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Original Article

The disturbed serum mineral profiles in chronic kidney disease patients from Hail Region, Saudi Arabia.

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Abstract:

Chronic kidney disease (CKD) patients experience disturbed serum minerals concentrations. This study aims to investigate the serum minerals profile in CKD, and the possible causes for the disturbances.

The study was conducted at King Khalid hospital, Hail, Saudi Arabia. Clinical data of 276 CKD patients with results of serum calcium, phosphate, magnesium and potassium levels were included. The patients were distributed into 5 groups according to their estimated glomerular filtration rate. Statistical analysis was conducted by single ANOVA and regression analysis.

The majority of group 5 patients were male with older ages, and their serum phosphate levels were elevated by 26.96%, with the percentage of hyperphosphatemic patients increased from 2.30% to 37.61%. Moreover, the percentage of patients with hypermagnesemia rose from 4.6% to 22.93%. In contrast, the calcium was reduced by 9.69%, with the hypocalcemic patients raised from 37.93% to 81.65%. The serum potassium was significantly ($P < 0.001$) elevated, with the hyperkalemic patients increased to 28.44%. The serum phosphate, magnesium and potassium showed significant positive correlations with creatinine, whereas, calcium showed a negative correlation. Moreover, the magnesium showed significant positive correlations with phosphate and potassium, but not with calcium or sodium.

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Elevation of serum phosphate may start from as early as stage 3 and turns into hyperphosphatemia at stage 5, with a strong correlation between magnesium and phosphate. Thus, management of Mg and Phosphate levels from earlier stages of the disease can prevent vascular calcification. Moreover, restriction of dietary potassium intake can prevent the development of hyperkalemia.

Keywords: Chronic kidney disease, hyperphosphatemia, hyperkalemia, hypocalcemia.

Running Title: the disturbed minerals in chronic kidney disease.

Introduction:

Patients with chronic kidney disease (CKD) are known to experience disturbed plasma levels of calcium, phosphate, and potassium. The levels of parathyroid hormone (PTH) and vitamin D, which play the major role in their regulation are also disturbed. Magnesium is an essential mineral for human health that acts as a co-factor and activator for several enzymes that catalyze numerous metabolic reactions in the body. Low dietary magnesium intake was linked with increased risk of cardiovascular diseases [1]. Whereas, higher magnesium supplementation was shown to improve the control of blood pressure [2], improve insulin sensitivity [3], protect the endothelial function [4], and protect from the cellular damage induced by oxidative stress [5]. Under physiologic conditions magnesium is known to play a role in the secretion of PTH and activation of vitamin D. Higher magnesium level is known to suppress the PTH secretion by acting on the calcium-sensing receptors on the parathyroid glands [6]. Magnesium is also required for the hydroxylation of vitamin D into calcitriol [7].

The interrelation between serum magnesium levels and the homeostasis of calcium, phosphate and potassium in CKD patients is rather complex. While the prevalence of hypomagnesemia in the CKD patients is high and increases with progression of renal damage, the hyperphosphatemia is also highly prevalent. Both hyperphosphatemia and hypomagnesemia are involved in the further aggravation of the kidney damage and vascular calcification. The role of magnesium in the progression of these events was shown via its ability to inhibit the crystallization of calcium phosphate which leads to the detrimental tubular and vascular calcification. In a previous study we investigated the levels of vitamin D and PTH in the CKD patients of stages 1 to 4 in the Hail community. The study revealed severe deficiency of the vitamin D with hyperparathyroidism in the elderly patients [8]. Based on the previous findings, the present study aims to investigate the possible consequent prevalence of disturbances in the serum levels of phosphate, calcium, magnesium, and potassium in patients with stages 1 to 5 of CKD patients attending the kidney disease clinic at King Khaled Hospital, Hail. Saudi Arabia. Moreover, it aimed to investigate the possible interrelations between serum magnesium levels and the homeostasis of

calcium, phosphate and potassium in these patients.

Patients and Methods:

Sample frame:

This study was carried out at King Khalid hospital, Hail, Saudi Arabia, as a cross sectional study between January 2018 and April 2018. The project was in compliance with the Helsinki Declaration and was approved by the Research Ethical Committee, Faculty of Applied Medical Sciences, University of Hail. Saudi Arabia. The electronic database was searched for 276 patients with kidney disease attending the outpatient clinic of the hospital. From the records the files of patients with abnormal liver function, overt diabetes mellitus, or with history of thyroidectomy, and those who were taking calcium or vitamin D supplement were excluded. During their visit to the clinic, the patients' blood samples were received in the laboratory for their renal function tests. Following the release of results, a copy of the data was entered in our records and the residual serum samples were stored at -20°C for the assay of the various serum minerals utilizing the commercial kits. The estimated glomerular filtration rate (eGFR) was then calculated for each patient according to the CKD Epidemiology Collaboration Equation [9]. The patients were then classified into the 5 stages of the disease as groups 1 to 5. Group 1: (with eGFR ≥ 90), group 2: (eGFR= 89 – 60), group 3: (eGFR= 59 – 30), group 4: (eGFR= 29 – 15), group 5: (eGFR< 15). Then the patients distribution was as follows: Group 1: n = 87 (M = 36, F = 51), group 2: n= 47 (M = 15, F = 32), group 3: n = 16 (M = 9, F = 7), group 4, n = 17 (M= 11, F = 6), group 5, n = 109 (M = 84, F = 25). The lowest eGFR obtained was 8 ml/min/1.73m2. None of the patients was on hemodialysis.

Biochemical analysis:

The measurements of serum creatinine, urea, uric acid, calcium, phosphate, magnesium, sodium and potassium were carried out utilizing commercial kits with The Dimension Spectrophotometer (RxL XPAD-Germany).

Statistical analysis:

Results are expressed as means ± SD. The differences between the means were computed by one-way ANOVA using Statistical Package for Social Sciences version 16.0 (SPSS Inc, Chicago, IL, USA). The significance of differences between the means was carried out by Unpaired Student`s T-test. *P* values < 0.05 were considered significant. The regression

analysis between the various parameters was carried out by Spearman`s Regression analysis. *P* values < 0.05 were considered significant.

Results:

As shown in Table 1, a total of 276 patients were selected for the study and distributed into five groups representing the five stages of the kidney disease.

Table 1: The mean ages, gender distribution and the kidney function parameters in patients of the five stages of kidney disease. The presented data are means ± SD. a: significantly different from group 1, b: significantly different from group 2, c: significantly different from group 3 and d: significantly different from group 4. * P < 0.05, † P < 0.01 and ‡ P < 0.001.

Groups with eGFR		1 (≥ 90)	2 (89 -60)	3 (59 -30)	4 (29 -15)	5 (< 15)
Age (Years)		40.00±14.14	43.60±14.70	a* 48.68±17.52	a‡ b‡ 62.29±18.52	a‡ b‡ 55.08±18.31
Gender	M	36 (41.40%)	15 (32.90%)	9 (56.30%)	11 (64.70%)	84 (77.10%)
	F	51 (58.60%)	32 (68.10%)	7 (43.70%)	6 (35.30%)	25 (22.90%)
%of patients with ages (Y)	≥ 50	20.69%	38.29%	56.25%	88.23%	67.89%
	< 50	79.31%	61.71%	43.75%	11.77%	32.11%
Mean eGFR		128.73 ± 42.32	a‡ 78.30 ± 8.22	a‡ b‡ 47.12 ± 9.08	a‡ b‡ c‡ 20.00 ± 4.13	a‡ b‡ c‡ d‡ 9.56 ± 2.55
Serum Creatinine (umol/L)		59.46 ± 14.58	a‡ 84.08 ± 17.77	a‡ b‡ 138.18 ± 31.34	a‡ b‡ c‡ 298.78 ± 67.66	a‡ b‡ c‡ d‡ 800.80 ± 90.17
Serum Urea (mmol/L)		4.22 ± 1.58	a‡ 7.24 ± 2.08	a‡ b* 10.35 ± 4.33	a‡ b‡ 13.14 ± 3.75	a‡ b‡ c‡ d‡ 23.10 ± 4.68
Serum Uric Acid (umol/L)		231.40 ± 84.45	a* 268.50 ± 98.70	a‡ b† 331.15 ± 70.41	c* 289.28 ± 130.05	a‡ b‡ d† 355.96 ± 114.68

The percentage of males in group 1 was 41.40% which rose to 77.10% in group 5. Whereas, the percentage of female dropped from 58.60% in group 1 to 22.90% in group 5. The overall average age was 49.93 ±16.32 years. The mean ages in the individual groups increased concomitantly from group 1 to group 5 by up to 37.70%. The

percentage of patients with ages of 50 years or older was 20.69% in group 1, which rose to 67.89% in group 5, whereas, the percentage of patients with ages younger than 50 years was 79.31% in group 1 which dropped to 32.11% in group 5. The mean eGFR in group 1 patients was 128.73 ± 42.32 and was 9.56 ± 2.55 in group 5. The serum urea and uric acid levels significantly ($P < 0.001$) increased from group 1 to 5.

The changes in serum minerals profiles in the five groups with various stages of renal disease are shown in Table 2.

Table 2: The serum mineral profiles in patients with various stages of renal disease. The presented values are means ± SD. a: significantly different from group 1, b: significantly different from group 2, c: significantly different from group 3, and d: significantly different from group 4. * $P < 0.05$, ┼ $P < 0.01$ and ‡ $P < 0.001$.

Groups with eGFR	1 (≥ 90)	2 (89 - 60)	3 (59 - 30)	4 (29 -15)	5 (< 15)
Phosphate (mmol/L)	1.15 ± 0.25	1.08 ± 0.23	b* 1.23 ± 0.32	1.16 ± 0.39	a‡ b‡ d* 1.46 ± 0.58
Magnesium (mmol/L)	0.85 ± 0.11	0.84 ± 0.13	0.88 ± 0.18	0.87 ± 0.30	0.89 ± 0.17
Calcium (mmol/L)	2.37 ± 0.32	2.32 ± 0.58	2.24 ± 0.47	2.18 ± 0.46	a‡ b‡ c* 2.05 ± 0.26
Potassium (mmol/L)	3.99 ± 0.35	4.06 ± 0.41	4.13 ± 0.44	4.13 ± 0.53	a‡ b‡ c‡ d‡ 4.96 ± 0.57
Sodium (mmol/L)	137.62± 3.34	136.27± 4.15	135.25± 4.52	134.64± 4.55	134.66± 5.71

The serum phosphate levels were significantly elevated in group 5 compared to groups 1, 2 and 4 by 26.96%, 35.18% and 25.86%, respectively. However, the serum phosphate in groups 1, 2 and 4 were not significantly different from each other, whereas, that in group 3 was slightly higher than that of group 1 ($P < 0.05$). On the other hand, the serum magnesium concentration showed a trend of a slight increase in group

5 compared to groups 1 and 2, but was not statistically significant. In contrast, the serum calcium levels showed a trend of concomitant reductions in the groups 1 to 4, but were not statistically significant among each other. However, the calcium level in group 5 was significantly lower compared to groups 1, 2 and 3 by 9.69%, 11.25% and 8.48%, respectively. On the other hand, the serum potassium concentrations exhibited significant ($P < 0.001$) elevation in group 5 compared to the other four groups. However, the serum sodium level in group 5 showed a slight trend of decrease compared to groups 1 and 2, but was not statistically significant.

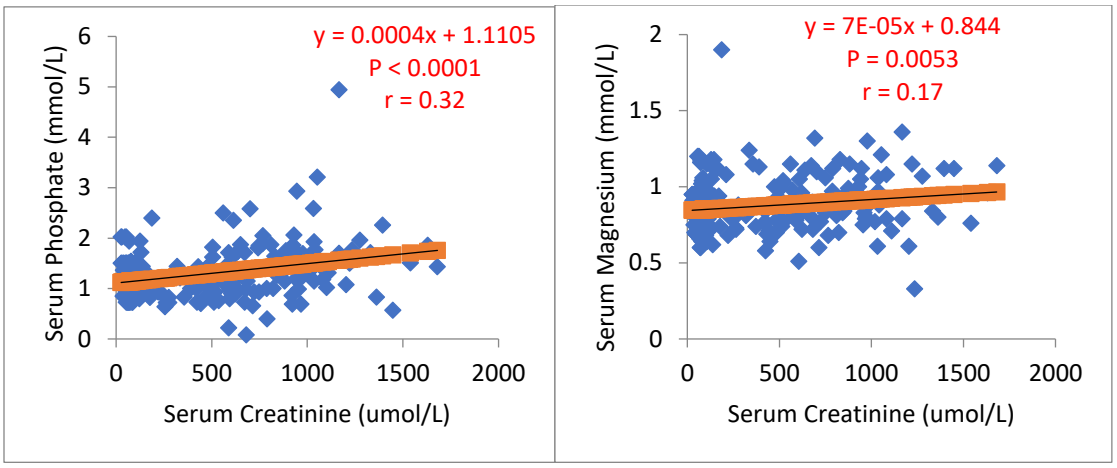
Table 3 exhibits the percentages of patients within each of the five groups with hyper-, hypo- or normal levels of the various serum minerals.

Table 3: Comparison between the percentages of patients with hyper, hypo- or normal levels of the various serum minerals in each group of patients with various stages of kidney disease. Presented data are percentages of patients from the total number in each group.

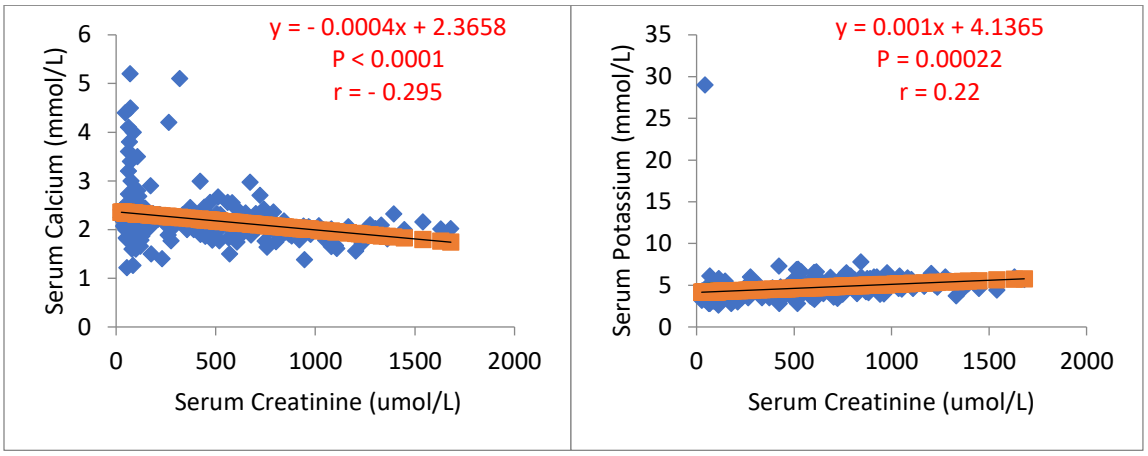
Groups with eGFR		1 ≥ 90	2 89 - 60	3 59 - 30	4 29 – 15	5 ≤ 14
No. of Patients		87	46	16	17	109
		% of patients with various mineral status				
Phosphate (mmol/L)	Hyper > 1.5	2.30	2.13	18.75	12.50	37.61
	Hypo < 0.8	2.30	10.64	0.00	6.25	4.59
	Normal	95.40	87.23	81.25	81.25	57.80
Magnesium (mmol/L)	Hyper > 1	4.60	12.76	25.00	17.14	22.93
	Hypo < 0.7	4.60	6.38	18.75	5.88	8.25
	Normal	90.80	80.85	56.25	76.47	68.81
Calcium (mmol/L)	Hyper > 2.75	8.04	4.26	12.50	11.76	1.83
	Hypo < 2.25	37.93	59.57	68.75	64.70	81.65
	Normal	54.03	36.17	18.75	23.53	16.51
Potassium (mm0l/L)	Hyper > 5.5	0.00	2.17	00.00	5.88	28.44
	Hypo < 3.5	9.20	12.16	12.50	23.53	4.59
	Normal	90.80	85.11	87.50	70.59	66.97

The percentage of patients with hyperphosphatemia showed an increase from 2.30% in group 1 to 37.61% in group 5 and the percentage of patients with normal phosphate levels fell from 95.40% in group 1 to 57.80% in group 5. Whereas, the percentage of hypophosphatemic patients showed a slight increase from 2.30% in group 1 to 4.59% in group 5. On the other hand, the percentage of patients with hypermagnesemia rose concomitantly from 4.6% in group 1 to 22.93% in group 5. Whereas, the percentage of patients with normal serum magnesium levels dropped from 90.80% in group 1 to 68.81% in group 5. However, 4.60% of patients in group 1 had hypomagnesemia and the percentage slightly raised to 8.81% in group 5. On the other hand, the percentage of patients with hypercalcemia was reduced from 8.04% in group 1 to 1.83% in group 5, whereas, the percentage of patients with normal serum calcium levels dropped from 54.03% to 16.51 %. However, the percentage of patients with hypocalcemia raised from 37.93% in group 1 to 81.65% in group 5. In contrast, the percentage of patients with hyperkalemia raised from 0.00% in group 1 to 28.44% in group 5, whereas, the percentage of those with normal serum potassium levels dropped from 90.80% in group 1 to 66.97% in group 5. However, the percentage of patients with hypokalemia was low and did not change significantly, ranging between 9.20% in group 1 and 4.59% in group 5.

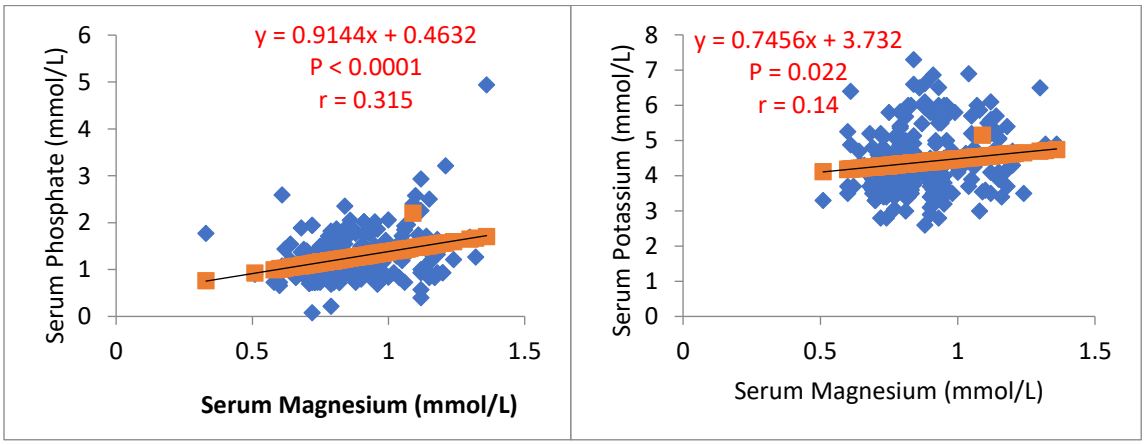
The straight- line correlation plots of creatinine or serum magnesium as independent variable and the different serum minerals as dependent variables are shown in the Figure 1.



A B



C D



E F

Figure 1: Straight line plots of regression analysis between: A) serum creatinine and serum phosphate, B) serum creatinine and serum magnesium, C) serum creatinine and serum calcium,

D) serum creatinine and serum potassium E) serum magnesium and serum phosphate F) serum magnesium and serum potassium in chronic kidney disease patients.

The serum phosphate and the serum magnesium levels showed significant positive correlations with creatinine as a kidney function marker ($P < 0.0001$, $r = 0.32$) and ($P = 0.005$, $r = 0.17$), respectively. On the other hand, serum calcium showed a significant negative correlation with the serum creatinine ($P < 0.0001$, $r = -0.296$), whereas, the serum potassium showed a significant positive correlation with creatinine ($P = 0.0002$, $r = 0.22$). On the other hand, the serum magnesium, as independent parameter, showed a significant positive correlation with the serum phosphate ($P < 0.0001$, $r = 0.32$), and a slight positive correlation with potassium ($P = 0.022$, $r = 0.14$). Whereas, there was no significant correlation between magnesium and calcium ($P = 0.82$, $r = 0.013$) or sodium ($P = 0.19$, $r = 0.07$).

Discussion:

The present study revealed that the average age of patients in group1 was 40 years whereas, that in group 5 increased to 55 years, and the female percentage in group 1 was 58% which dropped to 23% in group 5. This probably indicates that most of the females entering stage 5 of the disease are transferred to the dialysis unit in the hospital, whereas, older males continued follow-up in the outpatient department even-though they reached stage 5 of the disease. The present results also exhibited that the serum phosphate levels, which were only slightly raised in patients of groups 3 and 4, showed a significant elevation in group 5 by about 35% compared to that in group 2. This was in congruence with several reports that revealed elevation of serum phosphate levels in the CKD patients [10]. It is believed that in CKD patients initially the failure of tubular phosphate reabsorption causes increased urinary loss of phosphate. As a response, the parathyroid gland secretes the parathyroid hormone (PTH), and the fibroblast growth factor 23 (FGF23) is released from the bones to regulate the phosphate level [11]. Further progression of the tubular damage and failure of hormonal regulation causes the development of persistent hyperphosphatemia [12]. In the physiological conditions FGF23 maintains the phosphate balance by promoting its renal excretion, limiting its intestinal absorption by inhibiting the activation of vitamin D, and limiting bone reabsorption by blocking PTH secretion [13]. Furthermore, α-Klotho,

a membrane-anchored protein expressed in the kidney tubules, together with FGF-receptor 1 (FGFR1) form the receptor for FGF23 and thereby plays a key role in phosphate homeostasis [14]. However, during progressive kidney disease, the parathyroid gland becomes resistant to FGF23, favoring the secretion of PTH that aggravates the secondary hyperparathyroidism [15]. Moreover, in these patients the α-klotho expression is drastically declined causing failure of this cascade process of phosphate regulation and the ensue of hyperphosphatemia. In the present results the influence of the progression of renal disease on the development of hyperphosphatemia was exhibited by the significant correlation between serum creatinine and the phosphate levels ($P < 0.0001$, $r = 0.32$). Several studies have shown that the developed hyperphosphatemia plays a direct role in the further progression of the kidney disease [16, 17]. It was demonstrated that this induced hyperphosphatemia triggers the proximal tubular calcification by formation of calcium-phosphate crystals that aggravate the tubular damage and cell death [18]. These calcium phosphate crystals initiate the formation of primary calciprotein particles (CPPs) [19]. These primary CPPs particles contain amorphous calcium phosphate which is covered and protected by fetuin A, a protein formed by the liver, that prevents the ectopic calcification. During the progression of the kidney damage accompanied by deficiency of fetuin A, the primary CPPs aggregate to form secondary CPPs. The secondary CPPs are larger needle-shaped particle, that promote stable and more destructive calcification [20, 21].

Results of the present study also revealed that serum magnesium levels did not show any significant changes in patients of the five groups. However, those in group 5 exhibited a slight non-significant trend of increase. Moreover, the percentage of patients with hypermagnesemia in group 1 was 4.6% which raised to 23% in group 5 and those with hypomagnesemia raised slightly from 4.6% to 8.25%. Several studies have shown the prevalence of hypomagnesemia among CKD patients to range between 8% to 15% depending on the stage of the disease [22]. In the CKD patients, the hypomagnesemia is believed to be caused by the tubular dysfunction that impairs the magnesium tubular reabsorption, and the magnesium deficiency itself was shown to aggravate the progression of the kidney disease [23]. In the present results, the 23% of patients with hypermagnesemia

among stage 5 group probably indicates that those patients approaching stage 5 had their magnesium intake improved by consuming magnesium rich diets or taking additional magnesium supplements, which could not be verified in the present study. Our data also showed a possible role of magnesium in the phosphate homeostasis, which was exhibited by the highly significant correlation between the two minerals ($P < 0.0001$, $r = 0.32$). Under physiologic conditions magnesium is known to play a role in the regulation of PTH secretion. Investigators have shown that high serum magnesium can suppress the PTH secretion by acting on the calcium-sensing receptors on the parathyroid glands [24, 6]. In CKD patients with low serum magnesium levels, the developed hyperphosphatemia was shown to be associated with high risk of cardiovascular mortality, whereas moderate magnesium levels tended to abolish this association [25]. Moreover, in hemodialysis patients, high magnesium levels tended to reduce the levels of the inflammatory cytokines (tumor necrosis factor-α and interleukin – 6) [26]. Magnesium is believed to delay the maturation of CPPs, and consequently, suppress the phosphate-induced calcification of the renal tubules and the vascular smooth muscles [27, 28], and consequently, the serum magnesium level was strongly associated with the mortality rate in patients with CKD [29]. The serum calcium is the third mineral known to be disturbed in CKD patients which was investigated in the present study. The serum calcium levels showed a highly significant negative correlation with the serum creatinine ($P < 0.0001$, $R = - 0.30$). Although there was no significant change in the serum calcium levels in groups 1 to 4, there was a significant reduction in that of group 5 by 9.69% compared to group 1. Moreover, the percentage of patients with hypocalcemia in group 1 was about 38% which raised to about 81% among the group 5 patients. On the other hand, the percentage of patients with hypercalcemia dropped from 11% in group 1 to only 2.00% in group 5. Our findings were in line with the reports of several investigators who found that hypocalcemia was common in CKD patients and ranged between 30% to 85% depending on the stage of disease [30, 31], and that only 5% of the patients had hypercalcemia [30]. It is well stablished that, under normal physiologic conditions, vitamin D, PTH, and FGF23 play crucial role in the feedback loops that regulate plasma calcium and phosphate balance [32, 33]. The 25[OH]-vitamin D_3, is activated into 1,25[OH]2-

vitamin D_3 (calcitriol) by 1-α-hydroxylase enzyme in the kidney tubules. The active calcitriol stimulates the intestinal absorption of calcium by inducing synthesis of the intestinal calbindin which binds the calcium prior to its transport into the blood circulation via the sodium-calcium exchanger [34]. However, in the CKD patients 25[OH]-vitamin D_3 is known to be severely depleted that may lead to decreased plasma calcium levels. The hypocalcemia in turn, induces the PTH gene transcription and triggers the secondary hyperparathyroidism [35]. In a previous study which involved CKD patients of stages 1 to 4, we observed a concomitant reduction of vitamin D and increase of PTH level, where about 50% of the patients with older ages had severe vitamin D deficiency [8]. However, some authors have reported the prevalence of hypovitaminosis D among older ages to be as high as 93.8% [36]. Investigators have found it important to maintain adequate levels of the 25(OH)D3 at > 30 ng/mL, and recommended monitoring its serum levels every 6 -12 months [37]. The second important regulator of plasma calcium is the PTH, which is secreted by the parathyroid gland in response to a decrease in the plasma calcium level. The reduction in calcium level is sensed by calcium sensors located in the cell membranes of the parathyroid gland. The PTH acts to increase the plasma calcium concentration by stimulating bone resorption, enhancing intestinal absorption of calcium and phosphate by promoting the calcitriol formation and augmenting the active renal calcium reabsorption. However, in CKD all these regulatory measures fail due to loss of the sensitivity of the parathyroid gland to the hypocalcemia and the depleted vitamin D levels. On the other hand, the regression analysis revealed that magnesium which was strongly correlated with phosphate and potassium was not significantly correlated with calcium ($P = 0.82$, $r = 0.013$). Magnesium is known to be involved in the homeostasis of calcium under physiological conditions through its influence on the activity of the 1α-hydroxylase enzyme that activates 25-hydroxy-D3 into calcitriol. Magnesium acts as a cofactor and regulates several steps in vitamin D metabolism, and it is also required for the binding of vitamin D to its transport protein [38, 39]. However, in CKD since vitamin D is deficient, the influence of magnesium on calcium tubular reabsorption seems to be lost in spite of the apparently stable serum magnesium levels, which probably explains the loss of correlation between magnesium and calcium in this

study. In the present study the changes of serum potassium levels in these CKD patients were also investigated. Although the serum potassium levels did not change in the groups 1 to 4, however, a significant elevation by 23.44% was evident in patients of group 5. The percentage of patients with hyperkalemia in group1 was only 1.15% which raised to 41.00% in group 5, whereas, the percentage of those with normal serum potassium levels dropped from 95.41% in group 1 to 57.00% in group 5. Moreover, the influence of renal failure on the potassium homeostasis was exhibited by the significant correlation between serum creatinine and serum potassium levels (P = 0.0002, r = 0.22). It has been reported that in CKD patients the prevalence of hypokalemia is less frequent and of less clinical concern compared with hyperkalemia, making management of hyperkalemia a more public health concern [40, 41]. It is believed that a stable transmembrane potential of about −85 mV is critical for normal cardiac and skeletal muscle function, which requires a tight serum potassium homeostasis. Therefore, sudden alterations in the potassium levels may cause changes in the membrane potential that may lead to muscle paralysis and fatal arrhythmias [42]. In the CKD patients, hyperkalemia develops when the intestinal potassium absorption overtakes its renal excretion [43, 44]. At earlier stages of the disease, the kidney succeeds to maintain the potassium homeostasis by increasing the tubular secretion [43], and developing an additional mechanism of intestinal excretion of potassium [45]. These adaptation processes are successful to normalize the serum potassium levels until the glomerular filtration rate falls below 10–15 ml/min [44]. Thus, with progression of the kidney disease the ability of kidney to regulate the plasma potassium levels is fail leading to the development of hyperkalemia. Therefore, restriction of potassium intake in the diet is considered crucial in management of potassium levels in these patients. The association of magnesium with potassium homeostasis was exhibited as a weak but significant correlation between the two electrolytes (P = 0.02, r = 0.14). Several investigators have indicated the association of magnesium with potassium homeostasis. The combined roles played by the magnesium and potassium and their correlation were found crucial for the normal bodily functions [46], and similar correlation between the two minerals was also demonstrated in the hemodialysis patients [47]. This positive linear correlation between magnesium and potassium implies

that both markers shared similar metabolic pathways associated with the changes in their concentrations. Magnesium affects potassium homeostasis by acting as a cofactor and stimulator for the Na-K-ATPase, Na-K-Cl cotransport, and K transport channels [46]. In these transport mechanisms free ATP and magnesium bind to induce the conformational change of the enzyme that promote the catalytic pumping activity of the ATPase enzyme [48]. This probably explains the significant correlation observed between the two minerals.

Conclusion: The present results indicated that the majority of non-dialysis CKD patients of stage 5 were male with ages older than 50 years. It also demonstrated that moderate elevation of serum phosphate may ensue from as early as stage 3 of the renal disease which turns into severe hyperphosphatemia at stage 5. This may require close monitoring and management of the phosphate levels from earlier stages of the disease to avoid the secondary complications of vascular calcifications and rapid deterioration of the kidney function. Our data also showed a strong association of magnesium as a determinant factor with the phosphate levels which necessitates combined measurements of serum phosphate and magnesium regularly, since hypomagnesemia may enhance deterioration of the kidney function. Moreover, the data confirmed the association of hyperkalemia with the end stage disease, which requires close management through restricted dietary potassium intake in these patients. It is also important to monitor and manage the vitamin D deficiency, particularly in patients of older age, to avoid the fast deterioration of the renal functions.

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Availability of data: The data are available on request from the author.

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