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Positive Correlation between Parathyroid hormone-related Protein (PTHrP) and Vitamin D Bind Protein (VDBP)in Osteoporosis and Osteopenia patients in AL-Najaf city /Iraq

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Abstract---Severe and moderate osteoporosis is a common disease in the world. It is considered a silent disease that has no clear signs. The current study aimed to evaluate the correlation between Parathyroid Hormone-related Protein (PTHrP) with Vitamin D Bind protein(VDBP) in Osteoporosis and Osteopenia patients in AL-Najaf city /Iraq. To succeed in the desired goal, 100 patients (50 with Osteopenia and 50 with Osteoporosis) participated in this study, on the other hand, fifty healthy individuals were selected as a control group. Serum Parathyroid hormone-related protein (PTHrP), Parathyroid hormone (PTH), Vitamin D Bind protein (VDBP) and Vitamin D were evaluated using the Elisa technique. The study was unique in proving a Positive correlation between parathyroid hormone-related protein and Vitamin D Bind protein in Osteoporosis and Osteopenia patients. inverse correlation between parathyroid hormone and T-score. In addition, the results indicated that there was a significant decrease in the levels of Parathyroid hormone (PTH), Parathyroid hormone-related protein (PTHrP), Vitamin D and Vitamin D Bind protein (VDBP) in patients compared to the control group.

Keywords---parathyroid hormone, parathyroid hormone-related protein, osteoporosis, osteopenia, T-score, vitamin D and vitamin D binding protein.

Introduction

Osteoporosis and Osteopenia are considered dangerous indicators, as they lead to fractures and other complications that may lead to death [1]. Osteopenia is the first step toward osteoporosis, Osteoporosis is the more serious progression of osteopenia. This disease is affected and develops by the influence of many factors, the most important of which are the parathyroid hormone and vitamin D, which were included in this study, as well as the study of their relationship with the proteins associated with them. Parathyroid hormone is a protein with 84 amino acids [2]. It plays a main important role in maintaining calcium homeostasis in the body [3]. Secreted from the parathyroid gland normally and dependent on serum calcium and phosphorous [4]. Parathyroid hormone (PTH) is a chemical molecule that has the ability to improve bone regeneration in significant bone defects. This possibility stems from PTH's anabolic action on bone [5]. The other factor is Parathyroid hormone-related protein (or PTHrP) that is secreted by mesenchymal stem cells. It is a protein member of family of parathyroid hormone [6]. It regulates development of bone by maintaining the endochondral growing plate at a limited width [7].

(PTH), PTHR, and PTH-related peptide, their cognate G protein-coupled receptor show crucial roles in the balance of extracellular phosphate and calcium and in regulatory skeletal development and repair [8]. PTHrP bind to and activate the identical G-protein-coupled receptor [9]. Parathyroid hormone and (PTHrP) are proteins that have anabolic activities when managed intermittently [10]. Several studies have demonstrated that parathyroid hormone can be given to postmenopausal women to maintain bone integrity, as it stimulates osteoblasts, but at the same time it stimulates osteoclasts, but to a lesser degree. However, they proved that parathyroid hormone-related protein stimulates only osteoblast genesis [11]. Figure (1) shows the role of the Parathyroid gland in regulating calcium levels in the blood. Where the parathyroid hormone increases the absorption of calcium from the intestines and re-absorbs it from the kidneys. When a decrease in the parathyroid hormone level occurs, it causes calcium deficiency in the blood, which leads to an increase in its release from the bone, producing osteoporosis [12].

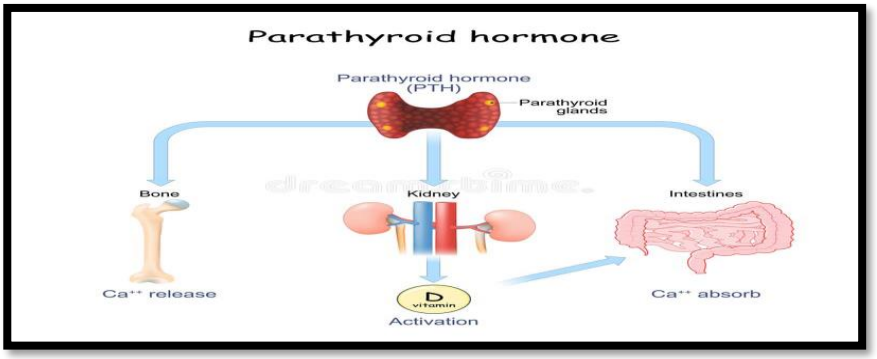

Figure 1. The role of the Parathyroid gland in regulating the level of calcium in the blood

Vitamin D (calciferol) found in a limited diets naturally and sold as a supplement [13]. It's a prohormone that is absorbed from food or supplements and produced in the skin after ultraviolet light exposure [14]. Adequate exposure to sunshine is essential for avoiding and curing vitamin D deficiency. Vitamin D lack has adverse health consequences, this vitamin is important for bone formation . Vitamin D insufficiency may lead to osteoporosis in older or postmenopausal women [15]. The GC gene encodes vitamin D-binding protein, which is a partly glycosylated alpha-2-globulin synthesized in the liver which has a Molecular weight (52-59) kilodalton [16]. The key responsibility of VDBP is to act as a transporter of vitamin D to target tissues in order to maintain calcium homeostasis via the vit D endocrine system` [17].

Vitamin D Binding Protein can be bound with high attraction to 88% of circulating 25-hydroxyvitamin D. Furthermore, VDBP is capable to bind with low affinity to almost 85% of 1, 25-dihydroxyvitamin, that is a most active metabolite of vitamin D. The residual part of V.D is bound to protein (albumin), and <1% of vitamin D exists in an unbound form into the bloodstream [18]. The results of the present study are identical to the results of previous studies, which showed a significant decrease in the levels of Vit D and VDBP in patients with osteoporosis compared to the control group. This result can be explained depending on the patient's history, most of the patients are women and their ages are beyond menopause, which indicates a decrease in their estrogen level. In addition to all of the above, aging is a major cause of this disorder, as it reasons a decline in the performance of hepatic in the synthesis of vitamin D-binding protein [19].

Subject and Method

One hundred patients with osteoporosis participated in the current study. Samples were collected from Medical Rehabilitation Center at Al-Sadr Hospital in AL- Najaf city, DEXA was used to diagnose Osteoporosis or Osteopenia disease for all patients participating in the study. On the other hand, fifty samples were collected from healthy people were elected as a control group for comparison with them. Parathyroid hormone (PTH), Parathyroid hormone-related protein (PTHrP), and Vitamin D Bind protein (VDBP) were measured by (ELISA Kit) supplied by

Elabscience®\USA company while Vitamin D was measured by (ELISA Kit) supplied by AccuBind®\USA.

Results and Discussions

The results in Table (1) appear decrease ($P<0.05$) in T-Score, Parathyroid hormone-related protein (PTHrP), Parathyroid hormone (PTH), Vitamin D binding protein and Vitamin D in patients as compared with the control group. On the other hand, the results show a significant increase in body mass index in patients as compared with the control.

Table 1
Level of the measured parameters in osteoporosis patients in comparison with the control group

Parameters	Patients	Control	P-Value
	Mean± SD	Mean± SD	
T-Score	-2.464±0.85	0.394±0.84	$2.1E^{-35}$*
Age	58.939±9.70	55.92±11.46	0.114281
BMI	27.733±5.19	30.15623±4.41	0.003494*
ESR	26.843±13.90	29.93617±12.32	0.179916
PTH	18.44±18.04	38.68±52.50	0.024286*
PTHrP	21.90±18.67	31.53±29.34	0.010563*
Vitamin D3	26.922±17.49	37.12504±25.07	0.011884*
VDBP	153.649±64.17	177.87±59.62	0.024286*

This result is expected for patients with osteoporosis for the important role of (PTH) and (PTHrP) for bone strength and mineralization since the main function of parathyroid hormone is to reabsorb calcium and stimulate the renal synthesis of 1,25 dihydroxy vitamin D [20],[21]. In addition, most of the patients are women and their ages are beyond menopause, which indicates a decrease in their estrogen level, estrogen has a direct effect on the concentration of vitamin D and vitamin D-binding protein, as some studies have shown that taking estrogen as a supplement leads to an increase in the level of protein related to vitamin D and maintains bone health from fragility [22]. Osteoporosis is an illness described by decreased bone strength which rises the danger of fragility fractures. Anabolic agents reduce the severity of the situation by increasing osteoblasts in proportions that exceed osteoclasts [23].

Several studies have demonstrated that parathyroid hormone can be given to postmenopausal women to maintain bone integrity, as it stimulates osteoblasts, but at the same time it stimulates osteoclasts, but to a lesser degree. However, they proved that parathyroid hormone-related protein stimulates only osteoblast genesis [24][25]. Table (2) indicates no significant relationship between PTH and VDBP, while the same table shows a significant positive association between PTHrP and VDBP. There are no prior studies that have proven a relationship

between vitamin VDBP and PTHrP, so the current study is considered unique to prove this relationship.

Table 2
The relationship between VDBP with both PTH and PTHrP

R	VDBP	P Value
PTH	-0.135	0.180
PTHrP	0.197	0.049

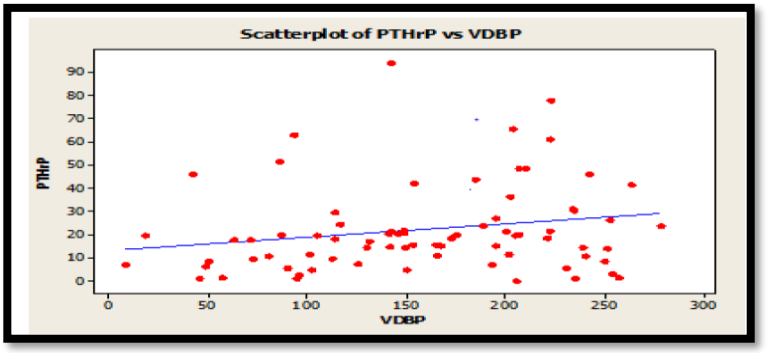

Figure 2. The correlation between VDBP with both PTHrP

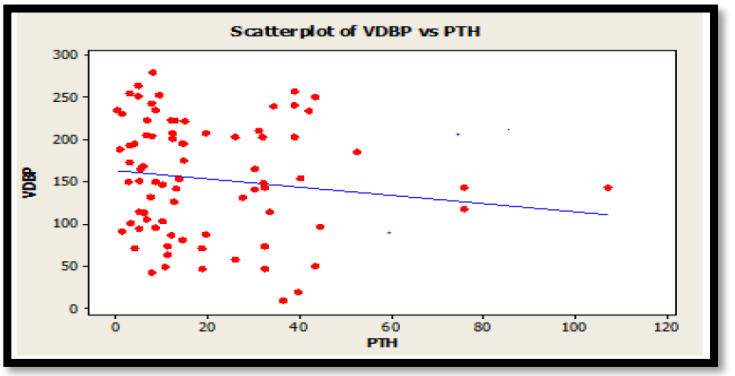

Figure 3. The correlation between VDBP with PTH

The current study demonstrated a significant inverse relationship between T-Score with PTH, while the results indicated no significant relationship between T-Score with PTHrP, as shown in table (3), figure (4), and (5) respectively.

Table 3
The relationship between T-Score and PTH and PTHrP

R	T-Score	P Value
PTH	0.194	0.053
PTHrP	-0.050	0.621

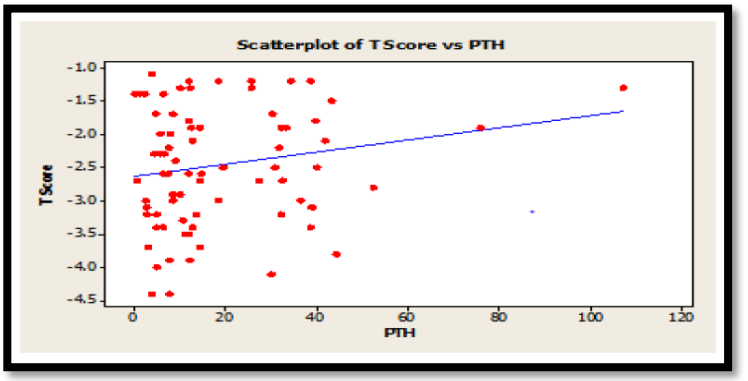

Figure 4. The correlation between T-Score and PTH

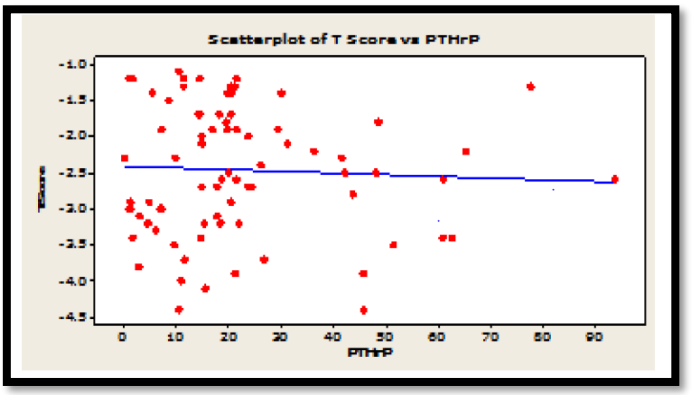

Figure 5. The correlation between T-Score and PTHrP

PTHrP is the same PTH but varies in numerous respects, such as being yields of separate genes, sequence deviation at the amino acid and level of nucleotide, and essentially different usual working. PTHrP is a typical product of osteoblasts and performances, like PTH, via the communal PTH-PTHrP receptor (also called the PTH-1 receptor or PTH1R) to activate osteoblast function and, indirectly, recruit osteoclast precursors. Both osteoclast-mediated bone resorption and osteoblast-mediated bone creation are stimulated by parathyroid hormone. This enhanced bone turnover is demonstrated by significant rises in biochemical indicators for production of bone [26].

Conclusions

Osteoporosis is a silent and dangerous disease that may lead to death. accompanied by a clear and significant decrease in bone density, in addition to a significant decrease in Parathyroid hormone-related protein (PTHrP),Parathyroid hormone (PTH), Vitamin D Bind protein (VDBP) and Vitamin D levels. The study was unique in proving a Positive correlation between parathyroid hormone-related protein and Vitamin D Bind protein in Osteoporosis and Osteopenia patients. on the other hand, the results indicated that there was an inverse correlation between parathyroid hormone and T-score.

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