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ESTIMATE OF BONE BIOMARKER ON OSTEOPOROSIS IN IRAQI POSTMENOPAUSAL WOMEN

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Abstract: Background; Osteoporosis (OP) is a chronic and a progressive disease characterized by low bone mass and micro-architectural deterioration of bone tissue, resulting in an increased risk of fracture .Dual-energy X-ray absorptiometry (DXA) is commonly used for diagnosis of osteoporosis. Bone turnover markers have advantages over DXA, as they are cheap, non-invasive and can detect changes in bone turnover rates earlier. **Aims of the study:** to investigate the significance of bone turnover biochemical markers; serum parathyroid, serum osteopontin and Vitamin D3 in evaluating osteoporosis for postmenopausal Iraqi women with and without history of vertebral fracture, as well as to explore the relationship of these markers with bone mineral density (BMD). **Methodology:** Forty-four (85) postmenopausal women were included in this study with age range (45-70years). Subjects were divided into three groups: osteoporosis postmenopausal women: (n=45), osteopenia postmenopausal women: (n=24) and healthy postmenopausal women (n=16) (serve as controls). Patients were diagnosed as osteoporosis and controls as normal by measuring bone mineral density (BMD), using dual energy x-ray absorptiometry (DXA). In addition, serum calcium, phosphorous and alkaline phosphatase measured by spectrophotometer. **Result;** BMD and T-score were significantly lower in osteoporotic postmenopausal group as compared with healthy group (p=0.009) (p=<0.001). Serum ALP levels were elevated significantly in osteoporotic postmenopausal group as compared with healthy group (p=<0.001). Serum Ca levels and serum PO4 levels were elevated significantly in Healthy postmenopausal group as compared with osteoporotic group (p=0.65) (p=0.957). **Conclusions**: The levels of ALP in serum could be used as a biochemical indicator in the early diagnosis of osteoporosis postmenopausal women.

Keywords: Osteoporosis, Osteopenia, Menopausal, Osteopontin, Calcium

Introduction

Bone is a specialized form of connective tissue that serves as both a tissue and an organ system within higher vertebrates. As such, its basic functions include locomotion, protection, and mineral homeostasis. Its cellular makeup includes osteoblasts, osteocytes, bone lining cells, and osteoclasts, and its matrix contains an organic and an inorganic component. Morphologically, bone is characterized either as cancellous (spongy, trabecular) or as cortical (compact) **(Downey., 2006).** Menopause is defined as the state of an absent of menstrual periods for 12 months in women's due to the ovary stop to release the estrogen, this can lead to bone loss and risk factors for osteoporosis after the menopause **(Fantasia et al., 2016)**. Osteoporosis, it is a bone skeletal disorder that is characterized by a decrease in bone mass and density which can lead to an increased risk of fracture. The clinical diagnosis combines evidence of fragility fractures with measurement of bone mineral density [BMD].

BMD correlates with bone strength, skeletal load- bearing capacity, and fracture risk. The widely used World Health Organization [WHO] definitions compare patient BMD to norms expressed as T-scores, the number of standard deviations [SDs] from the mean BMD in young white adult women. Osteoporosis is defined as a T-score at any site of -2.5 or lower, while osteopenia is defined as a T-score between (-1 and -2.5) **(Abdelmohsen,., 2017 ; Nuti., 2019).** The normal aging process and estrogen loss related to menopause increase a woman's risk for osteoporosis. Estrogen plays a significant role in the regulation of osteoblast and osteoclast production. However, when estrogen deficiency occurs this regulatory process is disrupted, and the result is a decrease in the production of osteoblast and an increase in osteoclast production. The effect is an increase in bone reabsorption **(Qureshi., 2010).** And is maintained through bone remodeling, bone remodeling is characterized by two opposite activities: formation and resorption. The rate of formation or resorption of the bone matrix can be assessed by measuring markers of bone turnover **(Garnero, P., 2009).** Bone turnover is characterized by the formation of new bone by osteoblasts followed by the resorption of older bone matrix by osteoclasts. In osteoporosis, bone turnover is altered, leading to bone loss and ultimately bone fragility. The development of serum and urinary assays for biochemical markers with improved specificity and sensitivity reflecting either enzymatic activities of osteoblasts and osteoclasts or breakdown products of bone tissue has been of great importance for the understanding of the complex pathways of bone turnover and their alterations in postmenopausal osteoporosis **(Pham., 2011).** Several population-based epidemiological studies have shown that bone turnover markers can predict bone loss and the incidence of osteoporotic fractures in women. Garnero, (2000). Individuals with increased bone turnover markers lose bone at a faster rate than subjects with normal or low bone turnover markers, **(Kronenberg., 2007)**. because of the physiological characteristics; the morbidity of osteoporosis is obviously higher in postmenopausal females than in males **(Walker., 2008).**

Methods

This is a cross-sectional study, conducted from November 2018 to June 2019, with eighty five postmenopausal Iraqi women whose ages are forty five years old and over, categorized into three groups: healthy postmenopausal women (n=16), mean age of (55.06±4.81 years), osteopenic postmenopausal women (n=24), mean age (55.63±5.25 years). and osteoporosis postmenopausal women (n=45), mean age (58.48±5.9 years). The postmenopausal osteoporosis subjects selected from patients who visited Rheumatology and Rehabilitation Outpatient Clinic in Baghdad Teaching Hospital, and healthy postmenopausal females were selected from general population. The postmenopausal status was defined as cessation of menses for at least 1 year. All participants were interviewed and examined by physicians in a Rheumatology and Rehabilitation Outpatient Clinic. In addition, information was obtained from each subject about medication and history of previous medical or surgical diseases. Subjects with diabetes mellitus, high or low blood pressure, primary hyperparathyroidism, hyperthyroidism, rheumatoid arthritis, and hepatic or renal dysfunction; which might cause changes in bone metabolism, were excluded. None of the subjects were taking any drugs or hormones that affect bone metabolism; including sex hormones, glucocorticoids, warfarin, vitamin K, raloxifene and bisphosphonates. Body mass index (BMI), was calculated from the height and weight information by dividing the weight of the subject, in kilograms, per square of his height, in meter. BMD in lumbar spine (anterior-posterior projection at T4-L4) of all subjects was measured by Dual Energy X-ray Absorptiometry, DEXA, (Stratos DMS, France) which was controlled by computer with auto-position fixing, auto-detecting and auto-data manipulating. In practical operation, the subject lay down in the middle of the detecting bed, with her head leaving 3 cm to the bed top,

her both hands on the sides of the body, and her two legs straightening and separating gently. The diagnostic criteria of osteoporosis proposed by World Health Organization (WHO) in 1994 were used, in which the T-score >-1.0 was considered as normal, -1< T-score <-2.5 considered osteopenia, and if T-score <-2.5 should be diagnosed as osteoporosis. Superficial vein blood of 5 ml was collected from the elbow, while all women were at fasting state and after an overnight fast. Blood samples were allowed to clotting at room temperature for approximately thirty minutes. The serum was separated by centrifugation (3,000 rpm) for 10 minutes, and then the serum was isolated, within an hour of blood collection, and stored at -20°C for subsequent analyses, hemolyzed samples were excluded, and before analyses, samples were allowed to attain the room temperature. All sera samples were analyzed for serum alkaline phosphatase, calcium and phosphorous by using spectrophotometric kit. Serum alkaline phosphatase was determined by colorimetric method for in vitro diagnostic measurement using kit manufactured by Horiba, France, serum calcium was determined by colorimetric method for the quantitative in vitro diagnostic measurement using kit manufactured by Horiba, France, serum phosphorous was determined by colorimetric method for the quantitative in vitro diagnostic measurement using kit manufactured by Fujifilm, Japan.

Statistical analysis

The collected data were analyzed statistically using student T-test to find the significant difference between means, and the correlation analysis to find the level of the correlation coefficient (r). P value less than 0.05 is considered as significant. All statistical analyses were performed with SPSS 25.0 software of IBM Company (SPSS, Chicago, IL, USA).

Results and Discussion

Results

The characteristics of the subjects enrolled in the present study are shown in Table 1.

The study showed the distribution of a set of biomarkers among the three groups: healthy, osteopenic, and osteoporotic. The number of participants in the three groups was 16, 24, and 45, respectively. It was noted that the mean age was close between healthy and osteopenic subjects (55.06±4.81 and 55.63±5.25 years, respectively) but was significantly higher in osteoporotic subjects (58.48±5.9 years, P=0.042). It was also found that the body mass index (BMI) was higher in the healthy group (36.58±5.81 kg/m2) and significantly lower in the osteoporotic group (31.43±5.67 kg/m2, P=0.009). On the other hand, bone density analysis (T-score) showed a gradual deterioration between groups, with healthy subjects recording -0.125±0.08, osteopenic subjects -1.79±0.42, and osteoporotic subjects -2.86±0.74 (P<0.001). Regarding calcium (Ca) and phosphate (PO4) levels, no statistically significant differences were found between groups (P>0.05), as the values were close. However, alkaline phosphatase (ALP) levels were significantly higher in both groups compared to healthy subjects (P<0.001).

Table1: Clinical characteristic of study groups.

Parameters	Healthy	Osteopenic	Osteoporotic	P Value
Number	16	24	45	-
Age, years	55.06±4.81a	55.63±5.25a	58.48±5.9b	0.042
BMI, kg/m2	36.58±5.81a	34.26±6.32a	31.43±5.67b	0.009
T-score (BMD)	-0.125± 0.08a	-1.79±0.42b	-2.86±0.74c	<0.001
Ca (mg/dL)	9.02±0.63a	9.06±0.81a	11.84±1.68a	0.65

PO4 (mg/dL)	4.27±0.83a	4.23±1.07a	4.2±0.69a	0.957
ALP (U/L)	73.98 ± 19.2a	90.85 ±16.78b	97.37 ±18.51b	<0.001

Discussion:

About 10% of the adult skeleton is remodeled each year; this turnover prevents fatigue damage and is important in maintaining calcium homeostasis. Bone loss results from imbalance between rates of resorption and formation **(Turki et al., 2013).** Estrogen and androgen are the major sexual hormones in human body, and they participate in the formation and growth of bone, and play a very important role in maintaining mineral balance and bone balance in the body. Frank, G. R. (2003). Estrogen and androgen exist in the blood of both men and women, and it is generally believed that estrogen may be related to the regulation of bone resorption, and androgen to the osteoblast differentiation **(Alexandre et al., 2005).** People lacking of sex hormone are prone to have osteoporosis caused by bone loss (**Riggs., 2003).** In addition, the ovary function of post-menopause women declines gradually near the age of menopause, testosterone is the most active androgen in women, and with the decrease of testosterone levels, the direct effect of androgen on maintaining bone quality will be lowered, and the amount of estrogen transformed from androgen will also be reduced, therefore, estrogen deficiency makes postmenopausal women at considerable risk for osteoporosis and related fractures. Fracture risk is higher in older individuals, indicating quality factors in addition to BMD contribute to bone fragility and increased fracture risk. The strength of bone is dependent on four factors, which are the bone mineral density, bone structure, bone matrix, and accumulation of micro cracks **(Tanaka et al., 2011).** The present study evaluates whether some biochemical markers of bone turnover could help to identify women with low BMD. The present study showed that elderly postmenopausal osteoporotic women have a significantly low BMD as compared with elderly healthy postmenopausal women; these results are in line with the findings of several researchers. The results of this study prove a significant correlation between BMD and the occurrence of osteoporosis in elderly postmenopausal women, which is similar to the results published by other researchers **(Allah., 2017; Al-Nejjar., 2015).** Furthermore, a significant low T-value in osteoporotic postmenopausal women was found comparing with healthy postmenopausal women, indicating bone loss with age and menopause, a rapid bone loss is commonly seen in elderly individuals and tend to be worsen with advancing age **(Ensrud., 1995).** The Results, which obtained from the present study, agreement with the results of the other studies, which found that osteoporotic is conventional in the postmenopausal women with low body weight. The Higher body weight (no obesity) is one of a common protective factor for osteoporosis **(Hui., 2002).** A high BMI level stimulate formation of bone by increasing the mechanical pressure on the bones and by increasing the excretion the hormones of sexual **(Karimifar., 2012).** The present study showed that the (mean ± SD) value of serum of calcium for postmenopausal osteoporosis women group, but there was no significance change between all the three studied groups **(Al-Maatouq., 2004).** The present study showed that the (mean ± SD) value of serum of phosphorus for postmenopausal osteoporosis women group, but there was no significance change between all the three studied groups. The analysis results of the present study did not find a significant correlation between the levels of phosphorous and the disease of osteoporosis in the three groups of postmenopausal women. Like our findings, several studies showed that serum phosphorus showed non significantly values between osteoporosis group and normal group for diagnosis of osteoporosis because their results were within normal range **(Al-Nejjar., 2015).** The present study showed that the (mean ± SD) value of serum alkaline phosphatase

for postmenopausal women with osteoporosis group is higher than osteopenia and healthy control groups. This study is congruous with some previous studies, which stated that there is a significant difference between women with fragility and healthy women at some point in the menopausal stage **(Allah., 2017).**

Conclusion

This study showed an obvious increase in bone turnover markers in Iraqi postmenopausal osteoporotic women, which revealed that serum ALP could be used as a biochemical markers for the diagnosis of osteoporosis in postmenopausal Iraqi women. **Ethical approval:** The research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq. **Conflict of interest:** The authors declare that they have no conflict of interest. **Funding:** Self-funding.

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