ± SEM of $Na^+$, $Ca^{2+}$, $Ca^{2+}/Mg^{2+}$ ratio, $K^+/Mg^{2+}$ ratio, $Na^+/Mg^{2+}$ ratio, $Na^+/K^+$ ratio and $Ca^{2+}/K^+$ ratio were significantly lower, whereas $K^+$, blood pressure (SBP, DBP), $Mg^{2+}$, $PO_4^{3-}$, PTH, eGFR, FBG, $Na^+/Ca^{2+}$ ratio were significantly higher in the CKD patients, compared to the controls. However, the mean ages and Adj Ca were similar in both CKD subjects and controls.

When the CKD patients were stratified by gender, serum $K^+$, creatinine and e GFR significantly increased whereas $Na^+/K^+$ ratio significantly decreased in the males, compared to the females. The following parameters were significantly decreased in CKD subjects with elevated PTH: DBP, $Ca^{2+}$, $Mg^{2+}$, $Na^+/Mg^{2+}$ ratio, $Na^+/Ca^{2+}$ ratio, $Ca^{2+}/Mg^{2+}$ ratio, $K^+/Mg^{2+}$ ratio and eGFR whereas serum creatinine increased significantly in CKD subjects with high PTH (Table 1).

### Electrolytes and electrolyte ratios based on stratification of CKD

Table 2 represents the demographic and biochemical parameters during various stages of CKD. Serum $K^+$, $Mg^{2+}$ and PTH levels increased from stages 1 to 5. The increases reached statistical significance at stage 1 and stages 3 to 5; stages 3 to 5, and stages 2 to 5 for $K^+$, $Mg^{2+}$ and PTH respectively. Serum phosphate decreased initially at stage 2, and increased reaching statistical significance at stages 3 to 5. $Na^+$, SBP and DBP decreased from stages 1 to 2 and increased afterwards. The decrease reaches statistical significance between stages 2 to 5; stages 3 and 5 for $Na^+$ and; SBP and DBP respectively. Adj Ca decreased from stage 1 to 5 reaching statistical significance at stages 4 and 5 respectively. Serum $Ca^{2+}/K^+$ ratio and $Na^+/K^+$ ratio levels increased significantly from stages 1 to 2 and decreased significantly afterwards. $Ca^{2+}/Mg^{2+}$ ratio, $Na^+/Mg^{2+}$ ratio, and $K^+/Mg^{2+}$ ratio decreased from stages 1 to 5, reaching statistical significance at stages 3 to 5 for $Ca^{2+}/Mg^{2+}$ ratio and $K^+/Mg^{2+}$ ratio; and stages 2 to 4 for $Na^+/Mg^{2+}$ ratio respectively (Table 2).

### Odds ratio of developing high and low electrolyte level

Table 3 represents odds ratios of high and low levels of electrolytes among controls and CKD subjects. The risk of developing hypermagnesaemia, hyperkalaemia and hyperphosphataemia was 36 folds (OR = 36.5; 95% CI =12.6-105.5), 9 times (OR = 9.3; 95% CI = 3.5 -24.5) and about 30 times (OR = 29.6; 95% CI = 12.5-70.0) high in the CKD subjects compared to the controls. However, hypernatraemia was less likely in the CKD patients compared to the controls (OR = 0.3; 95% CI = 0.1-0.6). Furthermore, the risk of hyponatraemia (OR = 9.06; 95% CI = 3.4-23.8) and hypocalcaemia (OR = 7.8; 95% CI = 3.7-16.3) were 9 and 8 times more pronounced in the CKD subjects compared to the controls. Conversely, the risk of hypophosphataemia was 14 times more pronounced in the controls compared to the CKD subjects (OR = 0.1; 95% CI = 0.0-1.5).

Figures 1 A-D shows a linear regression analysis of the various electrolytes and their ratios in relation to PTH. For every mmol/l increase in the serum concentration of $PO_4^{2-}$ ($r^2 = 0.78$, $p < 0.0001$) (Figure 1 A), $K^+$ ($r^2 = 0.28$, $p < 0.0001$) (Figure 1C) and $Mg^{2+}$ ($r^2 = 0.004$, $p = 0.0211$) (Figure 1 D) there was a corresponding increase in serum concentration of PTH with beta values of 0.005, 0.0007 and 0.001, respectively. However, there was no linear relationship between $Na^+$ and PTH ($r^2 =0.001$, $p = 0.6687$) (Figure 1 B). Conversely, there was a corresponding decrease in the serum concentration of PTH, for every mmol/l increase in the serum concentrations of $Ca^{2+}$ ($r=0.33$, $p < 0.0001$) (Figure 2 A), $Ca^{2+}/Mg^{2+}$ ratio ($r^2 = 0.33$, $p < 0.0001$) (Figure 2 B), $Na^+/Mg^{2+}$ ratio ($r^2 = 0.26$, $p < 0.0001$) (Figure 2 C) and $K^+/Mg^{2+}$ ($r=0.19$, $p< 0.0001$) (Figure 2 D) with beta values of -0.001, -0.003, -0.005 and -0.154 respectively.

Furthermore, as shown in Figure 3 A-C, there was an inverse relationship between $Na^+/K^+$ ratio ($r^2 = 0.04$, $p< 0.0151$), $Ca^{2+}/K^+$ ratio ($r^2 = 0.28$, $p < 0.0001$) and PTH with beta values of -0.005 and -0.0002 whereas for every mmol/l increase in $Ca^{2+}/Na^+$ ratio ($\beta = 0.0373$, $r^2 = 0.34$, $p < 0.0001$) there was an increase in PTH.

**Table 1:** Demographic and biochemical characteristics of the study population

| | | | | Stratification of CKD subjects | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Gender | | | Levels of PTH | | |
| **Parameter** | **Control (n=80)** | **Subjects (n=146)** | **P Value** | **Female (n=80)** | **Male (n=66)** | **P Value** | **Normal PTH (n= 20)** | **High PTH (n=126)** | **P Value** |
| Age (years) | 46.35 ± 1.96 | 50.18 ± 1.14 | 0.0720 | 49.46 ± 1.36 | 51.05 ± 1.91 | 0.4919 | 47.61 ± 3.90 | 50.55 ± 1.18 | 0.3953 |
| SBP (mmHg) | 120.70 ± 1.82 | 140 ± 3.84 | <0.0001 | 133.00 ± 2.58 | 131.40 ± 2.78 | 0.6740 | 135.00 ± 7.58 | 132.00 ± 1.9 | 0.6130 |
| DBP (mmHg) | 70.42 ± 1.25 | 90.32 ± 2.61 | <0.0001 | 81.96 ± 1.69 | 81.56 ± 1.80 | 0.8725 | 89.38 ± 6.22 | 80.83 ± 1.13 | 0.0281 |
| FBG (mmol/l) | 5.31 ± 0.17 | 8.75 ± 0.33 | <0.0001 | 9.00 ± 0.47 | 8.44 ± 0.47 | 0.4053 | 9.18 ± 1.09 | 8.69 ± 0.35 | 0.6423 |
| $Na^+$ (mmol/l) | 141.90 ± 0.61 | 137.10 ± 0.48 | <0.0001 | 137.10 ± 0.564 | 136.70 ± 0.85 | 0.6740 | 137.00 ± 2.15 | 136.90 ± 0.47 | 0.9590 |
| $K^+$ (mmol/l) | 4.25 ± 0.08 | 4.87 ± 0.05 | <0.0001 | 4.72 ± 0.06 | 4.98 ± 0.08 | 0.0144 | 4.93 ± 0.14 | 4.82 ± 0.05 | 0.5014 |
| $Mg^{2+}$ (mmol/l) | 0.80 ± 0.03 | 1.15 ± 0.03 | <0.0001 | 1.12 ± 0.04 | 1.19 ± 0.05 | 0.2743 | 0.81 ± 0.04 | 1.20 ± 0.04 | 0.0002 |
| t $Ca^{2+}$ (mmol/l) | 2.21 ± 0.03 | 2.04 ± 0.02 | <0.0001 | 2.02 ± 0.02 | 2.07 ± 0.04 | 0.2797 | 2.22 ± 0.03 | 2.01 ± 0.02 | 0.0030 |
| Adj Ca (mmol/l) | 2.14 ± 0.05 | 2.12 ± 0.02 | 0.7211 | 2.12 ± 0.03 | 2.12 ± 0.03 | 0.9683 | 2.34 ± 0.40 | 2.09 ± 0.02 | 0.0003 |
| $PO_4^{3-}$ (mmol/l) | 1.25 ± 0.05 | 2.27 ± 0.08 | <0.0001 | 2.16 ± 0.10 | 2.41 ± 0.14 | 0.1577 | 1.60 ± 0.13 | 2.37 ± 0.09 | 0.0026 |
| $Na^+/K^+$ | 33.29 ± 0.78 | 28.77 ± 0.32 | <0.0001 | 29.44 ± 0.42 | 27.93 ± 0.49 | 0.0198 | 28.17 ± 0.89 | 28.85 ± 0.34 | 0.4873 |
| $Na^+/Mg^{2+}$ | 203.60 ± 6.09 | 135.30 ± 4.15 | <0.0001 | 139.60 ± 5.76 | 130.00 ± 05.94 | 0.2536 | 178.00 ± 10.70 | 129.20 ± 4.24 | <0.0001 |
| $Na^+/Ca^{2+}$ | 63.93 ± 1.62 | 68.41 ± 0.87 | <0.0001 | 68.98 ± 1.05 | 67.70 ± 1.47 | 0.4700 | 61.94 ± 1.35 | 69.32 ± 0.95 | 0.0050 |
| $Ca^{2+}/K^+$ | 0.52 ± 0.01 | 0.43 ± 0.01 | <0.0001 | 0.43 ± 0.01 | 0.42 ± 0.01 | 0.5259 | 0.45 ± 0.01 | 0.42 ± 0.01 | 0.1604 |
| $Ca^{2+}/Mg^{2+}$ | 3.26 ± 0.10 | 2.06 ± 0.07 | <0.0001 | 2.09 ± 0.10 | 2.02 ± 0.11 | 0.6629 | 2.90 ± 0.12 | 1.94 ± 0.07 | <0.0001 |
| $K^+/Mg^{2+}$ | 6.19 ± 0.15 | 4.76 ± 0.15 | <0.0001 | 4.79 ± 0.20 | 4.71 ± 0.22 | 0.7861 | 6.47 ± 0.48 | 4.51 ± 0.14 | <0.0001 |
| PTH (pg/ml) | 49.33 ± 1.51 | 210.80 ± 13.72 | <0.0001 | 203.50± 17.15 | 219.80 ± 22.27 | 0.5575 | | | |
| e GFR (ml/min/ 1.73 $m^2$) | 92.40 ± 5.67 | 57.61 ± 4.15 | <0.0001 | 50.16 ± 4.12 | 66.79 ± 7.63 | 0.0460 | 134.70 ± 12.26 | 46.69 ± 3.46 | <0.0001 |

SBP= Systolic blood pressure; DBP = Diastolic blood pressure; FBG= Fasting blood glucose; t$Ca^{2+}$=Total calcium; Adj Ca=Adjusted calcium; PTH = Parathyroid hormone; eGFR=Estimated Glomerular filtration rate; CRT = Creatinine.

**Table 2.** Demographic and biochemical parameters during various stages of chronic kidney disease

| | CKD STAGE (ml/min/1.73m$^2$) | | | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **Controls (n=80)** | **1 (n=24)** | **2 (n=35)** | **3 (n=37)** | **4 (n=25)** | **5 (n=24)** | **P Value** |
| $K^+$ (mmol/l) | 4.25 ± 0.07 | 3.84 ± 0.08* | 4.60 ± 0.09 | 4.71 ± 0.10** | 4.80 ± 0.14** | 5.15 ± 0.10*** | <0.0001 |
| $Na^+$ (mmol/l) | 142.00 ± 0.61 | 136.30 ± 1.67*** | 138.10 ± 0.93* | 136.20 ± 0.66*** | 137.50 ± 1.11* | 135.30 ± 1.06* | <0.0001 |
| $Mg^{2+}$ (mmol/l) | 0.80 ± 0.02 | 0.81 ± 0.03 | 0.91 ± 0.04 | 1.25 ± 0.06** | 2.35 ± 0.21*** | 4.60 ± 0.22*** | <0.0001 |
| $PO_4^{3-}$ (mmol/l) | 1.25 ± 0.05 | 1.53 ± 0.06 | 1.39 ± 0.06 | 2.00 ± 0.09*** | 2.98 ± 0.10*** | 3.92 ± 0.10*** | <0.0001 |
| t $Ca^{2+}$ (mmol/l) | 2.21 ± 0.03 | 2.19 ± 0.03 | 2.18 ± 0.04 | 2.08 ± 0.03 | 1.88 ± 0.04*** | 1.78 ± 0.08*** | <0.0001 |
| Adj Ca (mmol/l) | 2.14 ± 0.05 | 2.28 ± 0.04 | 2.27 ± 0.04 | 2.17 ± 0.04 | 2.00 ± 0.03 | 1.78 ± 0.04*** | <0.0001 |
| $Ca^{2+}/Mg^{2+}$ | 2.91 ± 0.11 | 3.12 ± 0.20 | 2.62 ± 0.13 | 1.92 ± 0.14*** | 1.10 ± 0.05*** | 0.89 ± 0.06*** | <0.0001 |
| $K^+/Mg^{2+}$ | 6.19 ± 0.153 | 6.13 ± 0.38 | 5.51 ± 0.27 | 4.25 ± 0.28*** | 3.54 ± 0.21*** | 3.54 ± 0.21*** | <0.0001 |
| $Na^+/K^+$ | 33.29 ± 0.78 | 28.46 ± 0.96 | 29.74 ± 0.62*** | 29.32 ± 0.64*** | 28.76 ± 0.77*** | 26.80 ± 0.54*** | <0.0001 |
| $Na^+/Ca^{2+}$ | 63.93 ± 1.62 | 62.59 ± 1.54 | 63.80 ± 1.23 | 65.78 ± 0.86 | 74.11 ± 1.93*** | 79.05 ± 2.81*** | <0.0001 |
| $Na^+/Mg^{2+}$ | 203.60 ± 6.09 | 174.70 ± 8.56 | 163.00 ± 7.86*** | 122.90 ± 8.06*** | 116.20 ± 6.13*** | 94.41 ± 5.66 | <0.0001 |
| $Ca^{2+}/K^+$ | 0.53 ± 0.01 | 0.45 ± 0.10** | 0.47 ± 0.01** | 0.44 ± 0.01*** | 0.39 ± 0.01*** | 0.35 ± 0.01*** | <0.0001 |
| PTH (pg/ml) | 49.33 ± 1.51 | 69.03 ± 2.21 | 95.23 ± 3.14*** | 141.10 ± 7.43*** | 327.20 ± 14.91*** | 515.80 ± 7.20*** | <0.0001 |
| FBG (mmol/l) | 5.31 ± 0.17 | 8.19 ± 0.81 | 8.55 ± 0.85 | 8.95 ± 0.70 | 10.66 ± 0.93* | 7.28 ± 0.71 | <0.0001 |
| SBP (mmHg) | 120.70 ± 1.82 | 129.1 ± 3.38* | 126.00 ± 3.70 | 134.3 ± 3.82* | 135.6 ± 4.36 | 136.00 ± 4.36* | 0.005 |
| DBP (mmHg) | 70.21 ± 1.26 | 79.2 ± 2.70*** | 78.92 ± 1.85* | 79.43 ± 1.87* | 84.20 ± 2.80 | 90.50 ± 4.94*** | <0.0001 |

eGFR ≥ 90 ml/min/1.73 m$^2$ = stage 1; 60-89 ml/min/1.73 m$^2$ = stage 2; 30-59 ml/min/1.73 m$^2$ = stage 3; 15-29 ml/min/1.73 m$^2$ = stage 4; and < 15 ml/min/1.73 m$^2$ = stage 5

**Table 3.**Odds ratios of high and low levels of electrolytes among controls and CKD

| **Parameter** | **Control (n=80)** | **Subjects (n=146)** | **OR (95% CI)** | **P Value** |
|---|---|---|---|---|
| *High Electrolytes* | | | | |
| Hypernatraemia | 17/80 (21.25%) | 10/146 (6.85%) | 0.27 (0.12-0.63) | 0.0023 |
| Hyperkalaemia | 5/80 (6.25%) | 56/146 (38.35%) | 9.33 (3.55-24.5) | <0.0001 |
| Hypermagnesaemia | 4/80 (5.00%) | 96/146 (65.75%) | 36.48 (12.61-105.50) | <0.0001 |
| Hypercalcaemia | 5/80 (6.25%) | 8/146 (5.48%) | 0.87 (0.27-2.75) | 0.7746 |
| Hyperphosphataemia | 7/80 (8.75%) | 108/146 (74.00%) | 29.64 (12.55-70.00) | <0.0001 |
| *Low Electrolytes* | | | | |
| Hyponatraemia | 5/80 (6.25%) | 55/146 (37.67%) | 9.06 (3.45-23.81) | <0.0001 |
| Hypokalaemia | 1/80 (1.25%) | 0/146 (0.00%) | 0.18 (0.01-4.50) | 0.354 |
| Hypomagnesaemia | 1/80 (1.25) | 0/146 (0.00%) | 0.18 (0.01-4.50) | 0.354 |
| Hypocalcaemia | 10/80 (12.50%) | 77/146 (52.74%) | 7.8 (3.73-16.34) | <0.0001 |
| Hypophosphataemia | 3/80 (3.75%) | 0/146 (0.00%) | 0.07 (0.00-1.48) | 0.0433 |

OR=Odds ratio

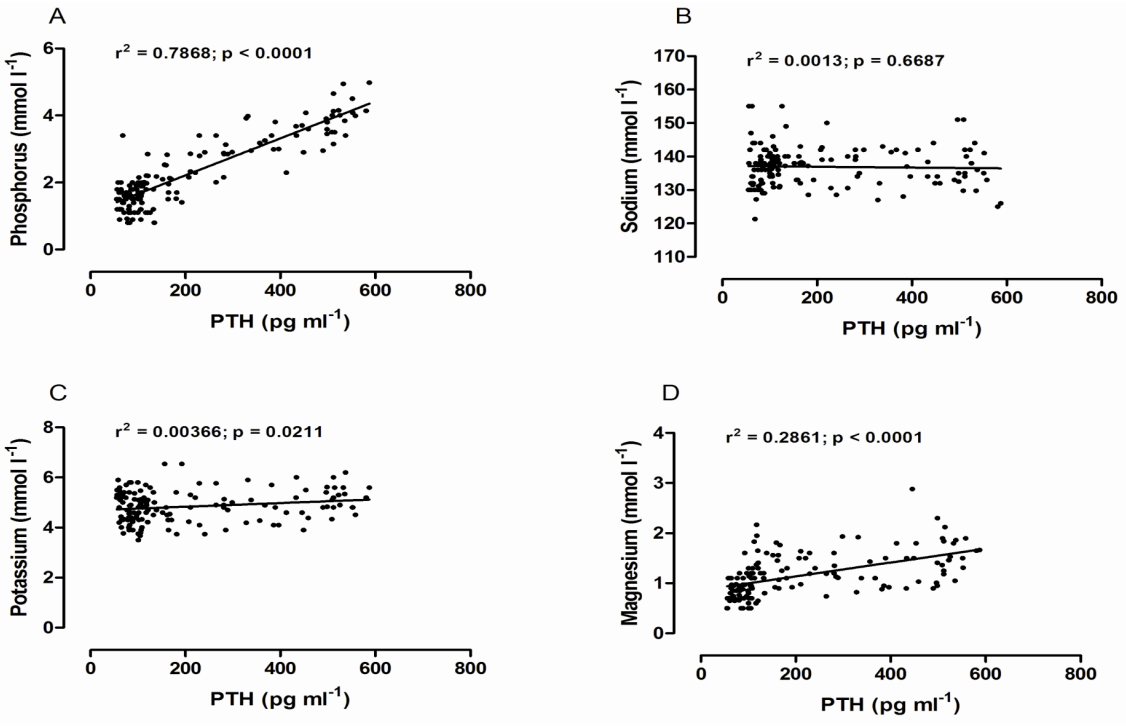


**Figure 1***: Linear regression graphs of phosphate (A), sodium (B), potassium (C), and magnesium (D) against parathyroid hormone (PTH).*

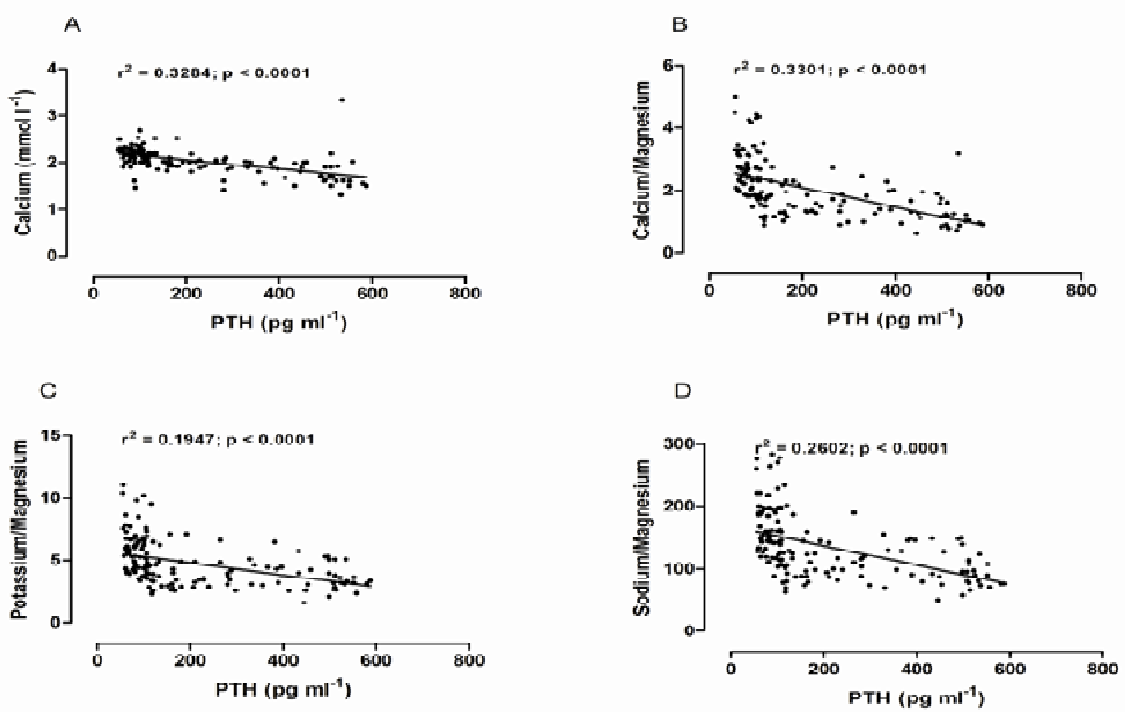


**Figure 2:** *Linear regression of calcium (A), calcium/magnesium (B), potassium/magnesium (C) and sodium/magnesium (D) against parathyroid hormone (PTH).*

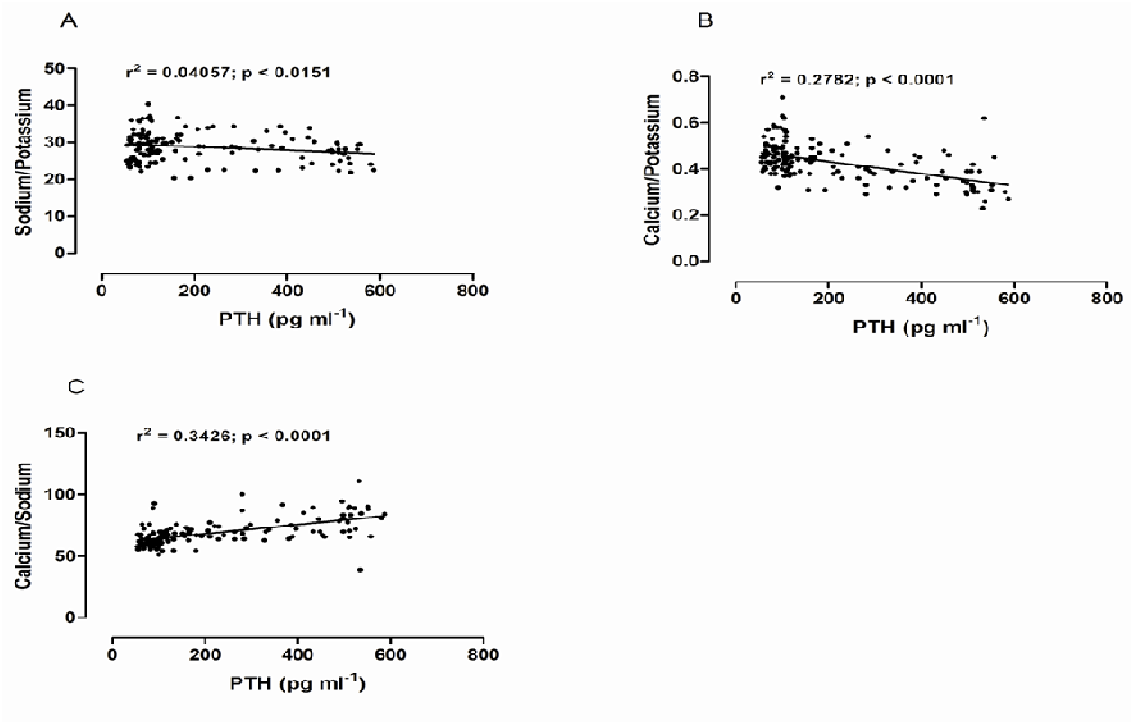


***Figure 3:*** *Linear regression graphs of sodium/potassium (A), calcium/potassium (B) and calcium/sodium (C) against parathyroid hormone (PTH).*

## Discussion

This study compared the relationship between serum electrolytes and their ratios with parathyroid hormone (PTH) in CKD patients. The significant increase in the serum PTH level observed in this study (Table 1) among the cohort of subjects with CKD compared to normal controls, as well as the progressive increase in the serum concentration of PTH as kidney function deteriorates (Table 2) has been observed in earlier studies (Pitts *et al*., 1988; Levin *et al*., 2007). Persistent increase in PTH is known to cause secondary hyperparathyroidism which has been implicated in a myriad of abnormalities including cardiovascular, metabolic, hematologic, and immunologic abnormalities (Meytes *et al*., 1981; Massry and Smogorzewski, 1994; Chiu *et al*., 2000).

In CKD patients, magnesium is mostly excreted via the renal route; consequently an elevated serum magnesium value is anticipated (Mountokalakis, 1990) even though normal or decreased values may be found as a result of decreased dietary intake, together with diminished absorption as a result of deficient synthesis of the active metabolite of vitamin D by the damaged kidney (Schmulen *et al*., 1980; Spencer and Osis, 1988). The serum magnesium levels were found to be significantly higher in this cohort of subjects with CKD (Table 1) compared to the controls, an observation that is consistent with earlier reports (Mountokalakis, 1990; Agus and Massry, 1994; Massry and Smogorzewski, 1994). Additionally, the CKD patients were several folds at risk of hypermagnesaemia from this study as compared to the controls (Table 3).

There have been inconsistent results studies of the relationship between Mg and PTH in CKD (Massry *et al*., 1970; Ferment *et al*., 1987). However, in this study we observed a positive linear relationship between magnesium and PTH, a finding which is consistent with some previous reports (Wei *et al*., 2006). Chronic hypermagnesaemia is known to suppress the excretion of PTH in end-stage CKD, which contributes to the calcification of the soft tissues including vascular calcification (Wei *et al*., 2006). Furthermore, in dialysis patients hypermagnesaemia is known to suppress PTH production, thus it is considered an important factor in the manufacturing of dialysis fluids.

As kidney disease progresses there is diminished filtration and excretion of phosphate resulting in hyperphosphataemia, a finding consistent with observations made in this study (Table 1). Initially this is surmounted by an elevation in the serum level of PTH which decreases proximal phosphate reabsorption. However, eventually there is hyperplasia and hypertrophy of the parathyroid gland as a result of this physiologic compensation, setting the stage for secondary hyperparathyroidism and the vast array of metabolic, vascular, rheumatologic, and cardiac complications that are associated with its onset (Slatopolsky *et al*., 1966).

The CKD cohorts in this study had significant hyperphosphataemia between stage 3 and 5 (Table 2) which is consistent with the findings of Block *et al*., (1998) who explained that in the latter stages of CKD the rate of intestinal phosphate absorption exceeds that of urinary phosphate excretion resulting in hyperphosphataemia. The linear relationship observed between PTH and phosphate in this study (Figure 1A) is in agreement with previously reported works (Slatopolsky and Delmez, 1994; Naveh-Many *et al*., 1995; Almaden *et al*., 1998).

Serum potassium is generally believed to rise above the normal limit only at the end stage of CKD (Allon, 1995). This finding is in agreement with observations made in this study (Table 2). Furthermore, the linear relationship between potassium and PTH observed in this study (Figure 1C) is in agreement with previously reported findings which explained that excess PTH increases basal levels of cytosolic calcium which affects the permeability of the cellular membrane to potassium thus decreasing extra renal disposal of potassium in CKD (Soliman *et al*., 1989). Moreover, potassium is known to stimulate the pancreas to release insulin (Bia and DeFronzo, 1981), an important regulator of extra renal disposition of potassium. Since SHPT of CKD impairs glucose-induced insulin secretion (Fadda *et al*., 1991), it is likely to interfere with potassium-induced insulin secretion which could result in the derangement of the extra renal disposition of potassium.

Serum calcium levels were found to be significantly lower in the cohorts with CKD than in controls (Table 1) due to impaired intestinal absorption and phosphate retention, a finding that is consistent with previously reported observations (Kurokawa, 1994). Furthermore, the CKD patients were about 8 times at risk of developing hypocalcaemia from this study as compared to the controls. Hypocalcaemia stimulated excess PTH secretion (Yamamoto *et al*., 1989) as observed in this study.

A lot of attention has been given to the effects of the variations in the inorganic composition of tissue fluids in the diseased kidney, because in the maintenance of health, balance plays an essential role. The understanding of mineral ratios is particularly interesting and probably offers more information than analyzing mineral levels alone. Electrolyte ratios have been linked to a number of endocrine abnormalities including thyroid and adrenal disturbances (Watts, 1989). Even though significant observations on the various electrolyte ratios were made in this study further focused studies may be required to further elucidate the role of electrolyte ratios in the pathophysiology and prognosis of diseases associated with hormonal imbalances.

## Conclusion

The results of the present study suggest that PTH is linked with derangements in the metabolism of electrolytes like calcium, magnesium, phosphorus and potassium in CKD and contributes to a plethora of complications. PTH should be measured early in CKD and the necessary interventions including dietary and pharmaceutical, concerning these electrolytes, provided to protect the CKD patient from any complication that will result as a result of PTH excess.

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