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Comparison between Vitamin D Deficiency and 17- β-Estradiol Decline in Postmenopausal Osteoporotic Iraqi Women

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Objective: Determining serum levels of 17-β-estradiol and Vit D in healthy and osteoporotic Iraqi women, exploring the degree of correlation of these parameters with BMD and make a comparison between them using correlation coefficient values.

Patients and Methods: Eighty-two Iraqi women recruited in this study. They categorized into two groups. The first contains 50 healthy postmenopausal women, and the second consists of 32 osteoporotic postmenopausal women. T-score was determined using the dual energy X-ray absorptiometry (DEXA) technique. Vit D and 17-β-estradiol were determined using ELISA methods.

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Results: Vit D and 17-β-estradiol were significantly p< o.ooo1 decreased in osteoporosis. A high significant decrement p< o.ooo1 in bone mineral density represented by the noticeable decline in T-score values reported. The R for the correlation between T-score and 17-β-estradiol was 0.8165 while the correlation coefficient between T-score and Vit D was o.7761 only.

Conclusion: Osteoporotic women in Iraq have depleted levels of 17-β-estradiol and Vit D with low levels of serum Calcium. There is a higher rate of correlation between T-score and 17-β-estradiol if compared with the interrelation between T-score and Vit D. Therefore, the estrogen replacement therapy in Iraq is advisable to reduce the high morbidity and mortality of osteoporosis.

Keywords: osteoporosis; postmenopausal; Vit D; 17 β-estradiol.

I. Introduction

Bone is a vital tissue formed commonly from collagen and Calcium phosphate (1). Accelerated bone loss is a hallmark of menopause transition (2). Menopause is a gradual process that occurs over a years in females who are between 45–55 years of age (3). Osteoporosis is a reduction in bone mineral density (BMD). A decline in 17-β-estradiol plays a role in decreased bone mass during menopause (4). The T-score of bone mineral density shows how much the bone density is higher or lower than the bone density of a healthy 30-year-old adult (5). In postmenopausal women, estrogen levels decrease, which became a marker of loss of ovarian function. The reduction in estradiol levels can cause a decrease in bone mass (6).

Bone is a dynamic tissue that is remodeled constantly throughout life. Bone provides a reservoir for Calcium, the essential element in the human body and is necessary for many cell functions. Adequate intake of Calcium is required to maintain bones. Calcium is absorbed in the small intestines with the aid of Vitamin D (7). Low levels of Vit D (25-OH-D)status, as the case in Iraqi population, leads to reduced efficiency in intestinal Calcium absorption, and the body reacts by increasing the secretion of parathyroid hormone (PTH) (8).

The current study is an attempt to highlight the problem of osteoporosis and its deleterious consequences in postmenopausal women in Iraq. The expected decrement in estrogen hormone and the measured reduction in Vit D levels in these females require more effort to explore the real dimensions of this dilemma and draw the outlines for finding suitable solutions. Thus, identifying risk factors and prioritize them by determining their correlation with the decrement of Calcium levels in bones has become of great necessity and one of the hot issues.

II. Patients and Methods

This study started in Sep-2017 and accomplished in Jan-2019. The patients were carefully selected from the outpatient's ward of Al-Sadder teaching hospital of Al-Najaf Governorate. Eighty-two Iraqi women were consecutively recruited in this study. They were categorized into two groups. The first group contains 50 healthy postmenopausal women (HPW). The second group consists of 32 osteoporotic postmenopausal women (OPW). Table 1 contains some of the participant's characteristics.

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Table 1: Basic anthropometry of osteoporotic and healthy women

Variable	HPW Mean ± SD	OPW Mean ± SD
Participants no.	50	32
Age (Year)	55 ± 5	57 ± 6
Smokers percent %	11	13
BMI (Kg/m^2)	26.7 ± 5.2	27.8 ± 4.5
Postmenopausal Period (Year)	8.1 ± 4.3	9.5 ± 5.7

Written agreements were required from all the recruited participants before the beginning of participation. The participants did not use hormone replacement therapy of any type, Calcium and Vitamin D supplement for nine months before enrolment in this study. They had no history of any other bone disease or on medicament that may affect bone mineral density. The information of table 1 was reported in addition to some other details taken from the participants as a history.

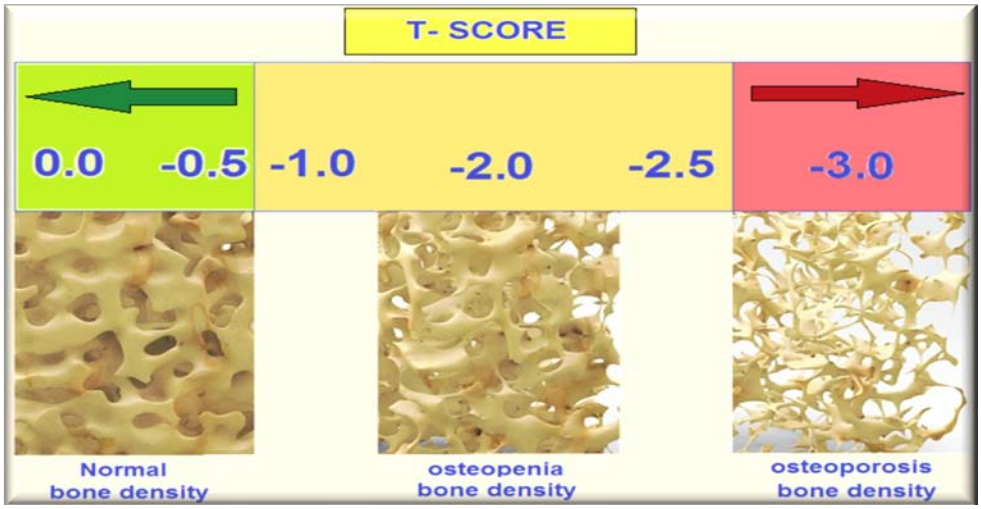

Figure A: Bone density in healthy and osteoporotic patients and related T-score values.

For dual-energy X-ray absorptiometry (DEXA) technique, Bone densitometer DEXXUM3- Dragon – China has used for bone mineral density (BMD) measurements (g/cm^2) at the lumbar spine in L1–L4 vertebrae. The radiologists in fractures and joints department assessed the results. The T-score is the standard deviation above or below values for a 30-year-old healthy population. Participants were diagnosed with osteoporosis according to the World Health Organization (WHO) definitions that use T-score assessment, as shown in figure A. For blood sampling, over-night fasting blood samples volume of 5 ml were obtained by venipuncture and transferred to serum collecting tubes. Samples were allowed to clot for 20 mins at room temperature (20-30°C) then centrifuged at 3500x g for 10 mins. 25-OH-cholecalciferol in sera was determined by the ELISA method. The kit purchased from Bioassay- China and measured by Bioteks ELISA reader.

17-β-estradiol was determined in serum using a competitive ELISA method with Streptavidin-Coated Plate following the instructions of the manufacturer Monobind Company- USA. Colorimetric assay with endpoint determination was used to measure serum Calcium levels. Arsenazo III reacts with Calcium in a slightly acidic solution to form a blue-purple complex that absorbs the light of wavelength at 650 nm, Intensity developed is proportional to the Calcium concentration. The endpoint determined by Auto Biochemistry Analyzer (AU240).

a) Statistical analysis

The results presented as mean ± standard deviation. Comparisons between two groups of data performed by Student t-test for paired observations (two-tailed). A p-value of <0.05 was considered significant and p-value of <0.0001 considered as a highly significant result. Correlation analysis using R^2 values and linear regression lines performed to determine the relationships between the variables. The figures and the relationships implemented using Microsoft Excel 2007.

III. Results

Table 2 contains the results of 50 healthy postmenopausal women (HPW) group and 32 osteoporotic postmenopausal women (OPW) group. It is evident from the values of p column in table 2 that there is a high significant $p< 0.0001$ declines in Vit D and T-score and significant $p<0.0085$ decrements in 17-β-estradiol in the osteoporotic postmenopausal women (OPW) group when compared to the healthy postmenopausal women (HPW) group.

In figure 1, there is a correlation between Vit D and T-score. In the scatter plot the Vit D was at the X axes and T-score at the Y-axes. The R-squared of the linear regression line was 0.6024.

Figure 2 represents the correlation between 17-β-estradiol and T-score and the obtained R-squared (R^2) value was 0.6666.

Table 2: 17-β-estradiol, Vit D, Calcium and T-score in healthy and osteoporotic women

Variable	HPW Mean ± SD	P <	OPW Mean ± SD
17-β-estradiol (pg/ml)	20.6 ± 10.8	0.0085	14.7 ± 7.5
Vit D (ng/ml)	21.41 ± 6.43	0.0001	8.37 ± 3.86
Ca^{2+} (mg/dl)	8.4 ± 0.8	0.0386	8.0 ± 0.9
T-score lumbar spine L1-L4	– 0.95 ± 0.45	0.0001	– 3.09 ± 0.26

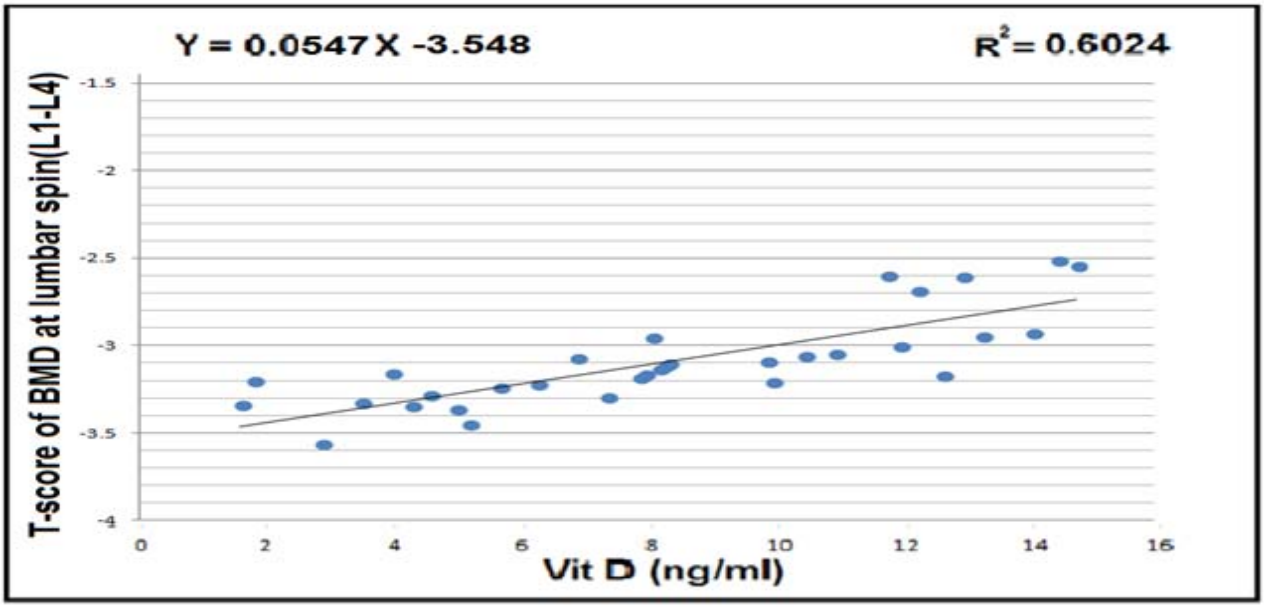

Figure 1: Correlation of Vit D and T-score of BMD at lumbar spin (L1-L4) in osteoporotic postmenopausal women

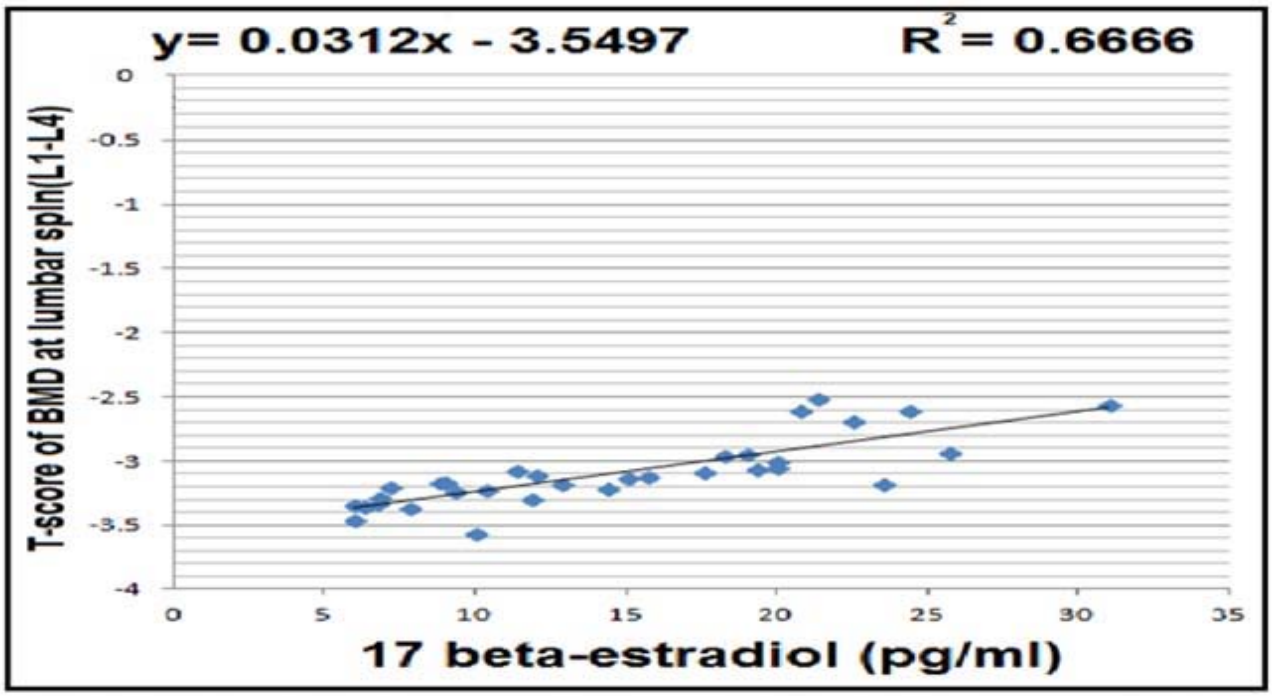

Figure 2: Correlation of 17 beta-estradiol and T-score of BMD at lumber spine (L1-L4) in osteoporotic postmenopausal women

Table 3: R^2 values for the correlations of T-score with each of Vit D and 17 β-estradiol

Variable	Vit D		17-β-estradiol	
	R	R^2	R	R^2
T-score	0.7761	0.6024	0.8165	0.6666

Table 3: shows R and R- squared values for the correlation of `T-score with each of Vit D and 17-β-estradiol.

IV. Discussion

The current study designed to assess the effects of parameters like Vit D and 17-β-estradiol on the osteoporosis of postmenopausal women especially when many other investigators reported that the level of Vit D in Iraqi population, in general, is under the normal range (9).

For 17-β-estradiol, the level in OPW group is significantly p< 0.0085 lower than its levels in HPW group. The postmenopausal ovary secretes androgens but virtually no estrogen. Although the ovary may still contain some oocytes, the follicles are predominantly incapable of responding to gonadotropins and of synthesizing 17-beta--estradiol (10). Levels of estradiol in women menopause are lower when compared to women of reproductive age in each phase of the menstrual cycle (11). After menopause, there is a reduction in 17-β-estradiol production by the ovaries. This reduction directly affects the bone status in these women (12). Loss of bone mass correlates with the duration of estrogen deficiency (13).

Vit D levels decreased significantly p< 0.0001 in OPW compared to HPW as shown in table 2. It has been considered that people residing in regions close to the equator, exposed to the sun without protection, have sufficient levels of Vitamin D. However, studies conducted in Turkey and Australia show the opposite results with Vitamin D levels of <17 ng/ml and <20 ng/ml, respectively (14). Vitamin D deficiency is a common condition, and therefore it has been considered as a global epidemic (15). This pathological decrement of Vit D becomes important due to its association with a low BMD, increased risk of osteoporosis and fractures (16, 17). It is estimated that one billion people suffering from osteoporosis. According to different studies, 100% of adult population of the United States and Europe have this condition, and

has been considered as a causal factor in many diseases, such as osteoporosis (18).

On the other hand, the decrement of serum Calcium concentration was slightly significant $p < 0.0386$ in OPW group in comparison with the HPW group. Khatak et al. (2013) reported that the level of serum Calcium was declined significantly in post-menopausal women concerning their age (19). It was concluded by Sadaf *et al*. (2014) that serum Calcium had a significant association with osteoporosis. They reported that the mean of serum Calcium level was 8.11 mg/dl in postmenopausal osteoporotic women, which is close to our result in table 2 (20). The overall mean of serum Calcium in the current study was 8.24 mg/dl it is comparable with the outcome that reported by Gallagher et al. (1979) who mentioned that intestinal Calcium absorption decreases with aging in post-menopausal women and results in decreased serum Calcium level. They observed that in osteoporotic women the active PTH was more over normal if compared with the age-matched controls (21).

Jowsey et al. (1974) reported that the decrement in the formation of the active structure of Vitamin D (calcitriol) in the kidneys, decrease blood Calcium, and could have an undesirable effect on bone mineral content and lead to exacerbating bone status (22).

There is a high significant difference $p < 0.0001$ between OPW and HPW in the T- score of BMD and that is expected because the patients with osteoporosis have lower Calcium content in their bone matrix when compared with healthy people.

For the correlation figures, each linear regression line was plotted to assess the degree of association between couple of parameters. Correlation factor R^2 only refers to the amount of association between two variables, which are assumed to be linear, whereas the regression line shows how a change in the first predictor variable affects the second predicting variable in the form of an equation. The figures 1 and 2 illustrate the mutual correlation between T-score of bones and each of serum Vit D and 17-β-estradiol respectively.

From table 3 the R^2 of the correlation between T-score and Vit D was 0.6024 while the correlation factor R^2 of T-score with 17-β-estradiol was 0.6666. Both reveal a high correlation (both ≥ 0.5) but 0.6666 is significantly higher than 0.6024, therefore, the changes in T-score or BMD in postmenopausal osteoporotic Iraqi women are more dependent on the decline of 17-β-estradiol than the deficiency of Vit D. this may be due to the substantial role of 17-β-estradiol as a potent antioxidant in different tissues (23). Therefore, depending on this comparison, it is suggested that the decrement in 17-β-estradiol in Iraqi women has a major impact on bone status than the deficiency of Vitamin D. Hence, estrogen replacement therapy should get more attention to avoid or minimize the risks of the expected fractures in the future.

Finally, the problem of osteoporosis and Vitamin D deficiency in Iraqi women after the age of menopause need to combine efforts and further intensive scientific cooperation to investigate the factors that exacerbate the disease and provide appropriate opportunities to treat or reduce the serious threat.

V. Conclusion

The current study shows that the participation of the decline in 17-β-estradiol to osteoporosis is significantly higher than the participation of Vit D deficiency to osteoporosis in postmenopausal osteoporotic Iraqi women. Although there is a significant decrement or pathological reduction seen in Vit D levels in these patients, the correlation between the decrement in bone mineral density and the retraction of 17-β-estradiol was more evident.

The osteoporotic women in Al-Najaf province in Iraq are deficient with Vit D. Lack of exposure to sun, insufficient intake of Calcium in food, no Vitamin D-fortified foods are available in the diet of most women many other factors inevitably increase the risk of Calcium loss from bone and ensure the high morbidity and mortality of osteoporosis.

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