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## Evaluation of some biomarkers of osteoporosis in women with breast cancer in Al-Najaf Governorate

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**Abstract:** Osteoporosis is a systemic disease that affects the mineral density of bones and their structure, which leads to an increase in the softness of the bones. One in three women after the age of fifty worldwide is affected. Both breast cancer and osteoporosis are common diseases in women. The cancer cells of the breast consider a public type of cancer in females, with (1) in (8) females developing breast cancer in their lifetime.

The study aimed to the evaluation of some biomarkers of osteoporosis in women with breast cancer represented by cathepsin K, parathyroid hormone, calcium and vitamin D. The current study was conducted at the National Cancer Center in Al-Najaf province for the period from 15/8/2022 to 20/1/2023. The study included 60 women with breast cancer and 30 healthy women free of diseases, and it was considered a control group. The ages of patients and healthy people ranged between (30-68) year old, vitamin D, calcium, parathyroid hormone, and cathepsin K were evaluated.

The finding showed no variance ( $p > 0.05$ ) among the two groups under study. The results a significant increase after the statistical analysis ( $p < 0.0001$ ) in the levels of calcium (Ca) and cathepsin K in infected women compared with healthy women. Likelihood ( $p < 0.005$ ) and calcium with a probability level ( $p < 0.0001$ ). In conclusion, the current study concludes that there is a high rate of osteoporosis in women with breast cancer. Prevalent. Also, rise in values of calcium in women with breast cancer, with no difference in parathyroid hormone, which is the most important biomarker for breast cancer diagnosis. An increase in the level of cathepsin K and its negative effect on the level of calcium in women that have breast cancer.

**Keywords:** osteoporosis, breast cancer, biomarkers, parathyroid hormone

## 1. Introduction

Breast cancer and osteoporosis are both common diseases among women worldwide[1]. One of every eight women develops breast

cancer during her lifetime. Most women are diagnosed with this disease when they reach menopause. In cases of the spread of the sickness in the body, marks appear: lymph glands swollen, bones pain in addition to

decrease the breath and the skin become yellow [2] Factors that increase the possibility of cancer the breast: sex, as females get breast cancer more than the men. Exercise reduction and obesity, alcohol drink and hormone treatment through menstruation, early puberty for females, not having children or having children at a late age, and family history for this disease [3]

Osteoporosis is a bone disease considered one of the most common metabolic, and the most prevalent type of osteoporosis is related to the deficiency in ovarian hormones in the case of menopause or surgical removal of the ovaries [4]. Osteoporosis is categorised by a lack of bone content and a decline inside a bone tissue, which results in bone fracture due to Bone Mineral Density (BMD) and a decrease in the mineral content of the bone. With new bone cells to regulate the elasticity and elasticity of the bone [5]. And that the imbalance between bone rebuilding and bone resorption leads to osteoporosis, in which bone resorption is more significant than its formation during bone reconstruction and restoration, and that among the factors that contribute to osteoporosis, including advanced age, lack of calcium intake, and the treatments used to curb stomach acidity [6].

The breast cancer standard treatments such as hormonal therapy or adjuvant chemotherapy cause losing the body bone mass, and risk of osteoporosis can be rise. Females premenopausal who are cured with chemotherapy often improve ovarian failure permanently or premature menopause.

Associated failure of the ovarian and speeded bone loss [7] occur in postmenopausal females' bone lack due to natural decline in levels of estrogen during age. But, inhibitors of aromatase (AIs), which are the regular cure for common in females with postmenopausal and estrogen receptor-positive of breast cancer, rise bone damage at double the level that occurs physiology with an increased danger of the breakability of the fractures [8] Bone loss is linked to with the extended-term aromatase

inhibitor treatment and ageing for females that have breast cancer. The remaining postmenopausal women with breast cancer (PBCS) are more likely to develop weakness fractures and osteoporosis than the additional postmenopausal females, whereas osteoporosis is not curable.

## **2. Methodology**

### **Study Samples**

The current study was conducted at the National Cancer Center in Al-Najaf province from 15/8/2022 to 20/1/2023. The study included 90 blood samples, including 60 blood samples from women with breast cancer, with ages ranged from 30 to 68 years old and 30 blood samples from healthy women as control group.

### **Blood samples collection**

Blood samples were collected by drawing 5ml of venous blood using medical syringes, and they were placed in gel tube, then separated using a centrifuge at a speed of 3000 revolutions per minute for 5 minutes to conduct biochemical tests.

### **Calcium concentration (Ca++) detection**

Serum calcium concentration was measured by a calcium measuring kit (Ca-kit) prepared by bioMerieux according to the method [9], a colourimetric method.

### **Estimation of cathepsin k level.**

The level of cathepsin K in the blood of women with breast cancer was estimated by following the steps provided with the Cathepsin K test kit and according to the manufacturer's instructions, BT LAB.

### **Estimation of parathyroid hormone level**

The levels of the parathyroid hormone level in the serum of the blood were measured by a measuring kit (parathyroid hormone -kit) prepared by bioMerieux according to the method [10].

### **Vitamin D concentration measurement**

According to the Vidas kit, the level of vitamin D measurement was determined by the Vidas automatic test device from the supplying company.

### Statistical Analysis:

Using the SPSS program version 28 and Excel version 2019 for the statistical analysis for the graphics, the statistical normal distribution analysis to differences among the groups and the data are stated as mean  $\pm$  SE (standard error).

The one-way ANOVA does the multiple comparisons among the groups with Tukey's post hoc. Still, the continuous variables are compared using the Independent T-tests, and the chi-square test analysed some other variables to calculate values of biomarkers by Binary and Nominal and found on the Odds ratio (OR) and 95% CI. And the Significance of differences identified at  $p < 0.05$  [11].

### 3. Results and Discussion

#### Comparison of some biomarkers between postmenopausal women with Breast cancer and control

The results in Table 1, show that levels of vitamin D and parathyroid didn't record any significant change ( $p > 0.05$ ) between (2) groups under study table [1].

The statistical analysis results exhibited a significant increase ( $p < 0.0001$ ) in the levels of calcium (Ca), and Cathepsin K in cancer women compared with healthy women table (1).

**Table. (1) The values of biomarkers for women with breast cancer compared with healthy women**

Variables	Patients n=60	Controls n=30	p-value
Vit D (ng/mL)	21.59 $\pm$ 1.2	24.33 $\pm$ 1.13	0.148
PTH (pg/mL)	27.45 $\pm$ 1.42	25.99 $\pm$ 1.6	0.527
Ca (mg/dL)	11.66 $\pm$ 0.14 *	9.61 $\pm$ 0.14	0.0001
Cathepsin k (ng/mL)	1.92 $\pm$ 0.03 *	1.41 $\pm$ 0.02	0.0001

\*Significant differences at p-value  $< 0.05$ .

- Mean $\pm$  standard error

The study results showed were a significant rise that there in values of calcium (Ca) and cathepsin K in infected women compared with healthy women, and this is explained by the fact that breast cancer causes osteoporosis, which causes an increase in the activity of osteoclast cells, and thus the liberation of calcium from the bones and causing an increase in its levels in the blood. Calcium-sensing receptor (CaSR) appearance in adenocarcinoma patients leads to raised levels of calcitonin receptors and the cathepsin K in osteoclasts, which in turn leads to degradation of the intercellular substance of bone [12].

In addition, Cat-K is consider be a powerful marker for wide-ranging perivascular epithelial neoplasms (PEComas), in addition to a potential differentiating factor for PEComas from other human cancers [13]as significantly increased Cat-K activity has been observed in metastases the bone, instead of in the primary tumours, possibly due to its involvement in bone resorption, which facilitates tumor metastasis, especially in breast and prostate cancers [14].

The raised levels can be detected for the CatK in tumor metastasis, whose primary function is related to the degradation of collagen, so helping in tumor invasion and proliferation [15].

#### The effect of the age in the Postmenopausal women with breast cancer group.

the level of vitamin D, a significant growth ( $p < 0.05$ ) was observed in its ranks in the age groups  $\leq 60$  and 41-50 years, compared with other age groups of the group of patients in Table (2). The results of the statistical analysis showed that there were significant differences ( $p < 0.05$ ). It represented a significant decrease in parathyroid hormone levels in the age group  $\leq 60$  compared with the rest of the age groups of the patients group. While there are no noteworthy differences ( $p > 0.05$ ) in the calcium values between the age collection of the groups of patients. With the level of vitamin D, a significant rise in its

values was detected in the age groups  $\leq 60$  and 41-50 years, compared with other age groups of the patients' group.

Table (2) showed no significant variances ( $p>0.05$ ) in the values of Kathepsin K among the different age groups of the patients' group.

**Table( 2) shows the effect of the age group on all the parameters studied in women with breast cancer.**

Variables	Age groups				p-value
	30-40 year n=16	41-50 year n=13	51-60 year n=20	$\geq 60$ years n=11	
Age	35.19 $\pm$ 0.83 d	44.38 $\pm$ 0.6 c	56.25 $\pm$ 0.74 b	67.36 $\pm$ 1.11 a	0.0001
Vit D (ng/mL)	18.79 $\pm$ 2.61 b	24.27 $\pm$ 3.23 a	20.77 $\pm$ 1.37 b	24.01 $\pm$ 2.72 a	0.054
PTH (ng/mL)	33.36 $\pm$ 3.26 a	25.69 $\pm$ 2.62 a	26.84 $\pm$ 2.24 a	22.07 $\pm$ 2.41 b	0.044
Ca (mg/dL)	11.94 $\pm$ 0.25	11.96 $\pm$ 0.41	11.6 $\pm$ 0.21	11.03 $\pm$ 0.2	0.124
Cathepsin k (ng/mL)	1.9 $\pm$ 0.06	1.88 $\pm$ 0.06	1.99 $\pm$ 0.05	1.88 $\pm$ 0.07	0.395

- different letters Significant differences at p-value  $<0.05$
- Mean $\pm$  standard error

Calcium in the bones and prevent osteoporosis caused by cancer. Vitamin D has been found in some test studies on cells of the tumour inside the rodents to have numerous actions that may block the growth of cancer cells or delay it, stimulating cellular differentiation, slowing the growth of tumour cells, and inducing cell death (apoptosis). The blood vessel formation decrease, also tumour development and metastasis reduce. Vitamin D is also found to defeat the immune cell that prevents the immune system from reacting violently to the cancer cells [16,17].

As for the results of parathyroid hormone levels, a significant decrease was found with age, and the reason for this may be due to high levels of calcium, and this was proven in the current study.

### Regression for Dependent Variable Cathepsin k (ng/mL) with other biochemical studied parameters in breast cancer patients.

Table. (3) shows is That value of PTH not effects and don't predict biomarker for increased cathepsin in **postmenopausal** women with breast cancer on parathyroid hormone, while an effect of cathepsins on both vitamin D was observed with a probability level ( $p < 0.005$ ) and calcium with a probability level ( $p < 0.0001$ ).)

**Table (3) displays the effect the cathepsin as dependent variable on some parameters studied in women with breast cancer.**

Independent Variables	Unstandardized Coefficients		Standardized Coefficients	t	P-value	95% CI
	B	SE				
Vit D(ng/ml)	0.011	0.004	0.137	2.956	0.005 *	0.004-0.019
PTH (pg/mL)	0.004	0.004	0.063	1.140	0.259	-0.003-0.011
Ca (mg/dL)	0.114	0.015	0.689	7.679	0.0001 *	0.084-0.143

- The reference category is: **postmenopausal** with Breast cancer. B: size effects. SE: standard error. 95%CI: Confidence Interval for OR.
- \* Significant differences at p-value  $<0.05$ .

It was also noted the effect of cathepsin K on both vitamin D and calcium, as it was found that the effect or association between cathepsin K and calcium and vitamin D could be because this protein is determined in the cells that destroy bone, and these cells that are in charge for the resorption of the bone, and since the increase in effectiveness osteoclast cells work to break down the bone, i.e. liberate calcium and minerals from the bone, and at the same time the rate of cathepsin k protein increases as a result of this activity. As for vitamin D, when it is high in the body, it works opposite to the

osteoclast cells, i. Reverse effect with cathepsin K [18].

## Conclusion

The current study determines that osteoporosis is at an excellent rate in women with breast cancer. Prevalent. Also, there is an increase in calcium values in women with breast cancer, with no difference in parathyroid hormone, which is the most important biomarker for breast cancer diagnosis.. associated between osteoporosis and breast cancer.

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