

VITAMIN D LEVEL AND ASSOCIATED FACTORS AMONG FEMALE PATIENTS WITH BREAST CANCER AT BAGHDAD MEDICAL CITY 2022

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ABSTRACT

Background: In recent years, epidemiologic and laboratory studies have implied that low vitamin D level has a role in the pathogenesis of breast cancer. studies have shown that 1, 25 (OH) vitamin D inhibits proliferation of breast cancer cells and makes them more differentiated; also, it seems to cause apoptosis.

objectives: The projected study aims to assess the vitamin D level and its role in association to tumor characteristics in females with breast cancer visiting oncology clinic in Oncology teaching hospital at Baghdad medical city. **Materials and Methods:** Across sectional study was conducted on females with breast cancer visiting oncology clinic in Oncology teaching hospital at Baghdad medical city/Iraq. Participants from age 18 years had been included for the study and selected by a convenient sampling technique. We used a pre-tested questionnaire list, vitamin D level measurement and tumor characteristics.

Results: A total of 75 female participants included in the study, the prevalence of low D3 level is 86.7% expressed some degree of deficiency ranging between deficient 44% and suboptimal 42.7%. **Conclusion:** In this study we found inverse association between vitamin D and breast cancer risk specially among postmenopausal women, the lacking in vitamin level more in progressing with staging and those with lymphatic involvement.

KEYWORDS: Vitamin D, Cancer, Breast, Obesity.

INTRODUCTION

Malignant tumor is a term used for steady and rapid developing cells that leads to the formation of groups of cells with uncontrolled division and spreading into the rest of the body.^[1]

Vitamin D is a fat-soluble vitamin and include 2 types D2 and D3. The first in vitamin D formation begins inside the human body from the 7-dehydrocholesterol, then by radiation reaching the skin is converted into pre-vitamin D3^[2]

Breast cancer has been considered as the most common type of cancer among the women within 161 countries, and the leading cause of females' cancer deaths worldwide. Known risk factors for breast cancer include age, family history, parity, overweight, the density of breast tissue, alcohol intake, and genetic risk factors such as BRCA mutations.^[3] In recent years, epidemiologic and laboratory studies have implied that low vitamin D level has a role in the pathogenesis of breast cancer.

studies have shown that 1, 25 (OH) vitamin D inhibits proliferation of breast cancer cells and makes them more differentiated; also, it seems to cause apoptosis.^[4] Experiments on animals have shown that dietary vitamin D can inhibit malignant effects of a high-fat diet on breast tissue. Furthermore, active vitamin D and its analogs can suppress the growth of breast cancer cells and prevent tumor progression induced by carcinogens.^[5] Recent studies suggest a low vitamin D in patients with breast cancer makes chemotherapy and radiotherapy less efficient as compared with those that had normal vitamin value.^[6] Anyhow, a number of factors contribute low circulating vitamin D levels, like age, low physical activity, race, obesity, smoking, skin type, and high altitudes living. Besides the mentioned mechanisms by which vitamin D may exert a protective effect against cancer, it has also been reported that vitamin D may partially facilitate the relationship between physical activity and breast cancer, through exposure to the sun.^[7]

Preclinical and clinical researches strongly propose that vitamin D deficiency increased risk of breast cancer

development and avoiding deficiency in addition to vitamin D supplements reduce cancer outcome risk. So, it is advised to maintain vitamin D store in survivors from breast cancer.^[8]

Vitamin D deficiency was found in many countries like China, USA and Iran.^{[9][10][11]} In Europe hypovitaminosis D was less as compared with other countries.^[8] The nature of indoor life with the sunny weather during most of the year in addition to the style of dressing play an essential role for hypovitaminosis D in Iraq. Therefore, measurement of serum vitamin D should be made routinely.

Patient and Methods

Study design, target population and setting: a comparative cross-sectional study was conducted on oncology clinic at oncology teaching hospital in Baghdad medical city.

Inclusion criteria: selected to decrease variation in vitamin D level associated with behavioral culture, diet and environment, included as following: females between the ages of 18 and 75 years, BMI (in kg/m²) ≤40, residence in Iraq for more than 5 years, absence of chronic diseases that might affect vitamin D metabolism, including hepatic, renal, endocrine and autoimmune diseases.

Exclusion criteria: male gender, recent consumption of vitamin D (patients who had taken oral vitamin D in the past 2 weeks, or injected vitamin D in the last 6 months), metabolic bone disease, renal and hepatic failure.

Sampling technique: breast cancer females from oncology clinic had been included for the study and selected by a convenient sampling technique.

Sample size: A total of 75 female patients agreed to participate in the study.

Data collection: The data were collected in three times per month during a period from first of December 2022 to 28th of February 2023. We use questionnaire list that consist of the following.

Part 1: sociodemographic information, consisting of age, marital status, schooling, smoking, parity, menopausal status, family history of breast cancer, all were obtained from direct questioning while weight and height were measured when participants wearing light clothes and without shoes. Body mass index (BMI) was computed as weight (kilogram) divided by squared height (meter).

Part 2: vitamin D level measurement classified according to reference ranges less than 20ng/ml as deficient, 20-30ng/ml as insufficient and more than 30ng/ml as sufficient value, we provide information about biochemical classification of D level according to instruments used in scientific laboratory of Nursing home hospital in Baghdad medical city.

Part 3: tumor characteristics and lymph node involvement.

Ethical issue: before data collection, official agreement had been taken, official agreement had been taken from Arabic council of medical specialty. Also, official agreement from oncology clinic in Oncology teaching hospital and laboratories of nursing home hospital in Baghdad medical city had been obtained. Verbal consent was obtained from every participated patient after explaining the aim and objectives of study and ensuring privacy of data and questionnaire filled without names.

Statistical analysis: data were entered and statistical analysis conducted by using SPSS program version 25. Data were presented in form of tables, numbers and percentages. Descriptive statistics (standard deviation and percentages) used for summarizing the study and outcome variables. Chi-square test (x²-test) and p value (equal or less than 0.05 was considered statistically significant) would be used for measuring association between the prevalence of low vitamin D level and breast cancer.

Proposed budget: No funded sponsors.

RESULTS

A total of 75 females with breast cancer participants had been included in this study. Sociodemographic characteristics as explained in table 1.

Table 1: Sociodemographic characteristics of participants.

		Frequency	Percent
education	Illiterate	11	14.7
	Basic education	33	44.0
	High school	31	41.3
smoking	Non smoker	64	85.3
	Ex-smoker	8	10.7
	Current smoker	3	4.0
Marital status	Single	3	4.0
	Married	49	65.3
	Divorce	2	2.7
	Widow	21	28.0
Parity	Nulliparity	8	10.7

	1-3	11	14.7
	4 and more	56	74.7
Menopausal status	Premenopausal	28	37.3
	Postmenopausal	47	62.7
Family history	Positive	32	42.7
	Negative	43	57.3
Vitamin D level	Deficient	33	44.0
	Insufficient	32	42.7
	Sufficient	10	13.3
Body mass index	Normal weight	5	6.7
	Overweight	26	34.7
	Obesity1	32	42.7
	Obesity2	10	13.3
	Obesity3	2	2.7
Staging	Stage1	6	8.0
	Stage2	37	49.3
	Stage3	26	34.7
	Stage4	6	8.0
Lymph nodes metastasis	No involvement	21	28.0
	Involving one or more	54	72.0
Total		75	100.0

Table 2: Association between D3 level and menopausal status.

D3level	menopausal		Total	Chi square	P value
	premenopausal	postmenopausal			
Deficient	7	26	33	7.107	0.029
	9.3%	34.7%	44.0%		
Insufficient	17	15	32	42.7%	
	22.7%	20.0%	42.7%		
Sufficient	4	6	10	13.3%	
	5.3%	8.0%	13.3%		
Total	28	47	75	100.0%	
	37.3%	62.7%	100.0%		

Table above shows significant association between D3 level and female menopausal state.

Table 3: Association between D3 level and breast cancer staging.

D3level	staging				Total	Chi square	Fisher exact test
	stage1	stage2	stage3	stage4			
Deficient	0	13	14	6	33	18.349	0.006
	0.0%	17.3%	18.7%	8.0%	44.0%		
Insufficient	6	17	9	0	32		
	8.0%	22.7%	12.0%	0.0%	42.7%		
Sufficient	0	7	3	0	10		
	0.0%	9.3%	4.0%	0.0%	13.3%		
Total	6	37	26	6	75		
	8.0%	49.3%	34.7%	8.0%	100.0%		

There is significant association between vitamin D3 level and staging in women with breast cancer as shown in table 3.

Table 4: Association between D3 level and lymph nodes involvement.

D3level	Lymph nodes		Total	Chi square	P value
	no involvement	involving one or more			
Deficient	5	28	33	4.849	0.089
	6.7%	37.3%	44.0%		
Insufficient	12	20	32	42.7%	
	16.0%	26.7%	42.7%		

Sufficient	4	6	10		
	5.3%	8.0%	13.3%		
Total	21	54	75		
	28.0%	72.0%	100.0%		

As shown above, there is significant association between low D3 level and involving of lymph nodes.

DISCUSSION

Breast cancer is one of the most malignant and prevalent type of neoplasms among females all over the world.^[12] In 2018, 2 million breast cancer cases and 626 deaths were recorded in 185 countries, the breast cancer in Iraq has gradually increasing in incidence (34.06%) while deaths reach (23.02%).^[12]

In the present study, the prevalence of vitamin D deficiency is 44% while insufficiency is 42.7%, our results show some agreement to study done in Kurdistan region of Iraq which found deficient insufficient vitamin level about 43.03%, 35.31% respectively among females.^[13] Previous studies explained the role of vitamin D as anti-proliferative and anti-inflammatory action in the tumors by attaching to vitamin D receptors, and down regulation of the vitamin D signal would take apart in the breast cancer progression and development.^[14]

In this study, there is high prevalence of vitamin D deficiency especially among the postmenopausal women that is about 34.7%. This result can be attributed to increase in age which is necessary factor for vitamin deficiency as like as gender, obesity and diseases. Mostly with aging, there is decreasing in skin production of the vitamin in addition to less sun exposure, reduce skin thickness, decrease intake, impair intestinal absorption, and insufficient hydroxylation in the liver and kidneys.^[15] Vitamin D3 deficiency elevate breast cancer risk among both premenopausal and postmenopausal females.^[3] A study done in Iran about vitamin level among newly diagnosed breast premenopausal women showed above than 50% of participants had deficiency.^[16] The vitamin D deficiency caused 7.5-fold greater risk among postmenopausal women complaining from breast cancer compared with control^[17], and this result agree with our study that has significant correlation between vitamin D level and menopausal state (p value 0.029).

There are some studies that yielded the correlation between vitamin D3 level and breast cancer, with some variations from this study to other. In a study done at 2011 by Yao et al, it was concluded that elevated vitamin levels were associated with decrease breast cancer risk about 63%.^[18] Our study clarifies the role of D3 deficiency in progression of breast cancer by comparison with vitamin D3 levels in early diagnosis and those with advanced breast cancer. We find the vitamin D had positive association with prognostic factors of breast cancer like staging (prevalence 26.7% for stage 3 and 4 collectively) and lymph node involvement (prevalence 37.3% of involving one or more lymph node), these

results similar to study done in Egypt and Jordan.^[2,3] Despite it was not causal, we conclude that females with early diagnosed breast cancer have elevated vitamin levels than those with advanced stages. The another contributing factors to hypovitaminosis D are dark skin, using sunblock, poor dietary intake and avoid performing activities in sunny areas.^[19]

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