Original Article

The Study of Fibroblast Growth Factor-23 in Renal Failure Patients Undergoing Dialysis with or without Corona Vaccine

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Abstract

Background: In the past 10 years, FGF23 has emerged as a potential symptomatic, prognostic biomarker, and restorative objective in several circumstances. Vaccination is one of the best techniques to stop the pandemic. However, following COVID-19 vaccination, both new and recurrent renal disorders have been reported. In the current study, levels of FGF23 were explored in renal patients with and without the corona vaccine. Other inflammatory markers also correlated with these levels. **Objectives:** The goal of the current investigation was to estimate FGF23 levels in renal failure patients undergoing dialysis with or without corona vaccination, as well as the relationship between these levels and other frequently used biomarkers. **Materials and Methods:** Blood tests were gathered from 60 patients with renal disappointment disease with and without vaccination with age ranging from 30 to 65 years and 30 age-matched healthy controls were included the study. We examined how other parameters and serum FGF23 levels were related. **Results:** This study found a substantial link between FGF23 and these parameters in patients who received the corona virus vaccine and other biomarkers, and there was an inverse correlation FGF23 between patients who did not receive the corona virus vaccine and some other parameters. Patients with renal failure undergoing dialysis also had elevated levels of FGF23. FGF23 levels are higher in patients with kidney issues than in healthy individual, even if they have received the COVID-19 vaccine. **Conclusion:** FGF23 is a promising marker for tracking disease progression. However, FGF23 levels in patients who received vaccination did not differ significantly from those who did not.

Keywords: COVID-19, dialysis, fibroblast growth factor, renal failure, vaccine

Introduction

Chronic kidney disease (CKD) is common in many nations.[1] Patients experiencing renal failure develop a secure imperfection that remembers weakness for both intrinsic and versatile insusceptible reactions, including diminished neutrophil, bacterial action, monocyte hypo movement, disabled action of T cells, and a reduction in B lymphocyte counts. Compared with the general population, people with this immune impairment experience a hundredfold higher rate of infection-related deaths.[2] The key characteristics that contribute to an unusually safe status in individuals with CKD include the maintenance of uremic poisons, gastrointestinal dysmetabolism, dysbiosis, and dialysis.[3] End-stage kidney disease (ESRD) sulfates may actuate monocyte separation to support provocative, macrophages that promote fibrosis, prompting chronic inflammation.[4] Renal disease is becoming increasingly prevalent. With the possibility of acquiring a serious case of COVID-19,when exposed to SARS-CoV 2, patients with renal problems were given priority to obtain COVID-19 vaccinations.[5]

Vaccination campaigns have been conducted worldwide in response to COVID-19 vaccinations, and during the previous 2 years, a number of vaccinations have

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been approved for use in emergencies. These comprise adenovirus-vectored vaccines from Oxford-AstraZeneca and Janssen, mRNA vaccines from Pfizer-BioNTech and Moderna, recombinant vaccines from Novavax, and inactivated vaccines from CoronaVac.[6,7]

Osteocytes are the primary producers of FGF23, a 32 kDa peptide, that is, in circulation. It assumes a focal part affects phosphate homeostasis by its effects on the kidney of advance phosphate discharge and cutoff calcitriol creation. Past its physiologic consequences for the kidney, FGF23 may likewise prompt neurotic cardiovascular myocyte hypertrophy.[8] It is functionally regarded as phosphatonin, a hormone that controls phosphorus. Although the kidney is its primary target, FGF23 is also expressed in a various organs.[9] Patients with renal failure have higher plasma levels of fibroblast growth factor=23 (FGF23). FGF23 regulates Vitamin D and phosphate digestion.[10] Recent research suggests that FGF23 is an immune-regulating hormone that modulates the immunological response through direct action on immune cells, such as macrophages and polymorpho-nuclear neutrophils, has indirect effects on non-immune organs. Expanded irritation was correlated with elevated FGF23 levels. Increased FGF23 levels in patients cause resistance reactions *in vitro* in both human erythrocytes and experimental animal models.[11]A well-known biomarker of adverse outcomes in patients with FGF23. According to a number of studies, anemia in these patients may be linked to FGF23. It is a bone-inferred chemical that manage phosphate and Vitamin D digestion.[12] With declining renal function, FGF23 levels gradually increase, which appears to be an adaptive strategy for preventing hyperphosphatemia. In the previous 10 years, FGF23 has emerged as a potential marker (both demonstrative and prognostic) and restorative objective in a few circumstances: genetic diseases (conditions of FGF23 overabundance and conditions due to an FGF23 deficit, hypophosphatemia and hyperphosphatemic messes).[13] The goal of the current investigation was to estimate FGF23 levels in renal failure patients undergoing dialysis with or without corona vaccination, as well as the relationship between these levels and other frequently used biomarkers.

Materials and Methods

One case-control investigation was completed in 60 patients (30 patients with chronic renal disease receiving dialysis received the corona virus vaccine and 30 patients with chronic renal disease who had not received the vaccine), at ages between 30 and 65 years and 30 age -matched healthy controls were included in the study. Patients were referred to the outpatient clinic at Al-kadhmah Teaching Hospital (the dialysis unit) from June 2023 to September 2023, all patients remembered for this study were non diabetic, non-liquor abusers, and without viral hepatitis. The first group, denoted G1, comprised 30 individuals and served as the control group. A total of 30 individuals with (CKD) who had not received the COVD-19 vaccination made up the second group (G2). We collected 5 mL of venous serum to measure urea, creatinine, and UA level using a self-loader analyzer BA-88A (Korea). In addition, we used a serum sample to determine FGF23 levels using ELISA kits provided by the U.S. We manually measured alkaline phosphatase (ALP), alanine transaminase (ALT), and aspartate aminotransferase (AST) levels.

Statistical analysis

Using statistical software and Excel programs, all statistical methods in this study were conducted using the *t* test, one-way analysis of difference (ANOVA), and Pearson correlation value (*r*). *P* value of 0.05 was employed to evaluate statistical significance.

Ethical approval

Procedures involving human participants followed the ethical guidelines outlined by the Ministry of Health in Iraq. All participants provided verbal consent after receiving a detailed explanation of the aim of study, procedures, potential risks, and benefits. Attendants were assured of their voluntary participation and the confidentiality of their personal information.

Results

Our knowledge this is the first study to assess the levels of FGF23 in renal failure, both with and without the COVID-19 vaccine. Table 1 shows a significant change in serum levels of blood urea (BU), creatinine (Cr), and uric acid (UA) in contrast with healthy control.

There was a significant increase ($P<0.05$) in the convergence of BU and, serum creatinine, and no significant difference ($P \geq 0.05$) when compared to healthy controls. Table 2 showed the ANOVA analysis of FGF23, AST, ALT, and ALP levels for G_1, G_2, and G_3.

Table 1: ANOVA statistics of urea, creatinine, and uric acid for G_1, G_2, and G_3

Group parameters	G1	G2	G3	ANOVA *t* test
Urea	25.16 ± 6.80	113.4 ± 30.19	125.76 ± 32.15	Significant
Creatinine	4.016 ± 0.34	7.50 ± 1.46	7.453 ± 1.00	Significant
Uric acid	4.016 ± 0.343	4.32 ± 1.20	4.68 ± 1.14	Non sign.

G1: Control group, G2: group of patients without vaccine, G3: group of patients with vaccine

Table 2: ANOVA statists of aspartate aminotransferase, alanine transaminase, alkaline phosphatase and FGF23 for G_1, G_2 and G_3

Group parameters	G1	G2	G3	ANOVA *t* test
AST	25.4 ± 0.72	19.92 ± 0.36	19.41 ± 0.93	Significant
ALT	24.61 ± 1.32	20.1 ± 1.02	20.85 ± 1.10	Sign.
ALP	401.83 ± 12.29	377.6 ± 77.59	386.53 ± 47.44	Non. sign.
FGF23	121.24 ± 47.26	380.00 ± 92.64	413.35 ± 101.24	Significant

G1: Control group, G2: group patient without vaccine, G3: group patient with vaccine, ALP: alkaline phosphatase, ALT: alanine transaminase, AST: aspartate aminotransferase

Table 3: The statistical difference between G2 and G3 in all biochemical parameters

Parameters	Patients with vaccine	Patients with vaccine	P value
	Mean ± SD	Mean ± SD	
Age	59.07 ± 10.09	51.53 ± 14.97	No. sig
FGF23	413.35 ± 101.24	380.00 ± 92.64	No. sig
Urea	125.76 ± 32.15	113.4 ± 30.19	No. sig
Creatinine	7.453 ± 1.00	7.50 ± 1.46	No. sig
Uric acid	4.68 ± 1.14	4.32 ± 1.20	No. sig
ALK	386.53 ± 47.44	377.6 ± 77.59	No. sig
AST	19.41 ± 3.93	19.92 ± 3.36	No. sig
ALP	3.684 ± 0.285	4.206 ± 1.53	No. sig

No sign = $P > 0.05$, sig = $P \leq 0.05$, ALP: alkaline phosphatase, AST: aspartate aminotransferase

Table 4: A Correlation between FGF23 with all studied parameters in patients with vaccination

	R	*P* value
Urea	−0.29	Sig
Uric acid	−0.483	Sig.
Creatinine	−0.552	Sig.
AST	−0.169	Sig.
ALT	−0.193	Sig
ALP	0.576	Sig

No sign = $P > 0.05$, sig = $P \leq 0.05$, ALP: alkaline phosphatase, ALT: alanine transaminase, AST: aspartate aminotransferase

The results of FGF23 showed a significant decrease in AST and ALT in G3 and G2 compared to G1, and a considerable increase in G2 and G3 compared to G1. ALP levels were not significantly different between G2 and G3, in contrast to G1. From Table 3, we are investigating whether there was a non-significant difference between G2and G3 in all biochemical parameters. From Table 3, we investigated whether there was a non-significant difference between G2and G3 in all biochemical parameters.

Table 4, we show the relationship between FGF23 levels and all indicators in patients who received vaccination

From Table 3, we show a relationship between FGF23 and other parameters in all patients with vaccination indicating a positive correlation between FGF23 and other parameters in renal failure patients with corona vaccine. Table 5 shows that there was no significant association

Table 5: A correlation between FGF23 with all studied parameters in patients without vaccination

	R	P value
Urea	0.303	No sig
Uric acid	0.349	No sig.
Creatinine	0.531	No sig.
AST	−0.097	Sig.
ALT	−0.118	Sig
ALP	−0.145	Sig

Sign = $P \leq 0.05$, no sig = $P > 0.05$, ALP: alkaline phosphatase, ALT: alanine transaminase, AST: aspartate aminotransferase

between FGF2 and urea, UC, and creatinine, a while a substantial relationship existed between FGF23 and AST, ALT, and ALP.

Discussion

Serum levels of creatinine and urea should be used as markers to determine whether impairment of renal function causes higher levels of these substances.[14] Urea is the livers product of protein and amino acid catabolism, which is filtered by the glomerulus. Increased urea levels in patients, blood occurs as a result of decreased capacity of the kidneys to excrete urea and the diminished capacity of the glomerulus to filter it. Creatinine is a degradation of muscular creatinine, mixed by the liver and found in the blood and muscle skeleton that the kidneys excrete through urine. Creatinine excretion is influenced by muscle activity.[15]This study found that dialysis patients had lower mean serum transaminase (AST and ALT) levels than the monitoring group, which had normal renal function. A few studies have demonstrated that CKD patients have lower ALT and AST levels than those with typical renal function.[16,17] Glomerular lesion-related progression of renal failure and lower serum ALT levels has been hypothesized to be linked. Fabrizi *et al*.[18] revealed that patients undergoing hemodialysis had lower ATL levels than those with chronic renal disease receiving moderate therapy (predialysis); suggesting a relationship between reduced serum ALT levels and impaired renal function. Serum levels of fibroblast growth factor-23 (FGF23) are often high in patients with CKD. A phosphaturic substance called fibroblast development factor-23 stifles dynamic

Vitamin D, which prevents the resistive reaction, through a restraint of one alpha hydroxylase and a feeling of 24 hydroxylases. FGF23 is raised during irritation and can additionally exacerbate this condition by leaning toward the development of favorable to incendiary cytokines,[19] FGF23 can initiate the arrival of fiery cytokines from assorted supplies. In patients with persistent pneumonic illness, FGF23 levels are fundamentally expanded.[20] FGF23 has been shown to act on human bronchial epithelial cells in people with cystic fibrosis and causes the release of IL-8, an essential cytokine that causes persistent inflammation in these patients.[21] Han *et al*. later revealed that FGF23 likewise focuses on peritoneal macrophages to build the outflow of TNF-α, further increasing its role in inflammation.[22] Patients with end-stage renal disease (ESRD) exhibit elevated plasma levels of fibroblast development variable (FGF23), a protein chemical engaged with the guidelines for Vitamin D and phosphate digestion.[23]

Recent data suggest that FGF23 functions as a hormone that modulates immunity, directly affecting immune cells and influencing the immunological response, such as macrophages and polymorph nuclear neutrophils, as well as indirectly affecting non-immune organs. Elevated titers of FGF23 can lead to increased inflammation and immunological dysfunction. This effect was observed in human leukocytes cultured *in vitro* and in experimental mouse models. In addition, high plasma levels of FGF23 are linked to a higher infection rate than lower titers in clinical studies conducted in patients with ESRD and non-ESRD CKD.[24] Convective and diffusive transports were combined with hemofiltration. Patients receiving frequent HD have reduced APC-T lymphocyte interaction and T-cell immune responses. CD8+ HD dramatically decrease T lymphocytes.[25] The accumulation of uremic toxins and the ongoing production of mononuclear cells are both responsible for the immunodeficiency state observed in HD patients, in the long run causing apoptosis and accelerating the senescence of monocytes. Uremic immune dysfunction can be improved by hemofiltration, which eliminates inflammatory cytokines and enhances monocyte function. During the influenza season, a prospective study of chronic dialysis patients revealed that individuals treated with hemodiafiltration had longer-lasting seroprotection than those on HD.[26] A few reports have illustrated peritoneal dialysis could be more effective safeguard from declining provocative status and untimely maturation of the resistant framework in correlation with HD.[27] These irregularities can reduce the typical reaction to immunization and may require a promoter. The responses of dialysis patients' to SARS-CoV-2 vaccines were found to be less favorable than those of healthy individuals.[28,29]Several cases of interstitial nephritis or glomerulopathy such as collapsing glomerulonephritis, IgA nephropathy, localized glomerulosclerosis, and minimal change disease, have been reported in the general population after COVID-19 vaccination. It was discovered that renal complications associated with COVID-19 vaccination were either fresh or recurrent in an existing condition. There is also a chance of exposureing to these renal entanglements in formerly solid patients with subclinical or mysterious renal pathologies upon coronavirus immunization.[30–32] The causality between Coronavirus inoculation and these inconveniences remains unclear. Until this point, only a fleeting relationship has been established and different pathogenic components, including sub-atomic mimicry, postponed extreme touchiness, transient fundamental cytokine reaction, deregulated lymphocyte reaction and others, have been estimated to make sense of the event of renal complexities in coronavirus immunized people. The majority of cases were found to have been successfully treated with appropriate therapy, such as steroids.[33,34] Notwithstanding, early conclusion assumes a vital part in better administration and forestalling further deteriorating these entanglements.[35,36]

Conclusion

Our findings indicate a significant elevated levels of FGF23 in ESRD undergoing dialysis with and without corona vaccine when compared with healthy control, We investigated into the most probably immune-mediated theory of renal damage after COVID-19 vaccination and some researcher suggested that COVID-19 vaccination is related to renal side effects. Further investigation is required to fully understand the processes and causes of kidney disease after COVID-19 vaccination. In addition, the association between FGF23 and other laboratory parameters in vaccinated persons was examined in our investigation versus those without vaccination except for ALT, AST, and ALP. However, there was no notable difference in fibroblast growth factor-23 levels between the two patient groups that received the vaccine and that did not.

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Conflicts of interest

There are no conflicts of interest.

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