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Study Level of Some Biochemical Markers in Male and Female Osteoporosis Patients

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ABSTRACT

Osteoporosis and consequent fracture are not limited to postmenopausal women. There is increasing attention being paid to osteoporosis in older men. Men suffer osteoporotic fractures about 10 years later in life than women, but life expectancy is increasing faster in men than women. Thus, men are living long enough to fracture, and when they do the consequences are greater than in women. The main purpose of this study is the measuring serum level of (CX3C, Bone sialoprotein, Gelsolin, Cathepcin K, Vitamin D, Calcium, Phosphorous and Alkaline phosphatase) in 100 patients (20 men and 80 women) and 50 as control group (19 men and 31women). The statistical analysis of results showed that the serum level of (CX3C, Gelsolin and Cathepcin K) increase in female osteoporosis patients and no significant increase in male osteoporosis patients compared to control group. The results also showed a rise serum level of Bone sialoprotein and Alkalin phosphatase in male and female osteoporosis compared to control group. The results also showed no significant difference in serum level of (vitamin D, Calcium and Phsphorouse) in male and female osteoporosis patients compared to control group. In conclusion The Cathepcin K, Gelsolin and Bone sialoprotein play an important role in bone metabolism and increase level in osteoporosis patients.

Key words: Osteoporosis, CX3C, Cathepcin K, Gelsolin, Bone sialoprotein

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INTRODUCTION

Osteoporosis is a progressive skeletal disorder whereby the bone strength (bone density and quality) is compromised thereby predisposing an individual to an increased risk of fractures which could occur spontaneously or after minor injuries. It is associated with low bone mineral density (BMD) and loss of structural and biomechanical properties that are vital for the maintenance of bone homeostasis [1]. Osteoporosis is the most prevalent bone disorder in humans and is a major global public health issue [2]. Osteoporotic fractures are associated with increased mortality [3]. In addition, fractures are associated with increased disability, reduced physical functions, and poor quality of life besides an increased financial burden [4]. Globally, approximately 9 million new and 56 million prevalent cases of osteoporotic fractures were estimated in the year 2000.5 In Taiwan, the prevalence of osteoporosis between 2001 and 2011 increased by about 7.6%.6. BMD is a valuable clinical diagnostic index for osteoporosis and the best tool for osteoporotic fracture prediction. Osteoporosis is associated with several genetic and nongenetic factors [1]. some of which include age [5], sex [2], Menopausal status [6], educational level [7], coffee drinking [5], smoking, exercise, alcohol consumption, diet [1], and body mass index (BMI) [8].

SUBJECTS AND METHODS

This study was carried out on patients attended to Bone Density unit in one hospital which is Marjan Medical City in Babylon Governorate. This study includes 150 females and males. They had been divided into two groups, the first group included 100 patients (80 females and 20 males) with OP and the second group included 50 relatively healthy (females and males) ,the age was of both groups was matched and ranged between (20- 80) years. Venous blood samples were drawn from patients and control subjects by using disposable syringes. Five ml of blood was obtained from each subject, 2 ml was placed into EDTA tubes and the remaining (3ml) pushed slowly into disposable gel containing tubes. Blood in the EDTA tubes was stored in(-20˚C) in order to be used later in

genetic part of the study, while blood in the gel containing tubes was allowed to clot at room temperature for 15minutes and then centrifuged at 3000 rpm for approximately 10-15.minutes , after that sera was obtained (Barbara and Anna,2012)and stored at -20˚C.

Biomarkers analysis

Quantitative detection of CXC3, gelsolin, cathepcin K and bone sialoprotein, in serum was done according to the industrial company (Bioassay Technology Laboratory (China) , that depended on the technique of the quantitative sandwich enzyme immunoassay (ELISA)) and (vitamin D) was assayed in serum according to the industrial company AccuBind ELIS Microwells (USA).that also depended on the technique (ELISA).Calcium and alkaline phosphatase was assayed in serum according to the industrial company BIOLABO (France).

Statistical analysis

Analysis of data was made by using Statistical Package for Social Science (SPSS) system/ version 20 Results expressed as mean ± Standard Error S.E.

RESULTS

The levels of biochemical parameters in osteoporosis patients and healthy groups according to gender (mean ± S.E)

In the Table 1 which describe levels of biochemical parameters showing that in osteoporosis patients markedly rise in level biochemical parameters that measured in the study, where the significant increase ($p \leq 0.05$) in CX3C in female, and significant increase in bone sialoprotein concentration for both genders when compared with healthy control group .and insignificant increase ($p \leq 0.05$) in gelsolin and cathepsin K level in female osteoporosis and no significant difference in male.

This study show no significant difference level of vitamin D , calcium and phosphorous in both gender while there is significant increase at ($p \leq 0.05$) in alkaline phosphatase in both gender (Figures 1A to Figure 1D).

Table 1: Levels some of biochemical parameters in osteoporosis patients and healthy according to gender.

Groups	Gender	Male	Female
Parameters		Mean ± S.E	
CX3C(ng/ml)	Patient	10.16 ± 1.3	11.53 ± 2.6
	Healthy	9.76 ± 1.5	3.46 ± 0.6
p-value		0.121	0.02
Bone sialoprotein (ng/ml)	Patient	47.53 ± 6.7	45.36 ± 12.4*
	Healthy	31.45 ± 5.1	19.32 ± 9.8
p-value		0.005	0.008
Gelsolin (ng/MLS)	Patient	50.06 ± 10.2*	75.61 ± 12.5*
	Healthy	48.13 ± 8.1	42.46 ± 10.5
p-value		0.09	0.02
Cathepsin K (ng/ml)	Patient	3.07 ± 0.2	4.77 ± 0.6*
	Healthy	2.99 ± 0.1	1.25 ± 0.8
p-value		0.41	0.04
Vit. D3(ng/ml)	Patient	18.44 ± 4.3	15.26 ± 2.2*
	Healthy	20.48 ± 4.4	20.66 ± 3.4
p-value		0.215	0.06
Ca (mg/dL)	Patient	8.46 ± 1.3	8.22 ± 0.8
	Healthy	8.43 ± 1.4	9.38 ± 2.2
p-value		0.687	0.311
PO4 (mg/dL)	Patient	4.74 ± 0.8	4.70 ± 0.9
	Healthy	3.77 ± 0.7	4.18 ± 1.1
p-value		0.567	0.244
ALP (Iu/L)	Patient	93.07 ± 15.2	114.5 ± 17.8
	Healthy	79.00 ± 11.7	69.85 ± 12.1
p-value		0.06	0.002

*Significant difference at ($p \leq 0.05$)

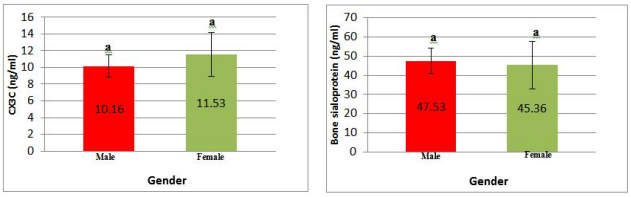

Figure 1A: Level some of biochemical parameters in osteoporosis patients according to gender.

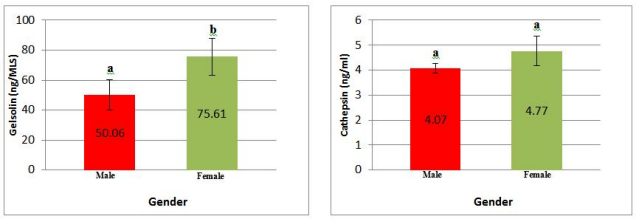

Figure 1B: Level some of biochemical parameters in osteoporosis patients according to gender.

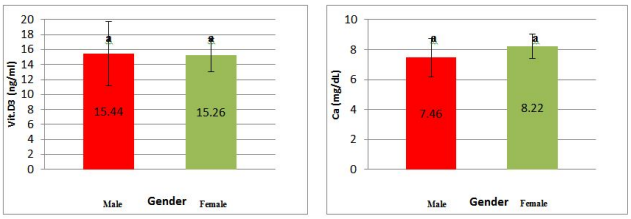

Figure 1C: Level some of biochemical parameters in osteoporosis patients according to gender.

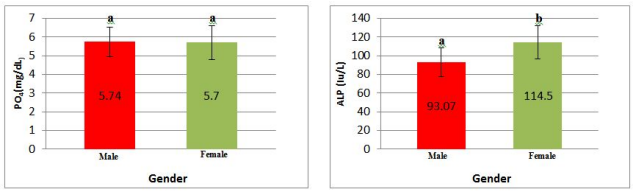

Figure 1D: Level some of biochemical parameters in osteoporosis patients according to gender.

DISCUSSION AND CONCLUSION

Sex is a well-established nonmodifiable factor for osteoporosis [9]. The risk of osteoporosis is greater in women than in men [1].

For instance, using data from the National Nutrition and Health Survey in Taiwan (2005-2008), the estimated prevalence of osteoporosis was 23.9% and 38.3% in men and women, respectively [10]. One major reason for sex differences in osteoporosis prevalence is menopause [9].

Menopausal women are estrogen deficient and more likely to have bone loss, osteoporosis, and fractures than premenopausal women. Results in this study recorded that women are more affected than males Table 1.

Women suffer from osteoporosis mainly due to the effects of menopause. CX3CL1 (also called fractalkine, FKN) is the only known member of the CX3C subfamily [11]. Unlike all other chemokines, CX3CL1/FKN exists as both a transmembrane protein and a soluble chemoattractant and is widely expressed on natural killer (NK) cells, monocytes and T cells [12]. So far the potential involvement of CX3CL1/ FKN in bone remodelling processes has been explored in only a few studies. Han et al. [13] found that the CX3CL1– CX3CR1 axis plays a pivotal role in osteoclast recruitment and subsequent bone resorption [13]. Also, inhibition of the CX3CL1-CX3CR1 axis through using anti-CX3CL1 mAb could inhibit osteoblast-guided differentiation of osteoclasts in vitro [14]. In addition, it has been identified that the CX3CR1–CX3CL1 axis plays an important role in the maintenance of osteoclastic precursors [15]. The result study showed signifigant increase in the serum CXC3 concentration in the female osteoporosis compared to control this finding, agreeing with its mention Yi-Ding Chen et al. [16] that FKN concentration in serum was elevated in postmenopausal osteoporotic patients compared with postmenopausal non-osteoporotic females and healthy controls.

Elevated serum FKN levels in osteoporosis patients were correlated with attenuated BMD, increased bone turnover markers, inflammation markers The CX3CL1/CX3CR1 axis plays a principal role in osteoclast maturation and binding them with immune cells to the surface of the bone tissue. It promotes the development of inflammation and production of many inflammatory cytokines near the bone surface (i.e., TNF-α, IL-1β, and IL-6). High concentrations of CX3CL1 in serum are directly proportional to increased concentrations of bone turnover and inflammatory factors in human blood serum (TRACP-5b, NTx, IL-1β, and IL-6) [17]. Bone sialoprotein (BSP) is a novel parameter of bone metabolism, BSP is a non collagenous bone matrix protein produced by osteoblasts [18].

However, presently it is not clear whether serum levels of bone sialoprotein reflect bone formation or bone resorption, respectively. Although it has been suggested that BSP levels reflect processes preferentially related to bone resorption [19,20]. Our study showed higher significant in male and female osteoporosis patients compared with the control group. Serum BSP was signi cantly elevated in postmenopausal osteoporosis compared to that of healthy perimen- opausal controls. Serum BSP decreased after diVerent antiresorptive treatments and this decrease paralleled the decrease of bone resorption markers , circulating BSP appears to be a valuable marker of bone resorption and monitoring therapy with antiresorptive drugs in postmenopausal osteoporosis. Pietschmann et al. [21] showed significantly decrease in the level of BSP in the men with idiopathic

osteoporosis .BSP is expressed during early phases of bone deposition therefore it is tempting to speculate that in male idiopathic osteoporosis most aspects of bone formation are normal while there appears to be a defect at distinct stages of osteoblastic differentiation. The possibility of a different metabolism of BSP in males and females subjects also should be considered. GSN plays an important role in severing and capping actin filament in actin cytoskeleton organization [22]. It was critical for podosome assembly, rapid cell movements and signal transduction [23]. Podosomes are cytoskeletal structures where a rapid polymerization/depolymerization of actin occurs [24]. Which are of great importance for cell adhesion, mechanical perception and matrix remodeling in osteoclasts, activated endothelial cells, macrophages and dendritic cells [25]. Osteoclast can degrade bone matrix including extracellular matrix and some mineral composition, which are critical for bone remodeling and maintenance of calcium balance [26]. The activation of osteoclast for bone resorption process relies on the integrity of the actin cytoskeleton and adhesion and motility function of podosomes [27]. Previous study showed that GSN deficiency would lead to the inability to produce podosomes, the abnormal actin cytoskeletal architecture; and the reduced rates of osteoclast motility; and blocked podosome-related signal transduction; and eventually cause decreased bone resorption; and increased bone mass and strength [28]. Plasma GSN level presented no significant difference between two genders. However, significant differences in plasma GSN level were observed between high and low BMD subjects in the females specifically. The results of the current study showed a clear increase in the GSN concentration in female osteoporosis patients compared with the healthy group, this finding, agreeing with its mention Wen et al. [29], that plasma GSN levels were significantly higher in extremely low BMD subjects than high BMD in Chinese postmenopausal women and there are significant differences in plasma GSN level were observed between high and low BMD subjects in male and the females specifically .The findings imply that the function of GSN is probably influenced by gender-specific factors, e.g., sex hormones. Previous study suggested that GSN serves as a regulator in regulating androgen-mediated effects on osteoclastogenesis and bone resorption [27]. Whether GSN interact with estrogen to influence bone metabolism and BMD is unknown and has yet to be investigated in the future. Cathepsin K is one of the main catalytic enzymes expressed and secreted by the osteoclasts. It plays a predominant role in the degradation of bone type I collagen, and consequently is a drug target in osteoporosis [30]. It is a lysosomal enzyme synthesized as a procathepsin K, which is activated in the lysosomes through a process involving autocatalytic cleavage at low pH, and then released into the resorption lacunae [31]. It may be possible that some of cathepsin K, is further released in the circulation and could be a specific biological marker of osteoclast activity. Several assays have been developed, although it remains unclear whether they detect the proenzyme, the active form or both. The results of the current study showed a clear increase in the cathepcin Kconcentration in male and female osteoporosis patients compared with the healthy group, this finding, agreeing with its mention Meier et al. [32], shown that serum cathepsin K is increased in patients with osteoporosis and Paget's disease. The data of this study showed no significant difference in the level of serum Calcium between osteoporosis patients and control group Our work agrees with Najlaa et al. [33] who found no significance difference in calcium level in osteoporotic women and in control group and agree with Muhammad et al. [34] who found no significance difference in calcium level in osteoporotic men and women and in control group. In the current study serum phosphorus showed no significantly difference between women osteoporosis and control group this agree with Selvapandian et al. [35] and this may be serum Ca and P was regulated and homeostasis is maintained in serum regardless of their store in bone relation of phosphorus with BMD [36] and agree with Muhammad et al. [34] who found no significance difference in level serum phosphorus in osteoporotic men and women and in control group. Serum alkaline phosphatase showed higher in osteoporotic groups compared with control group this agree with Ramesh et al. [37]. This may be due to ALP can be drain from osteoblast which is rich with ALP also it found in plasma membrane of the cell in the liver, intestine, and placenta, all of which is may contribute to the total amount of alkaline phosphatase and agree with Muhammad et al. [34] who found significance difference in ALP level in osteoporotic men and women and in control group. The result of this study showed difference in vitamin D between osteoporosis patients and control group this agree with Ramesh et al. [37]. The decrease of serum vitamin D levels may be due to less outdoor activities of the women also with decrease exposure to sun light and due to our habits in wearing long dress this will prevent the vitamin D in the skin [38] to induce and convert to the active form which is the major storage form of vitamin D consecutively it is important for calcium and phosphorus absorption, when it is level decrease lead to increase parathyroid hormone which lead to decrease calcium absorption then effect on bone health.

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