Fibroblast growth factor 23 levels before and after renal transplantation

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Background
Fibroblast growth factor 23 (FGF23), a novel bone-derived hormone that inhibits phosphate reabsorption and calcitriol production by the kidney, has uncovered primary regulatory pathways and new systems biology governing bone mineralization, vitamin D metabolism, parathyroid gland function, and renal phosphate handling.
Aim of the work
The aim of the present prospective study was to investigate FGF23 levels in patients with end-stage renal disease before and after a successful renal transplant and their probable association with the markers of bone and mineral metabolism.
Patients and methods
A total of 40 patients were studied for 6 months and divided into two groups (hemodialysis vs. renal transplant patients). Serum FGF23, calcium, phosphorus, and intact parathyroid hormone (iPTH) were estimated for both groups. We compared the changes in serum FGF23, calcium, phosphorus, and iPTH in renal transplant patients 3 and 6 months after successful renal transplantation.
Results
The serum FGF23 decreased significantly after renal transplantation. iPTH and P levels also decreased significantly after renal transplant, whereas Ca level increased.
Conclusion
FGF23 levels were markedly increased in patients with end-stage renal disease associated with an increase in phosphorous and iPTH levels. FGF23 levels decrease dramatically after successful renal transplantation and remain within the normal limits when graft function is good. iPTH and P levels also decrease significantly after renal transplantation, whereas Ca increases.

Keywords:
chronic kidney diseases, CRF, fibroblast growth factor 23, renal transplantation

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Introduction

Fibroblast growth factor 23 (FGF23), a novel bone-derived hormone that inhibits phosphate reabsorption and calcitriol production by the kidney has primary regulatory pathways and new systems biology governing bone mineralization, vitamin D metabolism, parathyroid gland function, and renal phosphate handling [1].

The assessment of FGF23 has been predicted to become a diagnostic marker as well as a therapeutic target for the management of disordered bone mineral metabolism [2].

Disordered phosphate homeostasis with elevated circulating levels of FGF23 is an early and pervasive complication of chronic kidney disease (CKD) [3]. FGF23 has been responsible for hypophosphatemia and inappropriately low calcitriol levels observed after renal transplantation [4].

Patients and methods

This cohort, prospective, observational study was carried out on 40 patients with end-stage renal disease (ESRD) on maintenance hemodialysis (21 males, 19 females). The patients were divided into two groups:

(1) Group A, which included 20 Hemodialysis (HD) patients on maintenance HD.

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(2) Group B, which included 20 HD patients scheduled for renal transplantation; patients were followed up 3 and 6 months after successful renal transplantation. Group B was further divided into the following:
   (a) Group B0, which included chronic renal failure (CRF) patients on regular hemodialysis scheduled for renal transplantation.
   (b) Group B3, which included patients who underwent renal transplantation after 3 months.
   (c) Group B6, which included patients who underwent renal transplantation after 6 months.
   (d) The study protocol was approved by the ethical committee of our faculty.

All the patients were recruited from the Dialysis Unit of Kasr El-Aini Hospital, Cairo University. The patients with ESRD had been undergoing hemodialysis three times weekly on standard bicarbonate dialysis with low-flux dialyzers.

All patients will be subjected to the following:

(1) History taking and physical examination to exclude any disease that might affect the parameters to be investigated.
(2) BMI, calculated as weight in kg/square of height in meters.
(3) Quantification of FGF23 (pg/ml) concentration by using enzyme-linked immunosorbent assay.
(4) Serum calcium, phosphate, parathyroid hormone (PTH), albumin, and creatinine by using colorimetry in a routine clinical laboratory.

All laboratory investigations were carried out again for group B, 3 and 6 months after renal transplantation, to compare the results.

Inclusion criteria

(1) Patients of both sexes with ESRD on regular hemodialysis.
(2) Age more than 18 years and less than 65 years.
(3) Renal transplant patients with normal kidney functions after transplant.

The allograft types in renal transplanted patients were living donor allograft; approval for the same was obtained from the local ethical committee.

They received triple drug immunosuppressive treatment consisting of cyclosporine (5mg/kg initially, maintenance dose based on blood trough level), prednisolone (200mg initially, tapered to 5mg), and mycophenolate mofetil (2×1000mg/day).

Exclusion criteria

(1) Renal impairment after transplantation.
(2) Age less than 18 years and more than 65 years.

Parathyroid hormone test

Serum samples were prepared promptly from blood and stored temporarily on ice or refrigerated at 4°C. PTH-EASIA (Roche Diagnostics, Indianapolis, Indiana, USA) – a solid-phase enzyme-amplified sensitivity immunoassay performed on a micro titer plate for the determination of intact human PTH from serum or plasma – was carried out according to the manufacturer's guidelines.

The fibroblast growth factor 23 enzyme-linked immunosorbent assay

As the intact FGF23 molecule was highly unstable (resulting in a decreased immunoreactivity over time), specimen collection and assay or storage procedures were conducted expeditiously. As recommended, samples were collected in the morning from patients who had fasted for 12h. The collected samples were centrifuged, and the plasma or the media were separated from the cells. They were assayed immediately or stored at −70°C or below. The serum levels of intact FGF23 molecules were measured using the two-site (NH2-terminal/C-terminal) enzyme-linked immunosorbent assay (Immutopics Inc., San Clemente, California, USA). To assay the sample in duplicate, 300μl of plasma or culture media were collected. The human intact FGF23 enzyme-linked immunosorbent assay (Immutopics Inc.) was carried out according to the manufacturer's guidelines. Intact parathyroid hormone (iPTH) levels were determined by using the enzyme-amplified sensitivity immunoassay (Roche Diagnostics).

Statistical analysis

(1) All the collected questionnaires were revised for completeness and consistency. Precoded data were fed in the computer using 'Microsoft Office Excel Software' program (2010) for Windows (Microsoft Corporation). Data were transferred to the Statistical Package of Social Science Software program, version 21 (SPSS; IBM Corp., Armonk, NY) to be statistically analyzed.

Table 1 Comparison between group A and group B0 as regards different parameters

	Group A	Group B0	*P*-value
Age (years)	36.2±12.6	24.1±7.0	**0.001 (HS)**
Sex [*n* (%)]			
Male	10 (50.0)	11 (55.0)	1.0 (NS)
Female	10 (50.0)	9 (45.0)	
BMI (kg/m^2)	23.6±2.9	22.2±2.7	0.1 (NS)
Duration of dialysis (years)	4.4±2.7	0.9±0.5	<**0.001 (HS)**
Creatinine (mg/dl)	10.5±2.5	9.3±2.0	0.1 (NS)
Calcium (mg/dl)	7.2±1.1	7.2±0.5	0.8 (NS)
Phosphorus (mg/dl)	6.2±0.8	6.4±0.8	0.6 (NS)
FGF23 (pg/ml)	625.3±18.2	604.5±39.4	**0.04 (S)**
Albumin (mg/dl)	3.3±0.3	3.5±0.4	0.09 (NS)
PTH (pg/ml)	497.0±228.8	447.6±188.8	0.5 (NS)

Comparing group A and group B0 at different parameters, there was a statistically significant *P*-value ($P<0.001$) as regards age of patients in both groups; there was a statistically significant *P*-value ($P<0.001$) as regards duration of dialysis; and also statistically significant *P*-value ($P=0.04$) was found on comparing FGF23 level of the two groups. FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

Table 2 Comparison between group A and group B3 as regards different parameters

	Group A	Group B3	*P*-value
BMI (kg/m^2)	23.6±2.9	22.9±2.1	0.4 (NS)
Creatinine (mg/dl)	10.5±2.5	0.96±0.26	<**0.001 (HS)**
Calcium (mg/dl)	7.2±1.1	8.5±0.4	<**0.001 (HS)**
Phosphorus (mg/dl)	6.2±0.8	4.3±0.6	<**0.001 (HS)**
FGF23 (pg/ml)	625.3±18.2	242.3±9.5	<**0.001 (HS)**
Albumin (mg/dl)	3.3±0.3	4.0±0.2	<**0.001 (HS)**
PTH (pg/ml)	497.0±228.8	214.0±37.7	<**0.001 (HS)**

On comparing group A and group B3 as regards different parameters, we found a statistically significant *P*-value ($P<0.001$) as regards level of creatinine (10.5±2.5 to 0.96± 0.26), statistically significant *P*-value ($P<0.001$) as regards level of phosphorous (6.2±0.8 to 4.3±0.6), statistically significant *P*-value ($P<0.001$) as regards level of FGF23 (625.3±18.2 to 242.3±9.5), statistically significant *P*-value ($P<0.001$) as regards level of PTH (497.0±228.8 to 214.0± 37.7), statistically significant *P*-value ($P<0.001$) as regards level of albumin (3.3±0.3 to 4.0±0.2), and statistically significant *P*-value ($P<0.001$) as regards level of calcium (7.2± 1.1 to 8.5±0.4). FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

Table 3 Comparison between group A and group B6 as regards different parameters

	Group A	Group B6	*P*-value
BMI (kg/m^2)	23.6±2.9	22.9±2.1	0.4 (NS)
Creatinine (mg/dl)	10.5±2.5	0.92±0.21	<**0.001 (HS)**
Calcium (mg/dl)	7.2±1.1	8.6±0.3	<**0.001 (HS)**
Phosphorus (mg/dl)	6.2±0.8	4.4±0.5	<**0.001 (HS)**
FGF23 (pg/ml)	625.3±18.2	136.3±9.8	<**0.001 (HS)**
Albumin (mg/dl)	3.3±0.3	4.2±0.2	<**0.001 (HS)**
PTH (pg/ml)	497.0±228.8	92.5±19.2	<**0.001 (HS)**

On comparing group A and group B6, we found a statistically significant *P*-value ($P<0.001$) as regards the level of creatinine (10.5±2.5 to 0.92±0.21), statistically significant *P*-value ($P<0.001$) as regards the level of phosphorous (6.2±0.8 to 4.4±0.5), statistically significant *P*-value ($P<0.001$) as regards level of FGF23 (625.3±18.2 to 136.3±9.8), statistically significant *P*-value ($P<0.001$) as regards the level of PTH (497.0±228.8 to 92.5± 19.2), statistically significant *P*-value ($P<0.001$) as regards the level of albumin (3.3±0.3 to 4.2±0.2), and statistically significant *P*-value ($P<0.001$) as regards the level of calcium (7.2±1.1 to 8.6± 0.3). FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

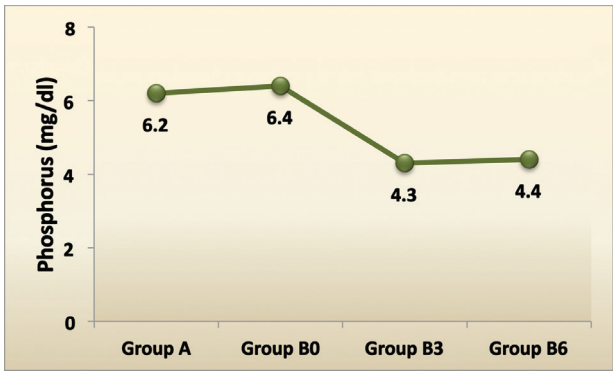
(2) Data were summarized using mean and SD for quantitative variables and frequency and percentage for qualitative ones.
(3) Comparison between the groups was carried out using the independent sample t-test or one way analysis of variance for quantitative variables, and the χ^2-test or Fissure exact test for qualitative ones.
(4) Repeated measurements were analyzed by using repeated measures analysis of variance test with the post-hoc Bonferroni test (for pair-wise comparisons).
(5) Pearson or Spearman's correlation coefficients were calculated to determine the association between parametric or nonparametric quantitative variables, respectively.
(6) P-values less than 0.05 were considered statistically significant, and less than 0.01 were considered highly significant.

Results

As shown in Tables 1–3 and Figs. 1–3, group A and groups B0, B3, and B6 were compared as regards different parameters, and a comparative analyses of the percent of changes for group A and group B at the beginning and at the end of the study were carried out.

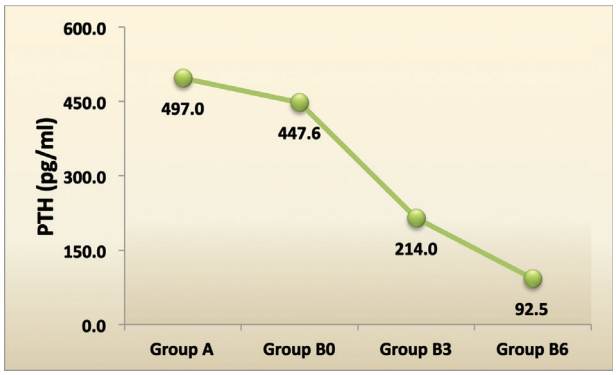
(1) As presented in Table 1, there was a statistically significant *P*-value ($P<0.001$) as regards age of patients in the two group. There was a statistically

Figure 1



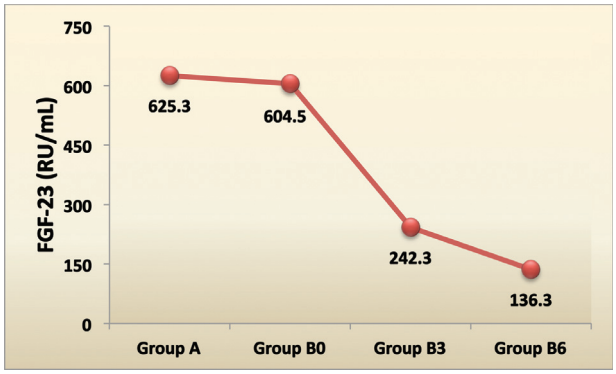
Comparison between group A and groups B0, B3, and B6 as regards phosphorous.

Figure 2



Comparison between group A and groups B0, B3, and B6 as regards parathyroid hormone (PTH).

Figure 3



Comparison between group A and groups B0, B3, and B6 as regards fibroblast growth factor 23 (FGF23).

significant *P*-value ($P<0.001$) as regards duration of dialysis, and also a statistically significant *P*-value ($P=0.04$) on comparing the FGF23 levels for the two groups.

(2) As shown in Tables 2 and 3, on comparing group A with groups B3 and B6 on different parameters, we found a statistically significant *P*-value ($P<0.001$) as regards the level of creatinine, phosphorus, FGF23, PTH, albumin, and calcium.

(3) As shown in Tables 4 and 5 and Figs. 1–3, on comparing groups B0, B3, and B6 on different parameters show a statistically significant *P*-value ($P<0.001$) as regards the level of creatinine, phosphorous, FGF23, PTH, albumin, calcium.

(4) We found that there was a statistically significant *P*-value ($P<0.001$) with different parameters (calcium, phosphorous, FGF23, PTH, serum creatinine) on comparing groups B0 and B3 with groups B0 and B6.

(5) There was a statistically significant *P*-value ($P<0.001$) as regards the level of FGF23 and PTH on comparing group B3 and group B6.

Discussion

CKD is often accompanied by dysregulated phosphate metabolism, which is usually first indicated by high circulating levels of FGF23, which become apparent with an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2. Hyperparathyroidism and hyperphosphatemia develop in more advanced stages of CKD, which is associated with an increased risk for cardiovascular morbidity and mortality [5].

In the recent years, there has been an increasing appreciation of the existence of a 'bone-vascular axis'. This term refers to the existence of a bidirectional flow of information between bones and vessels through an exchange of cells, hormones, and other metabolic signals. Investigators have proposed that promoters and inhibitors of bone mineralization, such as vitamin D, PTH, phosphorus, FGF23, and others, are also involved in the pathogenesis of vascular calcification [6].

FGF23 is identified as a 'phosphatonin' that is thought to be implicated in the systemic balance of phosphate maintained by the interaction of the kidneys, intestine, and bone. As a result, FGF23 excess is characterized by hypophosphatemia, with increased renal phosphate wasting and inappropriately low calcitriol levels [7].

After successful kidney transplantation, kidney function resumes and waste products and electrolytes are excreted and regulatory hormones return to the normal levels. Important mineral metabolites and regulatory hormones in the bone and mineral metabolism include calcium, phosphate, PTH, FGF23, and vitamin D. Improvement of bone and mineral metabolism are expected in most patients and,

Table 4 Comparison between group B0, group B3, and group B6 as regards different parameters

	Group B0	Group B3	Group B6	0–6 (*P*–value)
Creatinine (mg/dl)	9.3±2.0	0.96±0.26	0.92±0.21	<**0.001**
Step P-value	–	<**0.001**	0.3	
Calcium (mg/dl)	7.2±0.5	8.5±0.4	8.6±0.3	<**0.001**
Step P-value		<**0.001**	0.1	
Phosphorus (mg/dl)	6.4±0.8	4.3±0.6	4.4±0.5	<**0.001**
Step P-value	–	<**0.001**	0.6	
FGF23 (pg/ml)	604.5±39.4	242.3±9.5	136.3±9.8	<**0.001**
Step P-value	–	<**0.001**	<**0.001**	
Albumin (mg/dl)	3.5±0.4	4.0±0.2	4.2±0.2	<**0.001**
Step P-value	–	<**0.001**	**0.004**	
PTH (pg/ml)	447.6±188.8	214.0±37.7	92.5±19.2	<**0.001**
Step P-value	–	<**0.001**	<**0.001**	

Step *P*-value=*P*-value of comparison of the measurement with its previous time measurement. On comparison group B0, group B3, and B6 as regards, we found a statistically significant *P*-value ($P<0.001$) as regards the level of creatinine (9.3±2.0 to 0.92±0.21), statistically significant *P*-value ($P<0.001$) as regards the level of phosphorous (6.4±0.8 to 4.4±0.5), statistically significant *P*-value ($P<0.001$) as regards the level of FGF23 (604.5±39.4 to 136.3±9.8), statistically significant *P*-value ($P<0.001$) as regards the level of PTH (447.6±188.8 to 92.5±19.2), statistically significant *P*-value ($P<0.001$) as regards the level of albumin (3.3±0.3 to 4.2±0.2), and statistically significant *P*-value ($P<0.001$) as regards the level of calcium (7.2±0.5 to 8.6±0.3). We found that there was a statistically significant *P*-value ($P<0.001$) as regards different parameters (calcium, phosphorous, FGF23, PTH, serum creatinine) on comparing group B0 and B3 with group B0 and B6. There was a statistically significant *P*-value ($P<0.001$) as regards the level of FGF23 and PTH only on comparing group B3 with groupB6. FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

Table 5 Correlation of FGF23 with other parameters before transplantation

	FGF23 before Tx	After 3 months	After 6 months
Age			
r	0.238	0.362	0.085
P-value	0.139	0.117	0.722
BMI			
r	–0.203	0.073	–0.192
P-value	0.209	0.761	0.417
Duration of dialysis			
r	**0.338**		
P-value	**0.033**		
Creatinine (mg/dl)			
r	0.145	0.025	–0.019
P-value	0.373	0.918	0.936
Calcium (mg/dl)			
r	**–0.446**	–0.168	0.108
P-value	**0.004**	0.478	0.652
Phosphorus (mg/dl)			
r	**0.652**	0.196	0.201
P-value	<**0.001**	0.407	0.397
Albumin (mg/dl)			
r	**–0.362**	**–0.476**	–0.144
P-value	**0.022**	**0.034**	0.544
PTH (pg/ml)			
r	**0.111**	0.160	–0.091
P-value	**0.007**	0.500	0.702

We found a positive correlation between duration of dialysis and the level of FGF23 ($P=0.033$); there was a negative correlation between the level of calcium and that of FGF23 ($P=0.004$); there was a positive correlation between the level of phosphorous and that of FGF23 ($P<0.001$); there was a negative correlation between the level of albumin and that of FGF23 ($P=0.022$); there was a positive correlation between the level of PTH and that of FGF23 ($P=0.007$). FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

as a result, the progression of vascular calcification also attenuates. However, persistent abnormalities remain in some patients [8].

In our prospective study, FGF23 levels were determined in renal transplant recipients with stable renal function 3 and 6 months after the transplant.

Intact FGF23 was measured to avoid the measurement of fragments that accumulate in ESRD and do not probably reflect endogenous FGF23 production.

In our study, patients with ESRD on regular hemodialysis had statistically significant correlation between the level of FGF23 and that of phosphorous, PTH, and calcium.

Patients with ESRD had high levels of FGF23, phosphorous, and PTH, and low levels of calcium. This was in agreement with the findings of a study by Silver and Naveh-Many (2013) [9], in which patients with CKD exhibited marked elevations of circulating FGF23, and, also, serum phosphate was found to be one of the main regulators of FGF23 levels in uremic patients on maintenance HD, which suggests that the production of FGF23 in the bone is continuously stimulated by phosphate load.

In our study, we observed significant reduction of FGF23 levels 3 months after transplantation (625.3± 18.2 vs. 242.3±9.5, $P<0.001$), and at 6 months there was a slight further decline in the FGF23

levels (242.3±9.5 vs. 136.3±9.8, $P<0.001$). Hypophosphatemia, which is the major stimulant for FGF23 secretion, was resolved. This was in agreement with a study by Economidou *et al.* (2009) [10], in which they found out that FGF23 levels decreased by 89% at 3 months after transplantation (346±146 vs. 37±9pg/ml, $P<0.01$) and then remained stable for 12 months.

Our results were in agreement with those of a study by Pahnwat and Sinee [8], in which they reported a rapid reduction in FGF23 levels during the first 3 days up to 3 months after transplantation; the average FGF23 level was still higher than the normal level, resulting in almost 90% of the patients with functioning graft experiencing hypophosphatemia at some point. The degree of hypophosphatemia was mild to moderate (1.5–2.3mg/dl) in 20% and severe (≤1.5mg/dl) in 60% of the patients.

This was in contrast to the results obtained by Krocker *et al.* (2006) [11] who reported that the patients with chronic renal failure and secondary hyperparathyroidism, who had undergone renal transplantation, produced greater quantities of FGF23 in the first trimester after transplantation, until osteoblasts become inactive and bone metabolism is suppressed; the researchers also reported that corticosteroids, calcineurin inhibitors, and mTOR inhibitors stimulate FGF23 production, even though in the first months after transplantation, with the use of higher doses of these drugs.

Evenepoel *et al.* (2011) [4] also recognized persistent elevation of FGF23 level after transplant and explained that the uremic bone may develop resistance to feedback inhibition of FGF23, perhaps caused by the preceding years of chronic phosphate retention, which stimulates FGF23 secretion.

In our study, we observed that before transplantation, FGF23 level significantly correlated with phosphorous and iPTH levels. Moreover, we observed negative correlation with calcium levels.

There was no significant correlation between FGF23 level and phosphorous, calcium, and iPTH levels at 3 and 6 months after transplant.

This was in contrast to the findings of a study by Andrea *et al.* (2011) [12]. Pretransplant iPTH levels were significantly higher in patients developing hypophosphatemia after renal transplantation. Pretransplant levels of FGF23 were not associated with sPi at the time of transplantation. In addition to PTH, elevated FGF23 may contribute to hypophosphatemia during the early postrenal transplant period. Our results were also in contrast to those of a study by Economidou *et al.* (2009) [10], where they found phosphate levels 3 month after transplantation to be significantly correlated with FGF23 levels after transplantation.

In our study, mean iPTH levels decreased at 3 months after transplantation and remained low, but higher than the normal level at 6 months. This was in agreement with the findings of a study by Andrea *et al.* (2011) [12], in which they found that iPTH concentrations decrease progressively after renal transplantation. However, resolution of secondary hyperparathyroidism remained incomplete 1 year after transplantation.

In our study, a significant correlation was observed between pretransplantation iPTH and Ca and P levels and their levels at 3 and 6 months after transplantation.

This was in agreement with Heaf (2003) [13], who indicated that successful renal transplantation, by normalizing urinary phosphate and β2-microglobulin excretion and renal calcitriol production, reverses many of these abnormalities in mineral and bone metabolism, including the following:

(1) A fall in the plasma phosphate concentration to the normal level.
(2) A reduction in plasma PTH levels.
(3) A decrease in plasma alkaline phosphatase levels, indicating less bone resorption.
(4) Mobilization of soft tissue calcifications, as a correction of hyperphosphatemia markedly lowers the calcium–phosphate product.
(5) Improvement in aluminum bone disease.
(6) Prevention of progression of amyloid osteodystrophy.

In our study, we achieved a statistically significant *P*-value ($P<0.001$) on comparing phosphate level before transplantation with that at 3 and 6 months after transplantation. We also had temporary mild hyposphosphatemia in 20% of our patients at 3 months and 6 months after transplantation.

This was in agreement with Economidou *et al.* (2009) [10], who reported temporary mild hyposphosphatemia in 28% of their patients at 3 months after transplantation. Phosphate levels and $TmPO_4$/glomerular filtration rate were strongly correlated, indicating that the low P levels after renal

transplantation were a result of renal phosphate wasting.

In their study, Evenepoel *et al.* (2011) [4] showed that the patients that developed hypophosphatemia tended to have higher pretransplantation and post-transplantation iPTH levels, as well as higher pretransplantation FGF23 levels. These findings suggest that FGF23 and iPTH could act synergistically to cause phosphaturia.

In our study, we found a statistically significant relation ($P<0.001$) on comparing calcium level before transplantation with that at 3 and 6 months after transplantation. We noticed an increase in the serum calcium level after transplantation. This was in agreement with Saji *et al.* (2009) [14], who indicated that those patients who present with an increase in serum calcium, the plasma calcium concentration frequently begins to rise during the first 10 days after transplantation; however, this response can be delayed for 6 months or more.

In their study, Borchhardt *et al.* (2007) [15] explained that hypercalcemia developed after transplantation as persistent hyperparathyroidism is the most common cause. In addition to hyperparathyroidism, other factors can also contribute to an elevation in the plasma calcium concentration:

(1) Resorption of soft tissue calcium phosphate deposits, which is often associated with persistent hyperphosphatemia.
(2) Normalization of calcitriol production, which both increases the PTH effect on bone and directly enhances intestinal calcium absorption.
(3) Enhanced tubular calcium resorption.
(4) To a lesser degree, a rise in the plasma albumin concentration (due to better nutrition).

Our study had some advantages. One was that FGF23 levels were determined by using an assay that does not detect C-terminal fragments. Another was that we conducted serial measurements of FGF23 after renal transplantation. Possible limitations, on the other hand, were the small number of patients included in the study and the use of activated vitamin D analogs and calcium salts, which may have confounded our results.

Conclusion

FGF23 levels decrease dramatically after successful renal transplantation and remain within normal limits when graft function is good. iPTH and P levels also decrease significantly after renal transplantation, whereas the calcium level increases.

The recent identification of FGF23 as a physiological regulator of phosphate and vitamin D metabolism has greatly advanced our understanding of mineral and bone disorders in CKD.

FGF23 plays a central role in the pathogenesis of altered mineral metabolism and secondary hyperparathyroidism in CKD patients and post-transplant hypophosphatemia in kidney transplant recipients.

Further elucidation of FGF23 function and regulation will help to establish a more rational approach for the management of the mineral and bone disorders that are associated with the high burden of morbidity and mortality in CKD patients and also in renal transplant patients.

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Cairo University. The manuscript has been read and approved by all authors.

Conflicts of interest

There are no conflicts of interest.

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