Correlation of Fibroblast Growth Factor 23 and Parathyroid Hormone in Chronic Kidney Disease patients

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Abstract

Chronic kidney disease (CKD) is a growing international health concern with high mortality rate in the world today characterized by alterations in either kidney structure or function or both for a minimum of 3 months duration. Levels of PTH (Parathyroid hormone)and the FGF23(Fibroblast growth factor 23), increase early in CKD . This study was designed to show the Correlation of FGF23 and PTH in chronic kidney disease patients. One hundred blood samples have been collected from Al-Yarmouk Teaching Hospital, Baghdad Teaching Hospital and Al-Karama Teaching Hospital during the period from December 2021 to March 2022 besides 50 samples as apparently healthy control. The age groups in the current study was at 33-75 years for CKD patient and 30-65 years for control. Then the blood samples were taken from patients and healthy volunteer groups to screen fibroblast growth factor 23 by ELISA method and PTH by cobas e411 analyzer. The current study shows that the increase level of FGF23 was correlated with PTH. PTH, FGF23 is statistically highly significant at p-value =0.001. The receiver operation characteristic (ROC) curve results revealed the sensitivity and specificity for FGF23 was 100%.The conclusion of the current study appear that the FGF23 in CKD patients was higher when correlated with PTH.

Keywords: chronic kidney disease, Parathyroid Hormone, fibroblast growth factor 23

1. Introduction

Kidney failure, is a medical condition in which the kidney are functioning at less than 15% of normal levels [1].The kidney failure is classified into two types ,acute renal failure(ARF) and chronic renal failure(CRF). Acute renal failure is a life-threating disease with high mortality percentage ,patient may be recover and others cases subsequently develop to CRF[2]. Reducing kidney function leads to various complications such as water and salt imbalance, anemia and the accumulation of waste products in the body[3]. Fibroblast growth factor 23 is a 251 amino acid phosphatonin, which promotes phosphaturia by decreasing phosphorus re absorption through inhibition of Na/P cotransporter type II activity in proximal tubules and by decreasing phosphorus absorption in the gut by inhibiting generation of active vitamin D in proximal tubules through inhibition of renal 1 alpha hydroxylase. Reduced active vitamin D facilitates PTH secretion, which further promotes renal phosphorus excretion [4]. FGF23 is released by bone generating the concept of an osteo-renal axis for phosphorus balance control that has changed traditional paradigms[5]. In human chronic kidney disease (CKD), plasma FGF-23 appears to be a sensitive biomarker of abnormal renal phosphate handling, as FGF-23 levels increase during early stages of kidney malfunction [6].

Parathyroid hormone (PTH) is a hormone that parathyroid glands make and release to control the level of calcium and phosphorus and vitamin D blood[7] .

Elevated FGF-23 levels increase fractional phosphate excretion, reduce serum phosphate levels, and reduce 1α-hydroxylase activity, which reduces 1,25(OH)2D3 formation thereby increasing parathyroid hormone (PTH) secretion. FGF-23 thus has a key adaptive role in maintaining normal phosphatemia. Plasma FGF-23 continues to increase as CKD progress [8].

2. Materials and Methods

This case-control study was carried out on patients who attended AL Yarmouk Teaching Hospital, Baghdad Teaching Hospital and AL karama Teaching Hospital of the period from December 2021 to March 2022.one hundreds of Patients with renal failure selected in our study with age (35-75) years were diagnosed as chronic renal failure based on previous medical reports, laboratory tests and clinical examination by consultant nephrologists. The results of those patients were compared with 50 healthy age (30-65) years as appearntly healthy control group without diabetes mellitus or hypertension and without a history of kidney disease depending on previous medical reports and laboratory investigation. A level of significance of a=0.05 was applied to test. SPSS v.23 programs used to analyze current data

3. Results

A total of 100 blood specimens from (57males and 43 females) were investigated during the study period in addition to 50 samples as contro (table 1). showed the means age of renal disease patients was 55.07±10.5 versus 48.34±8.15 for control group, this differences was highly significant with p-value ≤ 0.001.Also the results of age groups in this table observed 33(33%) cases out of 100 were attacked with renal disease in age group(53-62) yrs, but the high number and percentage 22(44%) in control group was appear in 43-52 years. while the less

doi.org/10.31838/hiv22.02.241 Received: 12.05.22, Revised: 13.06.22, Accepted: 23.08.22

age group were attacked with the renal disease were the age group >72 years ,but in control group at age 63-72 years was 1(2%),this differences was highly significant with p-value ≤ 0.001.On the other hand, The results in this study demonstrated that the male group were more than female with 57 (57.0%),43 (43.0%) respectively with a male to female ratio of 1:1.3, this differences was non-significant with P-value >0.05

Table 1: Demographical Picture of studied group

Parametr		Patient (N=100)	Control (N=50)	Sign
Age (Years)	M± SD	55.07±10.5	48.34±8.15	T-test=3.95 P-value≤ 0.001 (H.S)
(33-42)	N (%)	15 (15,0%)	12(24.0%)	F.E.P=20.13 P-value ≤ 0.001 (H.S)
(43-52)	N (%)	24 (24.0%	22 (44,0%)	
(53-62)	N (%)	33 (33.0%)	15 (30.0%)	
(63-72)	N (%)	27 (27.0%)	1 (2.0%)	
>72	N (%)	1 (1.0%)	0 (0.0%)	
Gender N (%)	Male	57 (57.0%)	25 (50.0%)	Chi-sequare=0.65 P-value=0.1 (N.S)
	Female	43 (43.0%)	50.0%)	

Table (2) appear that all the patients in this study 100 cases (100%) had increased levels of FGF23>900(mg/dl) with increased level of PTH >65 (pg/ml) in there sera when categorized these parameter according to its cutoff points.

Table 2:Comparision means of studied parameter among cases and control

Parameter	Study Groups	NO	Mean	Std. Error	T-test	P-value
PTH (pg/ml)	Case	100	352.27	23.27	13.44	<0.001 H.S
	Control	50	38.54	1.75		
FGF23 (pg/ml)	Case	100	2225.41	100.74	16.45	<0.001 H.S
	Control	50	535.56	19.82		

Our study resemble with previous Pakistan study submitted representative by[9] showed that from 265 patients were enrolled for final analysis in this data with a male to female ratio of 1:1.03 (146/121),and another study in India by PARMAR et al. [10] Showed that mean age of the patients was 42.57 that this result was lower than our result 55.07±10.5. but[11].

Showed that (79%)were females and the median age was 58 years old also[12] from Spain showed that more cases were in female (39.1%)than male (29.6%) with age group (49-67) .The result in these study match to our study.The variation with our study depend on the sample size which taken in each study ,geographic distribution , life style different from country to country.

It was proposed that growing prevalence of decreased renal function in older persons can be due to an increase in age-related risk factors for progression to the CKD such as diabetes, hypertension and cardiovascular disease However, Aging undergoes several changes in body that impact kidney function, so GFR declines with age [13]. Men may be at increased risk of reaching kidney failure sooner than women because of differences in hormone levels. Higher testosterone levels in men may cause a loss in kidney function. On the other hand, men's kidneys may not be protected by estrogen, which is higher in women until menopause[14].

[15]. From Saudi Arabia showed elevation of serum PTH showing hyperparathyroidism accompanied by significant hypovitaminosis D and hypocalcaemia was observed in the patients as compared to controls.

In Italy study by Albanese et al. [16]. Showed that 39.7% of patients with

CKD had FGF-23 levels above normal, 14.3% of patients had PTH value increased beyond the normal range. Phosphate retention due to a decline in renal function had been considered as the main trigger of secondary hyperparathyroidism. The retained phosphate leads to a triad of hyperphosphatemia, low Vit D and hypocalcemia which are well-known stimuli for PTH secretion that in turn enhances phosphate excretion and development of secondary hyperparathyroidism in advanced CKD [17]. Patients with chronic kidney disease (CKD) have been shown to have high levels of circulating FGF-23, which could be a mechanism to compensate for disturbed phosphorus metabolism [18]. In end-stage kidney disease, FGF23 fails to maintain phosphate homeostasis [19].

Table (3) appear that all the patients in this study 100 cases (100%) had increased levels of FGF23>900(mg/dl) with increase level of PTH >65 (pg/ml) in there sera when categorized these parameter according to its cutoff point

Table 3 : Distribution the levels of FGF23 according to the cutoff point with PTH among cases

Categorial FGF23 (pg/ml)			Categorial PTH >65	Total
	>900	NO	100	100
		%	100.0%	100.0%
Total		NO	100	100
		%	100.0%	100.0%

In concordance to other studies [20-23]. That showed increase in level of PTH and FGF 23 in CKD patients.

Some studies have shown that in CKD there is a progressive increase in FGF-23 levels associated with reduced renal function. Several factors may contribute to this phenomenon, such as hyperphosphatemia, hypercalcemia, secondary hyperparathyroidism (SHP). Serum levels of FGF-23 increase in the early stages of CKD as a compensatory mechanism to prevent the onset of hyperphosphatemia and secondary hyperparathyroidism .Even transient increase in phosphoremia, in the early stages of CKD, stimulates FGF-23 production, which then tends to normalize phosphoremia but at the same time causes a reduction in vitD resulting both in increased parathyroid hormone synthesis and secretion [16]. SHP is a common complication of CKD that induces morbidity and mortality in patients. CKD stimulates the parathyroid to increase parathyroid hormone (PTH) secretion[24].

Table (4) and figure (1) Present the area under curve (AUC) for Receiver Operative Curve (ROC) curve analysis for the FGF23 (pg/ml) were 1.0 among renal disease patients reflecting the great diagnostic power of tests. This table also observedthe high value of sensitivity and specificity of the FGF23 with 100%, 100% respectively under fifty percent, with 95% confidence with (p-value≤0.001).

Table 4 :ROC test for FGF23 test among studied groups

Area	Cutoff point	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval		Sensitivity	Specificity
				L,B	U.B		
1.000	972	**.000	**.000	1.000	1.000	1.000	1.000
(**) Highly Sig. at P<0.01; Non Sig. at P>0.05; C.I.: Confidence Interval; L.B.: lower bound							

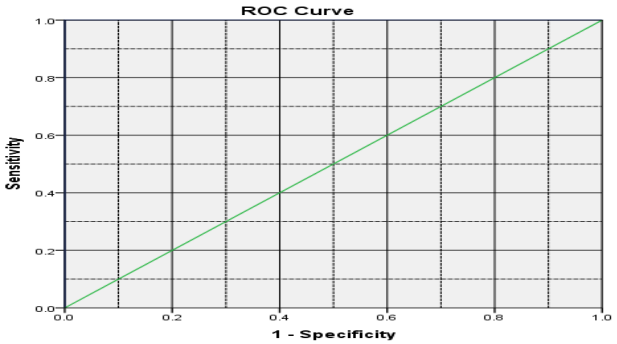

Figure1: ROC Curve Chart for the FGF23 marker among studied group (N=150)

[25] reportd that the FGF23 levels in the serum of patients were significantly higher and the cutoff point was 277 pg/mL. The calculated area under the ROC curves was 0.959 (95% confidence interval, 0.912–1.00); sensitivity was 94.0% and specificity was 84.0% (P < 0.001).

On the other hand [26]. showed that FGF23 has(sensitivity 80%, specificity 78.95%) while [27], patients had high FGF-23. (ROC) curve analysis showed serum FGF-23 has sensitivity 78%, specificity 76%.The current study was higher in sensitivity 100% and specificity 100% , this difference may be due in samples size, the relationship between the parameters that used in this study.

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