

Relationship between Vitamin D₃ Level and Body Mass Index in Postmenopausal Breast Cancer Patients

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Abstract

Background: Many studies have shown a relation between vitamin D₃ deficiency and breast cancer, others estimated an inverse correlation between vitamin D₃ and obesity. **Objectives:** This study aimed to verify the relation between vitamin D₃ level and obesity in postmenopausal breast cancer patients. **Materials and Methods:** This is a cross-sectional study included seventy-six postmenopausal patients with breast cancers who were diagnosed in the period from January 2020 to February 2022 who were divided into two groups: patients with body mass index (BMI) ≥ 30 and those patients with BMI < 30 . Vitamin D₃ level was estimated and compared between the two groups. We studied the correlation between vitamin D₃ level with the age of the patients and the parity. **Results:** the mean age of the included patients was 61 ± 7.7 years and the mean BMI was $32.3 \pm 4.3 \text{ g/m}^2$. The mean value of vitamin D₃ was 15.0 ± 5.4 for the patients with BMI ≥ 30 while it was 18.2 ± 4.3 for those patients with BMI < 30 and there was a significant difference between the two groups with $P = 0.007$. Furthermore, patients' vitamin D₃ levels showed significant inverse correlations with their age ($P = 0.008$) and BMI ($P = 0.001$). **Conclusion:** There is consistent evidence that deficiency of vitamin D₃ is associated with obesity in breast cancer postmenopausal patient; also, vitamin D₃ level has a negative correlation with the age and parity of the patients.

Keywords: Breast cancer, obesity, vitamin D

INTRODUCTION

Vitamin D₃ is a fat-soluble secosteroid that binds to a specific intracellular receptor called vitamin D receptor "VDR" which is a nuclear protein receptor that once it activated by vitamin D, leading to changes in transcription rate of specific target genes including those involved in maintaining mineral homeostasis in higher vertebrates^[1-3] in addition to genes which are playing important roles in vasoregulation, inflammation, and thrombosis^[4] The human body acquires the majority of vitamin D from skin after ultraviolet light exposure, (approximately 80%), while the rest comes from diet^[5,6] where it can be obtained either from vegetables in the form of vitamin D₂ (ergocalciferol) or from food such as dairy products and oily fish, or from vitamin D₃ (cholecalciferol) supplements.^[7] 25 hydroxy cholecalciferol "25(OH)D" is the main circulating form of vitamin D and is usually

estimated to determine the status of vitamin D in the human body.^[8]

The deficiency of vitamin D₃ is a worldwide health problem,^[9] as it is associated with an increased risk for several diseases, including osteoporosis associated fractures^[10] diabetes mellitus,^[11,12] cardiovascular diseases such as hypertension^[13,14] and some cancers such as breast cancer^[15] Breast cancer has a serious risk for women's health throughout the world, it's incidence is increasing during the last few years, according to the Iraqi cancer registry^[16] a lot of efforts have been directed to identify the risk factors which could lead to the development of breast

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cancer; aiming for prevention of its occurrence. Vitamin D is one of the factors that has been studied thoroughly to identify the relationship of its low level with the risk of breast cancer,^[17-19] some researchers concluded that keeping higher serum concentration of vitamin D₃ could have protective effect against breast cancer,^[20,21] since calcitriol (the biologically active form of vitamin D) can mediate the cell growth inhibition and differentiation by binding with vitamin D receptor in healthy breast cells (VDR).^[11]

Obesity is a recognized risk factor for adverse health diseases such as type II diabetes and cardiovascular diseases. The WHO estimates that more than 1 billion people worldwide are obese out of whom 650 million adults, 39 million children and 340 million adolescents, this number is still increasing and by the year 2025, approximately 167 million people (children and adult) will become less healthy because they are obese or overweight.^[22,23]

There is a close interrelation between vitamin D₃ and fatty tissues in both the pathogenic role of vitamin D on the development of obesity and the influence of fatty tissues and obesity on the vitamin D metabolism. In fatty tissues, vitamin D₃ increases the concentration of HDL-cholesterol, enhances changes in the adipokine profile such as leptin where vitamin D increases leptin levels which in turn inhibiting hunger, and this will diminish fat storage in adipocytes, in addition insufficiency of vitamin D₃ can result in an increase in fat mass by activation of lipogenesis.^[24,25] Both vitamin D₃ deficiency and obesity were associated with increased risk of mammary cancer development.

Aim of the study

The targeted goal of this work was to study the relationship between vitamin D₃ level and obesity, through the estimation of BMI, in postmenopausal breast cancer patients.

MATERIALS AND METHODS

Study type and design

This is a cross-sectional study.

Study population

The study population consisted of seventy-six postmenopausal women, who were presented with signs and symptoms of breast cancer, diagnosed histopathologically to have carcinoma of the breast with stage I, II or III, and attended to private oncology clinic immediately after doing surgical resection of the tumor (mastectomy or lumpectomy) and before giving adjuvant therapy, in the period from January 2020 to February 2022. The exclusion criteria of this study were those

patients with history of chronic medical condition, those patient taking D₃ supplement or metastatic disease.

Data collection

Every participant was asked to fill a questionnaire about personal and social data including; age, parity, menopausal status, education, place of residence whether urban or rural areas physical activity, and tonics intake including vitamin D supplement, the stage of the tumor at the diagnosis. Patients' body weight and height were recorded in order to calculate BMI for every patient. BMI = weight (in kg)/ height² (in m), A cutoff values of BMI ≥ 30 and <30 were regarded to differentiate between obese and non-obese patients, (BMI between 18.5 to 24.9 kg/m² regarded as normal weight and between 25 to 29.9 kg/m² regarded as overweight).^[26]

Sampling and laboratory technique

A random blood sample was taken from each patient for assessment of serum vitamin D₃ level using the ELFA (Enzyme Linked Fluorescent Assay) technique from bioMérieux (VIDAS® 25 OH Vitamin D Total). According to the Endocrine Society guidelines^[27] and based on the reference values of our study's assay, deficiency of vitamin D₃ was defined as level ≤20 ng/l (≤50 nmol/l); vitamin D₃ insufficiency was defined as level between 20–30 ng/l (50–75 nmol/l), while optimal vitamin D₃ levels were defined as between 30–40 ng/l (75–100 nmol/l).

Data analysis

Statistical analysis of our data was done using SPSS version 20, in which the population characteristics were exhibited as mean ± SD and the descriptive measures were shown as percentage and frequencies. Independent t-test was also used to compare between the patients' groups. Pearson's correlation was used to test correlation of vitamin D₃ levels in patients with age, BMI and parity. The level of significance used for all analyses was P value ≤ 0.05

Ethical approval

This study was conducted based on the principles of ethics that have their origin in the Declaration of Helsinki and it was approved by the scientific committee of training and human development center of Nineveh Health Directorate according to the document number 2022033 date 16 February, 2022 to get this approval.

RESULTS

The mean age of these patients was 61 ± 7.7 years, mean parity was 4.3 ± 2.4 and BMI was 32.3 ± 4.3 kg/m² as it is demonstrated in Table 1. The data of the patients regarding the stage of breast cancer show that five patients were diagnosed to have stage I (6.6%), forty-one patients

were diagnosed to have stage II (53.9%) while thirty patients were diagnosed to have stage III (39.5%) as it is demonstrated in Figure 1.

Deficiency and insufficiency of vitamin D₃ deficiency were reported in fifty-two patients (68.42%) and twenty-two patients (28.95%) respectively, while vitamin D₃ sufficiency (30–40 ng/mL) was reported in two patients (2.63%) as it is shown in Table 2. By comparing the mean

level of serum vitamin D₃ between the patients' group with BMI ≥ 30.00 ($n = 41$) and those patients group with BMI < 30.00 ($n = 35$) there was a significant decrease in the first group compared to the second group ($P = 0.007$) as it is shown in Table 3. Moreover, patients' vitamin D₃ levels have significant inverse correlation with their age ($r = -.302$, $P = 0.008$) and BMI ($r = -.375$, $P = 0.001$) while there was no significant correlation with parity, as it is shown in Table 4.

Table 1: Clinical data of the patients

Parameters	Patients (N=76) Mean $\pm$ SD
Age (years)	61 $\pm$ 7.7
Parity	4.3 $\pm$ 2.4
BMI	32.3 $\pm$ 4.3
Staging	2.3 $\pm$ 0.6

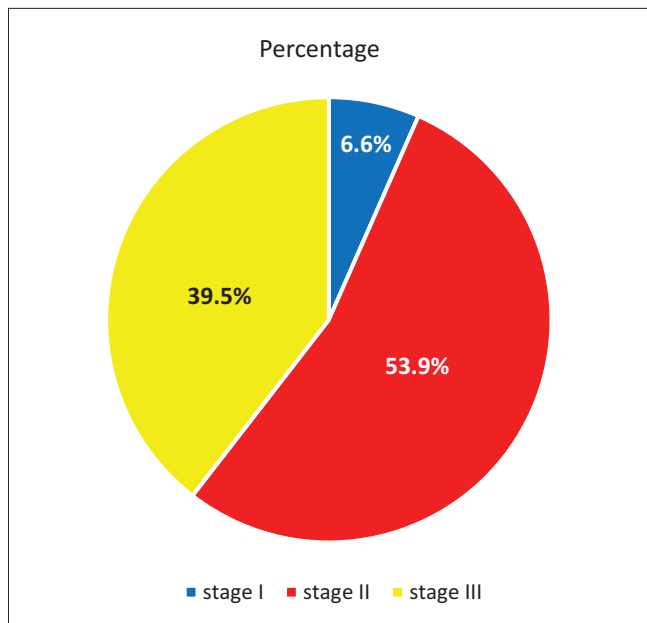


Figure 1: Shows percentages of disease's different stages

Table 2: Frequencies and percentages of the vitamin D₃ levels between the patients

Vitamin D3 Level	Frequency	Percentage
Deficiency <20 ng/mL	52	68.42%
Insufficiency (20–30 ng/mL)	22	28.95%
Sufficient (30–40 ng/mL)	2	2.63%
Total	76	100%

DISCUSSION

We conducted this study on seventy-six postmenopausal breast cancer patients where it shows that deficiency of vitamin D₃ is a common finding in breast cancer patients. Many pathophysiological conditions have been studied to uncover their relations to vitamin D status in human body including various neoplastic diseases such as breast cancer. Previous studies demonstrated that vitamin D₃ has anti-inflammatory and anti-proliferative effect in the tumors, through its attaching to vitamin D receptor (VDR),^[28] and down regulation of vitamin D signaling would take a part in the mammary cancer development and progression and this give a suggestion for the possible use of vitamin D supplementation as preventing agent for breast cancer development in young women.^[21]

In addition, this study shows a significant decrease in vitamin D₃ level in obese breast cancer patients (BMI ≥ 30.00) compared to the non-obese breast cancer patients (BMI < 30.00) and this result is quite expected since, there was a clear inverse association between the obesity and serum vitamin D₃ level as many studies have pointed to this fact^[29,30] and many efforts are going on to elucidate the pathophysiologic mechanism behind this, one of the suggested mechanism is the increase in the vitamin D metabolic clearance in the fatty tissues in a study conducted by Blum M et al, who found that vitamin D₃ level was significantly higher in fat tissue compared to serum level of vitamin D₃ in obese individuals,^[31] in addition, obese and elderly women were found to have less sunlight exposure, which is the most important rout to yield vitamin D

Table 4: Correlation of vitamin D₃ levels in all patients with age, BMI and parity

Parameter	Pearson correlation	Age $r = -.302$	BMI $r = -.375$	Parity $r = -.177$
vitamin D ₃ levels	P	0.008	0.001	0.125
	N	76	76	76

Table 3: Comparison of mean serum vitamin D₃ level between the patients with BMI ≥ 30 and those with BMI < 30

Parameter	BMI ≥ 30.00 $n = 41$	BMI < 30.00 $n = 35$	P-value
Vitamin D ₃ concentration (ng/ml) Mean $\pm$ SD	15.0 $\pm$ 5.45	18.2 $\pm$ 4.3	0.007

activation in human body and this could contribute to low vitamin D₃ in such people.^[32] Another important mechanism, which becomes evident, is called “volumetric dilution of vitamin D”, in fact vitamin D was found to be distributed mostly in the muscle and fat in obese people,^[33] due to increase in the volume of most body tissue (mainly the fatty tissues) this would result in low level of vitamin D₃ in to serum.^[29] Furthermore, Drincic A *et al.* showed that obese people, who had vitamin D deficiency, need more vitamin D supplementation than people with normal-weight to attain the same increment of vitamin D.^[34]

Another suggested mechanism for the inverse relation between obesity and low level of vitamin D₃ was contributed to the 1 α -hydroxylase and the 25-hydroxylase enzymes, which are important enzymes for hydroxylation of vitamin D converting it in to active metabolite 1,25 dihydroxyvitamin D, since the expressions of the genes of these two enzymes (25-hydroxylase CYP2J2 and the 1 α -hydroxylase CYP27B1) were shown to be decreased in subcutaneous adipose tissue of obese people which contributed to low level of vitamin D₃.^[35]

Similar to our result, Imtiaz S and Siddiqui N have found in their study, that deficiency of vitamin D₃ was very common among breast cancer women especially those with BMI >30 and consumed that vitamin D₃ level was inversely related with high body mass index.^[36]

In addition, this study showed that vitamin D₃ deficiency is associated with increasing age of the studied population, this result is consistent to the result of many previous studies, one of these studies is a cross-sectional study, done in Thailand, reported that insufficiency of vitamin D was found in one-third of the studied elderly women.^[37] This commonly encountered vitamin D₃ deficiency in old age people is usually resulted from decreased nutritional vitamin D intake, decreased skin synthesis of vitamin D, and the decreased in the time spent in the outdoors' activities,^[11] and physical activity has been found to increase sun exposure, prevent muscle strength's loss and mass that are the main determinants of serum vitamin D₃ level. Because of the deleterious effect of low vitamin D₃ level on the health of elderly people, The European Menopause and Andropause Society (EMAS) recommended to keep serum vitamin D levels at 75–225 nmol/L for elderly people.^[38]

This study has some limitations; we had limited data on the current or previous jobs of the patients in addition to the detailed information on the daily physical activities which may have indirect effect regarding the degree of exposure to sunlight, in addition to the samples size as the results would be more precise with larger sample size.

CONCLUSION

The data of our study indicate that vitamin D₃ level is inversely associated with obesity (BMI $\geq$ 30) in female

breast cancer patients. Furthermore, vitamin D₃ has negative relationship with age and this encourage us to recommend vitamin D₃ monitoring and supplementation for obese patients with Breast cancer and for elderly.

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Conflicts of interest

There are no conflicts of interest.

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