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Biochemical Study On Fibroblast Growth Factor 23 (Fgf23) And Its Relation With Osteomalacia Disease

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Abstract

The research examined the relationship between FGF23 and a few osteomalacia-related biochemical markers (vitamin D, phosphate, albumin, calcium, glutathione GSH, alkaline phosphatase enzyme (ALP), and arylesterase ARE enzymes, malondialdehyde, ceruloplasmin) in serum blood patients compared to the control group. The results demonstrated a substantial rise in mean FGF23 concentration in patients (356.75 ± 168.99 pg/ml) as compared to the mean concentration in the control group (273 ± 188.5 pg/ml), whereas the concentration of (vitamin D, phosphate, albumin, calcium, ARE enzyme) were considerable decreased. The concentration of (Malondialehyde and ceruloplasmin) had been found to have significantly increased Comparing the patients to the healthy group, the results revealed a non-significant increase in ALP enzyme levels and a non-significant decrease in glutathione levels. Additionally, the coefficient of correlation between FGF-23 and those clinical parameters revealed a considerable negative correlation with calcium in the patients. The association between the outcome and the remaining biochemical indicators was non-significant. The findings also revealed a negative correlation between FGF23 and BMI in patients and a positive correlation between BMI and FGF23 in the healthy group.

Keywords:

FGF23, Hyperphosphatemia, vitamin D, calcium, BMI.

Osteomalacia is a defect that results from the body's inability to nourish the skeletal bone with the minerals necessary for their survival in good health and strength, which makes the bones soft and easy to break. Patients suffering from muscle weakness, cramps, skeletal muscle deformity, and lack of calcium and vitamin D in the individual's nutritional system are leading causes of deficiency that accelerate bone demineralization [1,2] FGF23, a polypeptide having a molecular weight of 32 kilodaltons and 251 amino acids, was originally identified in the year (2000) [3]. In the amino part of the protein, it has a polypeptide made up of (24) amino acids [4]. Seventy-two amino acids are used to create the carboxylic terminus [5]. When phosphate homeostasis or vitamin D3 levels rise, osteocytes and osteoblasts secrete it. [6]In patients with osteomalacia, FGF23 regulates the level of phosphate by binding to receptors (FGFR1C -α-Klotho) and subsequently interacting with proximal renal tubes. FGF23 inhibits the gene expression of an enzyme called 1-hydroxylase, which is necessary for the production of vitamin D, reducing phosphate absorption in the intestine. This is accomplished by preventing sodium phosphate transporters (Napi2c and Napi2a) from crossing kidney wall for phosphate re-absorption and subsequently increasing its extraction in the urine. [7,8]Antioxidants exist in both non-enzymatic and enzymatic forms in the intracellular and extracellular environment. ROS are responsible for oxidative stress in various pathophysiological conditions, and their impact on bone formation is linked to osteoclastic resorption [9,10].

Oxidative stress is caused by an imbalance between antioxidant ROS in the body. [11]Additionally, BMI and the development of low bone mass in fracture cases are correlated.[12]

Aim of Research

It was suggested to research FGF23's mechanism of action in patients and its association with the measured biochemical parameters because there had been very few studies in Iraq concerning its relations with the body's metabolism of phosphate, particularly in patients with Osteomalacia disease.

Experimental

In addition, (60) blood samples from healthy individuals and (30) samples of both sexes (females and men) were acquired from the Ibn-Sina Teaching Hospital. The Osteomalacia patients' ages ranged from (15 to 65 years) and over. Following its separation from samples, blood serum has been utilized in order to calculate the subsequent bio-chemical variables.

FGF-23 has been calculated with the use of the SHANGHAI YEHUA Biological Technology kit(China) through the enzyme-linked immuno-assay ELISA approach [13]

Phosphate –was determined with the use of a BIOLABO kit(France)[14]

Vitamin D- was determined with the use of a BIOMERIEUX kit(France)[15]

Calcium was determined with the use of a BIOLABO kit (France)[16]

Albumin was determined with the use of a BIOLABO kit (France)[17]

Alkaline phosphatase enzyme- was determined by using a BIOLABO kit (France)[18,19]

Glutathione reductase enzyme –was specified with the use of Ellman's reagent through the modified technique for the researchers (Lindsey & Sedlak;1968) [20]

Aryl esterase enzyme –which has been specified through the analysis of substrate phenylacetate into phenol and acetic acid.[21]

Ceruloplasmin –which has been specified with the use of (para-phenylenediamine) by modified approach for researchers(Menden et al.;1977) [22]

Malondialdehyde –has been determined with the use of the TBA by modified approach for the researchers (Shah & Guidet,1989)[23]

Data Analysis

To compare two values, the acquired data were examined with the use of a T-test; the standard deviation and mean were determined using normal statistical approaches; and the Pearson correlation coefficient (r) has been utilized in order to determine the relationship between FGF23 and other clinical parameters.[24]

Result and Discussion:

The FGF-23 concentration in the patients with the chronic kidney disease in comparison to controls:

Results have indicated that normal FGF-23 concentration has been (273.880 ± 188.50pg/ml) in the control group. In comparison, results have demonstrated a non-significant increase of FGF23 concentration in patients was (356. 75±168.99 pg/ml) in comparison to control group as it can be seen in fig.1 below, the reason may be due to all patients showed tumor this induced osteomalacia, which includes the elevation of the serum FGF-23, the majority of the lesions in the long bones are located in the epiphysis.[25,26,27].

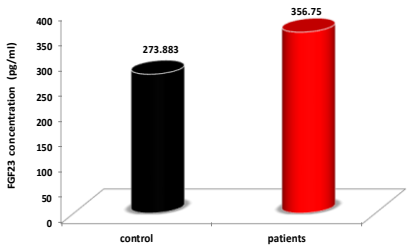

Fig1: concentration of the FGF-23 in the controls and the chronic kidney patients

Some of the clinical parameter concentrations in the chronic kidney patients in comparison to the controls:

Table1's findings have revealed a considerable reduction in phosphate concentration, which might be

caused by tumor-induced osteomalacia, which represents one of the rare syndromes that is characterized by the hypophosphatemia, increased phosphate excretion in the urine, decreased phosphate reabsorption through the renal tubules, and decreased vitamin D levels.[28]

Because vitamin D deficiency is linked to skeletal muscle defects, fractures, and bone loss, the results also revealed a significant decline in vitamin D levels, which could have contributed to the development of osteomalacia in adults and the subsequent development of hyperthyroidism. The results [10,29,30], consistent with the research findings[2,8,30], also showed a significant decrease in calcium and a non-significant increase in alkaline phosphatase enzyme. Low levels of vitamin D, calcium, and phosphate elevated parathyroid (PTH), increased alkaline phosphatase and osteocalcin, and low vitamin D levels indicate osteomalacia. However, bone alkaline phosphatase is the most important parameter for bone formation, and the results showed a significant decrease in albumin in patients, even though albumin is present in the bone matrix. Additionally,[31] the results demonstrated a substantial reduction in arylesterase in patients compared to controls. This result is consistent with research [11]that the increase of arylesterase is a mechanism of protection against oxidative stress on bone formation associated with osteoclasts resorption and a non-significant decrease in Glutathione in patients. However, results have shown a considerable increase in he ceruloplasmin and malondialdehyde because ceruloplasmin (CP) is ferroxidase activity, increases inflammation, and increases reactive oxygen species (ROS) that result from lipid peroxidation, which increases the MDA in bones. [32,33]

Table1: clinical parameter concentrations in Osteomalacia patients and controls

Clinical Parameter	Controls	Patient Group
Phosphate gm/dl	2.77 ± 0.66	*** 1.28 ± 0.36
Vit. D ng/ml	30.39 ± 5.08	*** 15.63 ± 8.59
Calcium mg/dl	2.13 ± 0.6	*** 0.85 ± 1.37
Ceruloplasmin µmol/L	357.6 ± 227.40	* 412.07 ± 261.6
Albumin gm/dl	4.22 ± 0.71	***3.39 ± 0.81
ALP Iu/L	53.8 ± 13.69	59.74 ± 21.42
GSH µmol/L	2.06 ± 1.40	1.63 ± 0.93
ARE U/ml	111.84 ± 35.28	*** 35.41 ± 14.22
Malondialdehyde µmol/L	1.72 ± 0.96	* 3.72 ± 4.22

Significant difference at the values of *p<0.050, **p<0.010

Correlations between FGF-23 concentrations and some of the clinical parameters in the Osteomalacia disease compared to the controls

Results from table2 have revealed that the FGF23 had a significant negative connection to the calcium in patients. FGF23 demonstrated a non-significant link with the other biochemical parameters in patients and controls. However, PTH was released by calcium decrease and acts on the distal renal tubules to enhance calcium reabsorption. This result is consistent with the research findings [34]when FGF23 is regulatory in phosphate homeostasis.

Table2: Correlation between the FGF-23 concentrations and some of the clinical parameters in Osteomalacia patients compared to the controls

Clinical Parameter	Control's r-value	Patients r-value
Phosphate gm/dl	- 0.156	- 0.087
Vit. D ng/ml	- 0.209	- 0.022
Ceruloplasmin µmol/L	- 0.199	- 0.226
Calcium mg/dl	- 0.104	- 0.261*
Albumin gm/dl	- 0.061	- 0.09
ALP Iu/L	0.178	- 0.249
GSH µmol/L	0.022	- 0.027
ARE U/ml	- 0.249	0.08
Malondialdehyde µmol/L	- 0.074	0.025

* Correlation has been found significant at 0.050 level

Effect of BMI on the concentration of the FGF-23 in the patients and controls:

The finding in table (3) shows that reduced BMI in the patient group is associated with increased FGF23 concentration. This result is consistent with the previous findings [35]that low BMI raises the risk of fracture because low BMI is linked to poor BMD, high tissue softness, and weak muscles. The results revealed a rise in FGF-23 with higher BMI in the control group. This is because serum phosphate and fat mass have an inverse relation, but FGF23 was

positively connected with BMI in healthy individuals [36].

Table3: The Concentration of the FGF23 in the Osteomalacia patients in comparison to the controls, According to the values of the BMI:

BMI kg/m2	FGF23 conc. pg/ml mean + SD	
	Controls	Patient
18.50 - 24.90	264.18 ± 172.40	* 345.4 ± 174.2
25 - 29.90	271.18 ± 186.30	* 305.57 ± 197.18
30 - 39.9	398 ± 289	* 219.18 ± 123.15
⩾ 40	414.2 ± 19	** 198.2 ± 112.17

Significant differences at *p< 0.05, **p<0.01

Body mass index (BMI): The WHO defines BMI as a result of the operaion of the division of the body weight in kilogram by square of the height in meters. WHO classified BMI into 4 categories: overweight (25-29.90 Kg/M^2), normal weight (18.5-24.9 Kg/M^2), morbidly obese (⩾40Kg/M^2), and obese (30-39.90 Kg/M^2). [37]

Conclusion

In the presented work, FGF23 was found to increase in patients with osteomalacia in response to hypocalemia, hypophosphotemia, increased levels of the ALP enzyme and PTH, vitamin D deficiency, and oxidative stress. FGF23 also had an inverse correlation with BMI in patients and a positive correlation with BMI in the healthy group.

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There is none to be stated

Competing interests:

The authors declare that there is no conflict in interest

Author's Contribution

Younis N Th,and Abdulmaujood S A,gathred the data and drafted the manuscript .Younis N Th, finalized the manuscript.

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