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Inorganic Elemental Imbalance in Patients with Chronic Kidney Disease Assessment of Fe, Zn, Cu, Ca, Mg, and Phosphorus

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Abstract: ***Background***: Chronic kidney disease (CKD) is a disease of renal function, mineral metabolism and trace-element homeostasis. The present study was carried out to evaluate some selected biochemical parameters and their diagnostic value in patients with CKD in comparison to healthy persons. ***Methods***: The study was conducted among one hundred participants comprising 50 CKD patients and 50 healthy controls. Determination of serum concentrations of vitamin D3, Fe, Zn, Cu, Ca, Mg and P, serum urea and serum creatinine were made. Correlation and ROC curve analyzes were used to evaluate the relationships between the studied parameters and their ability to discriminate CKD patients from controls. ***Results*:** The age distribution was observed between the groups ($P \leq 0.01$), whereas sex distribution was not significantly different ($P = 0.31$). CKD patients showed significantly lower concentrations of vitamin D3, Fe, Zn, and Ca compared with controls ($P \leq 0.01$), while Cu and phosphorus were significantly elevated. Magnesium showed only a borderline difference ($P = 0.05$). Blood urea and creatinine were markedly increased in CKD patients ($P \leq 0.01$). Strong correlations were observed among Fe, Zn, Ca, Cu, Mg, phosphorus, urea, and creatinine, whereas vitamin D3 showed no significant correlations. ROC analysis demonstrated excellent discriminatory ability for phosphorus and urea (AUC = 1.000). Copper also showed strong diagnostic performance (AUC = 0.908), while magnesium showed limited discrimination (AUC = 0.599, P = 0.087). The low AUC values for vitamin D3, Fe, Zn, and Ca reflected excellent discrimination in the reverse direction because these parameters were reduced in CKD patients. ***Conclusion*:** CKD is associated with substantial alterations in mineral and trace-element homeostasis. Phosphorus, urea, copper, vitamin D3, Fe, Zn, and Ca demonstrated considerable potential for distinguishing CKD patients from healthy individuals.

Keywords: Inorganic, Elemental, Chronic Kidney Disease, Fe, Zn, Cu, Ca, Mg, Phosphorus.

Research Paper

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INTRODUCTION

Chronic kidney disease (CKD) is a slow loss of kidney function. The kidneys are important for filtration, excretion, reabsorption, acid-base control, vitamin D metabolism and mineral homeostasis. Thus, the decreased kidney function may significantly affect the blood concentrations of several inorganic elements [1]. The most well characterized abnormalities are calcium and phosphorus abnormalities which together account for a major component of CKD-mineral and bone disorder (CKD-MBD). As CKD progresses, phosphate excretion decreases and calcium balance is disrupted due to changes in vitamin D metabolism and parathyroid hormone regulation. These changes can lead to bone abnormalities and vascular calcification [2]. CKD can also interfere with the metabolism of iron, zinc, copper and magnesium. These elements participate in erythropoiesis, antioxidant defense, enzyme activity, immune function, energy metabolism and bone metabolism. Abnormalities of trace elements may become more pronounced with declining renal function [3]. Copper (Cu) is an important trace element of antioxidant material, iron metabolism, mitochondrial

energy production and connective tissue formation. Since kidneys are involved in regulation and excretion of trace elements, chronic kidney disease may disrupt copper homeostasis. Serum copper concentration changes may be important with CKD, possibly through the oxidative stress, inflammatory, and iron metabolism changes [4]. Zinc is an essential trace element that plays a role in antioxidant defense, immune function, DNA synthesis, protein metabolism and cellular repair. Zinc homeostasis may be disturbed in chronic kidney disease (CKD) and may be correlated with disease severity and complications. Lower zinc status CKD patients may have lower serum or plasma Zn concentrations due to altered metabolism, decreased dietary intake, inflammation and losses associated with renal replacement therapy [5]. Chronic inflammation is a hallmark of CKD. Zinc (Zn) plays a role in the regulation of immune and inflammatory responses, and altered Zn status might be associated with inflammation [6]. CKD has an important relationship with iron (Fe) as kidney dysfunction often results in iron deficiency and iron-restricted erythropoiesis, both of which contribute to anemia in CKD. Anemia, iron deficiency. Anemia is a common complication of CKD because of decreased production of erythropoietin (EPO) by damaged kidneys [7]. CKD-associated inflammation, driven by low available iron, elevates hepcidin, a hormone that blocks absorption of iron from the gut and sequesters iron in storage cells. Iron deficiency may further impair the production of red blood cells and worsen anemia. The total body iron may be normal, but insufficient iron is available for erythropoiesis. This is often called functional iron deficiency [8]. Phosphorus (P) is an essential mineral for bone formation, energy metabolism, cell membranes, and intracellular signaling. Its relation to chronic kidney disease (CKD) is especially pertinent in that the kidneys are the main [9]. Hyperphosphatemia, hyperphosphatemia in serum is a common complication of moderate to severe CKD Higher phosphorus levels are especially important for patients with advanced CKD and on dialysis. In early CKD, (FGF23) is increased to promote phosphate excretion and keep serum phosphorus relatively normal. This compensatory mechanism is inadequate with progression of renal disease. Furthermore, decreased phosphate excretion and vitamin D metabolism causes increased secretion of parathyroid hormone (PTH). This can result in secondary hyperparathyroidism [10]. Vitamin D metabolism Diseased kidneys do not produce active vitamin D (calcitriol) as well as healthy kidneys do. Low calcitriol leads to reduced intestinal absorption of calcium and disturbed calcium-phosphorus homeostasis. organs to control the phosphorus balance [11].

MARTIALS AND METHODS

A total of 50 venous blood specimens were taken from patients diagnosed with chronic kidney disease (CKD). As a control group, we collected 50 blood samples from healthy individuals. The study groups also comprised both male and female participants, aged from 31 to 72 years. Samples were collected from Baghdad Teaching Hospital between May 2025 and April 2026.

Analytical Principles

Iron (Fe):

Serum iron is released from transferrin and reduced to Fe2+. Fe2+ reacts with a chromogen such as ferrozine to form a colored complex. The absorbance is directly proportional to the concentration of the iron.

CKD Diagnostic Criteria (eGFR) was estimated from the serum creatinine concentration using the CKD-EPI equation., correcting for age and sex to give a more accurate measure of renal function. Normal range was defined as eGFR value of ≥90 mL/min/1.73 m2. Evidence of kidney damage such as Albuminuria/proteinuria, Persistent abnormalities of urine sediment, Structural abnormalities detected by imaging Histological abnormalities detected by kidney biopsy and Persistent abnormalities of kidney function markers.

Calcium (Ca):

Calcium reacts with a chromogenic reagent, commonly Arsenazo III or o-cresolphthalein complexone, producing a colored complex. The absorbance is proportional to calcium concentration.

Magnesium (Mg):

Magnesium reacts with a specific chromogenic reagent to form a colored complex. The analyzer measures the absorbance photometrically and calculates the Mg concentration.

Phosphorus (P):

Inorganic phosphate reacts with ammonium molybdate under acidic conditions to form a phosphomolybdate complex. The intensity of the resulting color is proportional to the concentration of inorganic phosphorus.

Serum Zinc (Zn) and Copper (Cu):

Concentrations were determined using a flame atomic absorption spectrophotometer equipped with appropriate hollow-cathode lamps. Venous blood samples were collected in trace-element appropriate tubes, allowed to clot, and centrifuged at approximately 3,000 rpm for 5–10 min.

Ethical Approval:

Written informed consent was obtained from all participants prior to the commencement of the study. Ethical approval was granted by the Medical Ethics Committee under Approval No. 211 on April 1, 2026.

Statistical-Analysis

Data are presented as mean ± standard error (SE), where the mean represents the sample average and

the standard error reflects the precision of the estimated mean. The SE indicates how closely the sample mean is expected to approximate the true population mean and is commonly used to assess the reliability of the estimate and to construct confidence intervals.

Inclusion Criteria

Persons aged 20 to 65 years. Patients with diagnosed chronic kidney disease (CKD). Volunteers who consented to take part in the study and signed a written informed consent.

Exclusion Criteria

Presence of acute kidney injury, active infection, autoimmune disease, malignancy, liver disease, pregnancy or surgery recently. Ongoing treatment with anti-inflammatory or immunosuppressive drugs.

RESULTS AND DISCUSSION

Demographic characteristics showed important variations between age and Healthy group (P ≤ 0.01). The cases were aged between 51 and 70 years (80%) and most controls were aged between 31 and 50 years (72%). This suggested that the CKD group was generally older than the control group. This can be explained by the increasing prevalence of chronic kidney dysfunction with increasing age. In terms of sex distribution, 58% of the cases and 48% of the controls were males and 42% and 52% were females, respectively. not important variations (P=0.31).

Table 1: Demographic properties of studied groups

Properties	Case		Control		P-value
	N	%	N	%	
(31-50)	10	20	36	72	
(51-70)	40	80	14	28	≤0.01
Male	29	58	24	48	
Female	21	42	26	52	0.31

Demographic results showed that there was a significant difference between the CKD cases and control group regarding age (P < 0.01). The most affected age group was 51-70 years (80%) in CKD patients versus controls (28%). Most of controls (72%) were from the age group 31-50 years. Older participants in this study had prevalent CKD. This finding is in line with the observations of (12. Tang, *et al*., 2024) who attributed the increased prevalence of CKD with aging to the progressive reduction in glomerular filtration rate and accumulation of age-related structural and functional changes in the kidneys [12. There was no significant difference in distribution of sex between the two groups (P=0.31). Cases were more often males (58% vs 48%). 42% of cases were women and 52% of controls. Sex was not statistically significant, i.e. the two groups were similar 13. Barras *et al*., (2025) proposed that sex is not likely to be a major confounder of the biochemical differences described in this study, but the significant difference in age should be considered when interpreting the results [13]. Table 2.Mean values of studied biochemical parameters in CKD cases (n=50) versus healthy controls (n=50). There was a significant difference in almost all the parameters studied with major changes in mineral, trace element, vitamin D and renal function profile in the cases. Mean serum vitamin D3 level in cases was significantly lower (15.38 ± 1.70) than controls (49.64 ± 2.20) with highly significant difference (t = 12.29, P ≤ 0.01). This fall may be due to defect in vitamin D metabolism in chronic renal failure. Demographic data showed significant difference in age of CKD cases and control group (p ≤ 0.01). The majority of CKD patients were in the age group of 51-70 years (80%) whereas only 28% of controls were in this age group. 72% were controls between the ages of 31 and 50 years. This could mean the higher prevalence of CKD in the elderly subjects in the present study. The present study is consistent with the progressive reduction of glomerular filtration rate with age and the development of age changes in kidney function which can be attributed to the higher prevalence of CKD with age [12]. However, no significant difference was observed in the sex distribution between the two groups (P=0.31). Males were more likely to be cases (58%) than controls (48%). Women made up 42% of the cases and 52% of the controls. The statistical analysis showed no significant difference between the groups, indicating that they were similar in terms of gender [13]. However there is a wide age difference and this should be taken into account when interpreting the results. Sex is unlikely to confound the biochemical differences observed in this study (Barras *et al*., 2007). Table 2 Mean level of biochemistry parameters studied in CKD cases (n=50) and healthy controls (n=50) In some cases, the majority of parameters studied were significantly different, with large changes in mineral profiles, trace elements, vitamin D and renal function. The mean serum vitamin D3 concentration (± SEM) was significantly lower (15.38 ± 1.70) in cases than controls (49.64 ± 2.20) and the difference between the means was highly significant (t = 12.29, P ≤ 0.01). The fall could be associated with a problem in vitamin D metabolism that is common in patients with chronic kidney disease. Reduced renal function can decrease the conversion of 25-hydroxyvitamin D to its active form and may also be accompanied by disturbances in calcium–phosphorus homeostasis.

Serum iron (Fe) was significantly decreased among cases (53.90 ± 1.50) compared with controls (109.42 ± 2.00; t = 22.14, P ≤ 0.01). The reduced iron concentration may be associated with the anemia and altered iron metabolism commonly observed in CKD.

Zinc (Zn) concentrations were significantly lower in cases (56.80 ± 1.02) than in controls (94.38 ± 1.50; t = 20.66, P ≤ 0.01). This finding may indicate altered trace-element homeostasis in CKD.

In contrast, copper (Cu) showed a significantly higher mean concentration in cases (132.88 ± 1.88) compared with controls (109.96 ± 1.39; t = 9.76, P ≤ 0.01).

The mean calcium (Ca) concentration was significantly lower in cases (7.94 ± 0.043) than in controls (9.41 ± 0.03; t = 26.94, P ≤ 0.01). Hypocalcemia is an important biochemical abnormality in advanced renal dysfunction and may be associated with impaired vitamin D activation, phosphate retention, and disturbances in parathyroid hormone regulation. The simultaneous decrease in vitamin D and calcium observed in this study supports the presence of disturbed mineral metabolism among the cases.

For magnesium (Mg), the difference between cases (2.33 ± 0.03) and controls (2.26 ± 0.02) was relatively small and reached the borderline level of statistical significance (t = 1.96, P = 0.05).

The concentration of phosphorus (P) was significantly higher in cases (5.61 ± 0.09) than in controls (3.49 ± 0.04; t = 20.38, P ≤ 0.01). As expected, the renal-function markers showed pronounced differences between the two groups. Blood urea was substantially elevated in cases (108.04 ± 3.22) compared with controls (25.32 ± 0.60; t = 25.20, P ≤ 0.01). Likewise, serum creatinine was markedly higher among cases (3.63 ± 0.12) than controls (0.88 ± 0.02; t = 21.26, P ≤ 0.01).

Table 2: Comparative the mean levels of studied parameters between cases (n=50) and control (n=50)

Tests	Groups	Mean	SE	T-test	P-value
D3 (ng/ml)	Cases	15.38	1.70	12.29	≤0.01
	Control	49.64	2.20		
Fe (µg/dL)	Cases	53.90	1.50	22.14	≤0.01
	Control	109.42	2		
Zn (µg/dL)	Cases	56.80	1.02	20.66	≤0.01
	Control	94.38	1.50		
Cu (µg/dL)	Cases	132.88	1.88	9.76	≤0.01
	Control	109.96	1.39		
Ca (mg/dL)	Cases	7.94	0.043	26.94	≤0.01
	Control	9.41	0.03		
Mg (mg/dL)	Cases	2.33	0.03	1.96	0.05
	Control	2.26	0.02		
P (mg/dL)	Cases	5.61	0.09	20.38	≤0.01
	Control	3.49	0.04		
B. urea (mg/dL)	Cases	108.04	3.22	25.20	≤0.01
	Control	25.32	0.60		
S. creatinine (mg/dL)	Cases	3.63	0.12	21.26	≤0.01
	Control	0.88	0.02		

The results agreed with (Annamalai, and Viswanathan, *et al*., 2025) who reported that the reduction in serum vitamin D3 in CKD patients may occur because impaired kidney function reduces the renal conversion of 25-hydroxyvitamin D into its biologically active form, 1,25-dihydroxyvitamin D (calcitriol). In addition, phosphate retention and reduced calcitriol production can disturb calcium–phosphorus balance, further contributing to vitamin D deficiency [14].

The reduced serum iron in CKD patients may be explained by chronic inflammation, impaired iron utilization, reduced dietary intake, and blood loss**,** particularly in patients with advanced kidney disease. These findings confirmed with (McDonnell, *et al*., 2025) who revealed that the inflammation can increase hepcidin levels, which limits intestinal iron absorption and traps iron within storage cells, making less iron available for erythropoiesis [15]. This reduction may be related to chronic inflammation and increased hepcidin levels in CKD, which reduce intestinal iron absorption and iron availability for erythropoiesis. Abe, *et al*., (2024) described, reduced dietary intake and blood loss may also contribute to iron deficiency in CKD patients [16].

On the other hand, the lower zinc level in CKD patients may be due to increased urinary zinc loss, reduced dietary intake, impaired intestinal absorption, and altered zinc metabolism associated with chronic inflammation and renal dysfunction**.** These findings are consistent with (Huang *et al*., 2025) who presented that the decreased zinc concentration observed in CKD patients may be attributed to increased urinary zinc excretion, inadequate dietary intake, impaired intestinal absorption, and disturbances in zinc metabolism resulting from chronic inflammation and impaired renal function [17]. In addition, protein loss and changes in protein binding can reduce circulating zinc concentrations. Lebedeva, *et al*., (2026) demonstrated that this reduction may be attributed to altered zinc metabolism in CKD, including increased urinary losses, reduced dietary intake and intestinal absorption, and

chronic inflammation. These factors can contribute to disturbed zinc homeostasis and decreased circulating zinc levels [18].

Furthermore, Adomako, *et al*., (2024) reviewed that the elevated serum copper in CKD patients may be related to chronic inflammation and altered copper metabolism**.** Inflammatory conditions increase the production of ceruloplasmin**,** the major copper-carrying protein in blood, which can raise circulating copper levels. Reduced renal function may also disturb the normal balance and distribution of trace elements. The present findings are in agreement with the findings of Aldalati *et al*., (2025) who have reported the major copper transporting protein in circulation responsible for the high serum copper levels. Impaired renal function can also affect normal homeostasis, distribution and clearance of trace elements and may alter circulating levels of copper [19]. This increase may be associated with chronic inflammation in CKD that may increase ceruloplasmin synthesis and thus circulating copper levels. Altered metabolism of trace elements and renal function may also explain the accumulation of copper [19]. Also, the small difference in magnesium may be because magnesium homeostasis is regulated by several mechanisms including intestinal absorption and renal excretion. CKD leads to decreased renal magnesium excretion, but compensatory mechanisms may maintain serum magnesium within or near the normal range, particularly in early stages of disease. CKD-related decreased renal magnesium excretion can increase serum magnesium levels [20]. Perhaps this explains the borderline difference. However there may be compensatory mechanisms which keep magnesium concentrations relatively stable. There may be a small difference between groups [21]. Impaired renal phosphate excretion. Serum phosphorus is frequently elevated. Phosphate retention may result in secondary hyperparathyroidism and abnormal calcium and vitamin D metabolism. The CKD group showed disturbed mineral and bone metabolism with increased phosphorus and decreased calcium and vitamin D3 [22]. Mitchell *et al*., (2026). Serum phosphorus was significantly increased in patients of CKD ($p<0.0001$) due to decreased excretion of phosphate and hence retention of phosphate due to poor renal function. Increased phosphorus can also increase PTH secretion and inhibit synthesis of active vitamin D, leading to decreased calcium absorption and hypocalcemia. Disturbed mineral and bone metabolism in CKD is indicated by high phosphorus levels with low calcium and vitamin D3 [23]. The results of correlation analysis revealed a statistically significant high correlation of the majority of the studied minerals and trace elements to the markers of renal function.

Vitamin D3 showed weak and non-significant correlations with all parameters ($P > 0.05$), suggesting that its variation was not directly associated with the other measured variables in this study. Fe and Zn demonstrated a very strong positive correlation ($r = 0.964$, $P < 0.001$), indicating that their serum levels tended to change in the same direction. Both Fe and Zn were also strongly and positively correlated with Ca, while showing strong negative correlations with Cu, Mg, phosphorus, urea, and creatinine ($P < 0.001$).

In contrast, Cu showed strong negative correlations with Fe, Zn, and Ca, but strong positive correlations with Mg, phosphorus, urea, and creatinine ($P < 0.001$). Similarly, Ca was strongly negatively correlated with Mg, phosphorus, urea, and creatinine. Phosphorus showed strong positive correlations with Mg, urea, and creatinine ($r = 0.936$, 0.923, and 0.913, respectively; $P < 0.001$). As shown in table 3.

Table 3: Correlation analysis of studied parameters

		D3	Fe	Zn	Cu	Ca	Mg	P	Urea	Creatinine
D3	r	1	-.181	-.175	.031	-.182	.121	.137	.083	.105
	P-value		.208	.223	.829	.207	.401	.342	.566	.466
Fe	r	-.181	1	.964**	-.861**	.966**	-.920**	-.965**	-.903**	-.894**
	P-value	.208		.000	.000	.000	.000	.000	.000	.000
Zn	r	-.175	.964**	1	-.876**	.953**	-.920**	-.972**	-.902**	-.889**
	P-value	.223	.000		.000	.000	.000	.000	.000	.000
Cu	r	.031	-.861**	-.876**	1	-.847**	.847**	.893**	.815**	.798**
	P-value	.829	.000	.000		.000	.000	.000	.000	.000
Ca	r	-.182	.966**	.953**	-.847**	1	-.883**	-.954**	-.888**	-.873**
	P-value	.207	.000	.000	.000		.000	.000	.000	.000
Mg	r	.121	-.920**	-.920**	.847**	-.883**	1	.936**	.904**	.891**
	P-value	.401	.000	.000	.000	.000		.000	.000	.000
P	r	.137	-.965**	-.972**	.893**	-.954**	.936**	1	.923**	.913**
	P-value	.342	.000	.000	.000	.000	.000		.000	.000

The lack of significant correlations involving vitamin D3 may be explained by the multifactorial regulation of vitamin D status in CKD**.** Vitamin D levels are influenced not only by renal function but also by sunlight exposure, dietary intake, supplementation, liver metabolism, and disease severity. Janoušek, *et al*., (2022)

Highlighted, changes in vitamin D3 may occur independently of the measured Fe, Zn, Cu, Ca, Mg, phosphorus, urea, and creatinine levels in this sample [24].

On the other hand, the strong positive correlation between Fe and Zn may reflect their shared dependence on nutritional status, intestinal absorption, protein transport, and trace-element homeostasis. In CKD, disturbances in these processes can cause Fe and Zn to decrease together. These results align with (Nakatani *et al.,* 2025) that documented that the strong positive correlation observed between Fe and Zn may be attributed to their shared dependence on nutritional status, intestinal absorption, protein transport, and overall trace-element homeostasis. In patients with CKD, disturbances in these physiological processes may contribute to a simultaneous reduction in circulating Fe and Zn concentrations [25].

Their positive association with calcium may reflect the overall preservation or disruption of mineral status, whereas their negative correlations with phosphorus, urea, and creatinine may indicate that greater renal dysfunction is associated with greater disturbances in Fe and Zn levels. Fe and Zn showed a very strong positive correlation ($r = 0.964$, $P < 0.001$), which may reflect their shared dependence on nutritional status, absorption, and trace-element metabolism, (Reszke, *et al*., 2021), [26].

Their positive correlations with Ca and strong negative correlations with Cu, Mg, phosphorus, urea, and creatinine suggest that disturbances in renal function may be accompanied by coordinated changes in mineral and trace-element homeostasis. The inverse relationships with urea and creatinine may particularly indicate that worsening renal dysfunction is associated with lower Fe and Zn concentrations. These results are similar to those reported by (Abdulhasan 2026) who presented that the positive correlations observed with Ca, together with the strong negative correlations with Cu, Mg, phosphorus, urea, and creatinine, suggest that impaired renal function may be associated with coordinated alterations in mineral and trace-element homeostasis. In particular, the inverse associations with urea and creatinine may indicate that progressive deterioration of renal function is accompanied by decreased serum concentrations of Fe and Zn [27].

These relationships can be explained by the progressive disruption of mineral and trace-element homeostasis as renal function declines. Elevated Cu may be associated with inflammation, while lower Fe, Zn, and Ca may reflect altered metabolism and nutritional status. Increased Mg and phosphorus can occur because impaired kidneys have reduced capacity to excrete these minerals. Similarly, the positive correlations of phosphorus, Mg, and Cu with urea and creatinine suggest that their levels tend to increase as renal dysfunction becomes more pronounced. These findings agreed with (López-Alonso *et al*., 2025) that indicated progressive mineral imbalance in CKD, with elevated Cu, Mg, and phosphorus and increased levels of renal dysfunction markers [28].

The strong negative correlations of Cu with Fe, Zn, and Ca may reflect the disturbed trace-element and mineral balance associated with CKD, while the positive correlations of Cu with Mg, phosphorus, urea, and creatinine may be related to renal dysfunction and chronic inflammation. The negative association of Ca with Mg, phosphorus, urea, and creatinine may reflect disturbances in calcium–phosphorus homeostasis caused by impaired kidney function. (Ortega-Romero, *et al*., 2025) who observed that the strong negative correlations of Cu with Fe, Zn, and Ca may reflect the disturbed trace-element and mineral balance associated with CKD, while the positive correlations of Cu with Mg, phosphorus, urea, and creatinine may be related to renal dysfunction and chronic inflammation. The negative association of Ca with Mg, phosphorus, urea, and creatinine may reflect disturbances in calcium–phosphorus homeostasis caused by impaired kidney function [29].

Furthermore, the strong positive correlations of phosphorus with Mg, urea, and creatinine suggest that reduced renal excretion contributes to their accumulation as kidney function deteriorates. These findings indicate that impaired renal function is closely associated with alterations in mineral and trace-element homeostasis [29].

Figure 1 illustrated that the scatter plot demonstrates a very strong positive linear relationship between serum phosphorus (P) and urea concentrations among the CKD patients. The fitted regression equation was $y = 19.408x$, with an R^2 value of 0.9881, indicating that approximately 98.81% of the variation in urea concentration is explained by its linear relationship with phosphorus in this dataset. This corresponds to an approximate correlation coefficient of $r = 0.994$, indicating an exceptionally strong positive association.

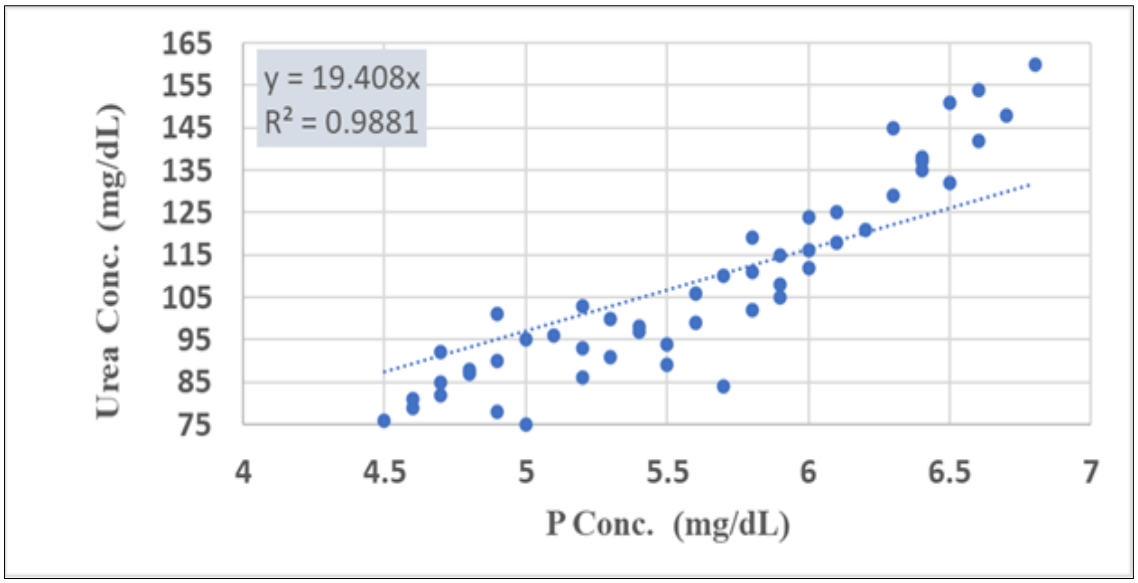


Figure 1: The scatter plot demonstrates

This association may indicate a progressive decline of renal function in CKD patients. In the nonfunctioning kidney phosphorus and urea are not excreted but are retained in the blood. Likewise, the high urea may be related to the high concentrations of phosphorus in the patients (Abbasi *et al*., 2026). Or the observed association may be due to the inter-related effects of reduced glomerular filtration, phosphate retention and abnormalities of mineral metabolism associated with CKD [30]. Increased urea deposition has also been associated with increased serum phosphorous levels that may be an indicator of declining kidney function (Prabhakar *et al*., 2024). However, this is a correlation analysis and the strong association should not be interpreted as supportive evidence that increased phosphorus leads to increased urea but rather a reflection of the underlying worsening of renal function [31].

The ROC curve analysis demonstrated that most of the studied parameters had significant diagnostic ability to discriminate CKD cases from healthy controls. Phosphorus and urea showed perfect diagnostic performance, with an AUC of 1.000, 100% sensitivity, and 100% specificity ($P \leq 0.01$).

Copper also demonstrated strong diagnostic performance, with an AUC of 0.908 (95% CI: 0.855–0.962), sensitivity of 70%, and specificity of 92% at a cutoff of 123.5 ($P \leq 0.01$). In contrast, magnesium showed poor-to-moderate discrimination (AUC = 0.599) and was not statistically significant (P = 0.087).

The AUC values reported for D3 (0.050), Fe, Zn, and Ca (0.000) indicate strong separation between cases and controls, but their direction is reversed because these parameters were lower in CKD cases than in controls. Therefore, the very low AUC values should be interpreted as excellent discrimination in the opposite direction rather than as an absence of diagnostic value. Their sensitivity and specificity at the reported cutoffs were 0% and 100%, respectively. As shows in table 4 and figure 2.

Table 4: ROC curve analysis of studied parameters between cases and controls

Test	Area	Cutoff	SE	P-value	95% C. I		SN	SP
					Lower Bound	Upper Bound		
D3	.050	89.9	0.023	≤0.01	.005	.096	0	100
Fe	.000	133	.000	≤0.01	.000	.000	0	100
Zn	.000	113	.000	≤0.01	.000	.000	0	100
Cu	.908	123.5	0.027	≤0.01	.855	.962	70	92
Ca	.000	10.08	.000	≤0.01	.000	.000	0	100
Mg	.599	2.45	0.058	.087	.486	.713	36	86
P	1.000	4.3	0.000	≤0.01	1.0	1.0	100	100
Urea	1.000	53.5	0.000	≤0.01	1.0	1.0	100	100

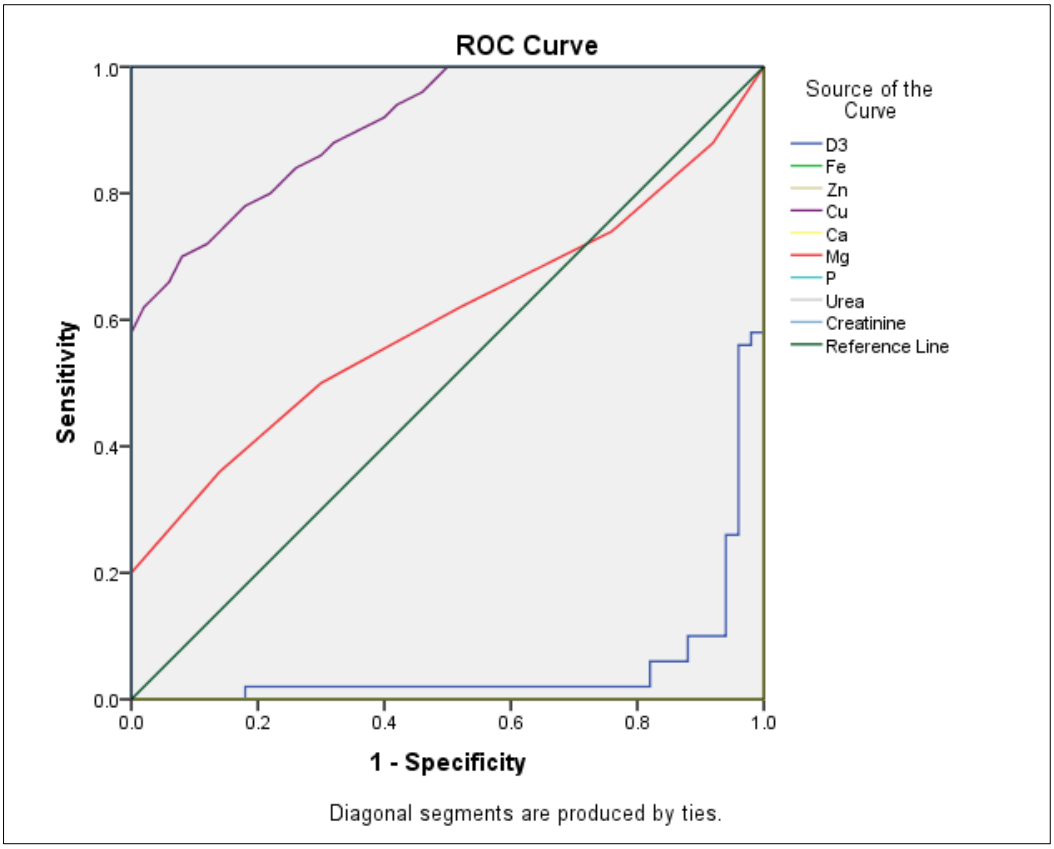


Figure 2: ROC curve analysis of studied parameters between cases and controls

The ROC findings indicate that copper has considerably better diagnostic value than magnesium for distinguishing CKD patients from controls. An AUC of 0.908 indicates excellent discrimination; the specificity of 92% indicates that the copper test identifies most of the healthy individuals correctly. The sensitivity of 70% demonstrates that copper can identify a large number of CKD cases but some patients may be missed at the selected cutoff [32]. This good performance could be related to the important elevation of copper observed in CKD patients, suggesting an altered copper metabolism and chronic inflammation. The present results are consistent with those published by (Liu, *et al*., 2025) who found that the robust diagnostic performance may be due to a significant elevation of serum copper in CKD patients which may be an indication of disturbed copper metabolism and the presence of chronic inflammation [33]. Magnesium showed a poor diagnostic performance (AUC 0.599, non-statistically significant P-value 0.087). One possible explanation is that the difference in magnesium levels between cases and controls was relatively small. This suggests a more tightly controlled serum magnesium that may be relatively stable with renal dysfunction. Therefore, in the present study, magnesium appears to be a less useful potential marker than copper to differentiate CKD cases from controls. These results are in agreement with (Khan *et al*., 2026) [34].

One important correction: P = 0.087 is not statistically significant at the conventional 0.05 level. Also, the reported sensitivity = 0% and specificity = 100% for D3, Fe, Zn, and Ca should be interpreted cautiously because the ROC direction/case coding may have been reversed [35].

The ROC analysis demonstrated very strong separation between CKD cases and controls for vitamin D3, Fe, Zn, and Ca. The AUC values were extremely low for D3 (0.050) and Fe, Zn, and Ca (0.000). These values should not be interpreted as indicating poor diagnostic performance. Rather, they indicate that the biomarkers have an almost complete ability to distinguish the two groups, but the direction of discrimination is opposite to the conventional ROC orientation.

This finding corresponded with (Dai, et al. 2026) and that consistent with the significantly lower concentrations of D3, Fe, Zn, and Ca observed in CKD patients compared with controls. Therefore, these parameters may have considerable potential for discriminating CKD patients from healthy individuals when the ROC direction is appropriately specified [36].

However, the reported sensitivity of 0% and specificity of 100% at the selected cutoffs should be interpreted with caution. This pattern may result from the classification direction used in the ROC analysis, particularly because these biomarkers were lower in

cases than in controls. Reversing the test direction would be expected to produce AUC values close to 1.00 and correspondingly meaningful sensitivity and specificity. Therefore, the ROC analysis should be checked to ensure that the case/control status and test direction were correctly entered before these results are presented as diagnostic performance measures [37].

CONCLUSION

1. CKD was associated with profound alterations in mineral and trace-element concentrations with decreased vitamin D3, Fe, Zn and Ca and increased Cu and phosphorus.
2. Urea and creatinine were significantly increased confirming substantial impairment of renal function among CKD patients.
3. Significant correlations between the analyzed parameters suggest the presence of mutual disturbances in mineral and trace-element homeostasis in the course of renal dysfunction.
4. The best diagnostic performance was found for phosphorus and urea (AUC=1.000) followed by Cu with high discriminatory ability (AUC=0.908), which indicates their potential value as biomarkers of CKD.

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