



VITAMIN D STATUS IN BREAST CANCER PATIENTS IN A TERTIARY CARE HOSPITAL

Biochemistry

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ABSTRACT

Background: Breast cancer is the most common cancer in women in India and accounts for 14% of all cancer in India. Evidence suggests that Vitamin D helps in the prevention of various cancers such as breast cancer, colorectal cancer, prostate cancer, head and neck cancer, and other cancers by reducing inflammation, antiapoptotic, and antiproliferative and decreasing aromatase activity. Several studies support that supplementation of vitamin D reduces the risk of breast cancer. The present study was conducted to determine serum vitamin D levels in breast cancer patients.

Material And Methods: The present study is a hospital based cross sectional study conducted in department of Biochemistry and Oncology department RIMS, Ranchi. In total, vitamin D was estimated in 100 patients; in which study group included 50 diagnosed cases of breast cancer and equal number of age and sex matched healthy persons were included in the control group. Serum 25-hydroxy Vitamin D was estimated by chemiluminescent microparticle immunoassay (CMIA). Statistical analysis was performed by SPSS version 19 software.

Results: The mean serum vitamin D level in the breast cancer patients was 15.38 ± 6.22 ng/ml and in the control group was 20.68 ± 5.27 ng/ml. Vitamin D deficiency was seen in 78% (39) breast cancer patients and in 50% (25) of the control group (P value < 0.05).

Conclusion: Our study suggests that the vitamin D deficiency is associated with risk of breast cancer.

KEYWORDS

Breast Cancer, Vitamin D Deficiency, 25-hydroxy Vitamin D.

INTRODUCTION:

Vitamin D is a fat soluble vitamin that plays a role in calcium and phosphorus homeostasis. Recently extensive research on its extra skeletal action has linked Vitamin D deficiency to an increased risk of infection, cardiovascular diseases, diabetes mellitus and many different diseases including oncological processes such as breast, prostate and colorectal cancer. Vitamin D has not only shown to strengthen our bones but it also has capability to modulate several features of cancer. Its anticarcinogenic properties include inhibition of cell proliferation, invasion, metastasis and angiogenesis and induction of apoptosis and differentiation.[1,2,3]

Breast cancer is the most common cancer in women in India and accounts for 14% of all cancer in India with age adjusted rate as high as 25.8 per 100000 women and mortality 12.7 per 100000 women. Breast cancer projection for India during time periods 2020 suggests the number to go as high as 1797900. Better health awareness and availability of breast cancer screening programs and treatment facilities would cause a favorable and positive clinical picture in the country.[4,5]

Several studies have been done to evaluate the association of vitamin D deficiency and breast cancer risk. Inverse associations have been suggested between serum 25-hydroxyvitamin D level (25(OH)D) and breast cancer development, risk for breast cancer recurrence, and mortality in women with early-stage breast cancer.[6,7] Studies have shown that serum 25(OH) D concentrations as well as treatment with vitamin D supplementation are significant independent predictors of breast cancer risk. Women with serum levels of 25(OH)D more than 50 ng/ml had a 50% lower risk of breast cancer compared to those with serum values less than 30 ng/ml.[8,9]. Another study suggests that vitamin D levels may affect breast cancer survival, but that both low and relatively high levels may have an adverse effect.[10]. However, not many studies have been done to evaluate the correlation between serum vitamin D and the incidence of breast cancer in Indian population. In this study, an attempt has been made to find out an association between serum vitamin D level and breast cancer risk in Indian population.

MATERIALS AND METHODS:

The hospital based case control study was carried out at Department of Biochemistry, Rajendra Institute of Medical Sciences, Ranchi from May 2014 to October 2015 comprising of 100 subjects. The present study was started after obtaining ethical clearance from the institutional ethical committee. All newly diagnosed breast cancer patients who presented to the Oncology department were taken as 'cases'. Written informed consent was taken from all the patients. Age matched healthy females who accompanied the non breast cancer patients to hospital were recruited as the "control group". Patients suffering from known bone diseases, liver diseases, cardiac diseases, renal diseases, respiratory diseases or any severe chronic illness were excluded from the study. The socio demographics were documented by direct questioning on to the performa for the whole study population. Postmenopausal status of females was defined as last menstrual bleeding at least 12 months before the date of interview or a history of bilateral oophorectomy. The histopathological diagnosis of breast cancer, grade, stage of the tumor, and hormone receptor status (estrogen receptor ER, progesterone receptor – PR, and Her2neu) was recorded from the pathology reports of breast cancer patients.

Venous blood was collected in plain vials. It was allowed to clot for 30 minutes. After clot formation the blood was centrifuged at 3000 rpm for 10 minutes. Serum was separated from cells and collected in a separate aliquot vial. Serum 25(OH) D assays were performed by architect i1000SR autoanalyser by chemiluminescent microparticle immunoassay (CMIA) method. The values were documented in ng/mL. The diagnostic cutoffs of levels of serum Vitamin D are as follow [11,12]:

Vitamin D status	Serum level of Vitamin D in ng/ml
Deficiency	<20
Insufficiency	21-29
Sufficiency	>30
Toxicity	>150

Statistical analysis: Data analysis was done by using SPSS version 19. Numerical data were expressed as mean and standard deviation or median and range as appropriate. Relation of vitamin D deficiency

with grades, stages, histology, and receptor status of tumor was determined by using the chi square test. Categorical variables in cases and controls like marital status, parity, grades, stages, histopathology, receptor status of tumor, exposure to sunlight, economic status, education status and vitamin D deficiency were presented in frequency and percentages. A P value of <0.05 was considered statistically significant.

RESULTS:

The present study was a hospital based case control study, comprising of 100 subjects (50 cases and 50 controls)

The mean age of the cases was 46.3±7.97 years and the mean age of the control was 46.3±5.37 years. Age, marital status, menopausal status, residential area, parda observing status, and body mass index was similar in distribution among cases and controls.

The mean serum vitamin D level in the breast cancer patients was 15.38±6.22 ng/ml and in the control group was 20.68±5.27 ng/ml. Vitamin D deficiency was seen in 78% (39) breast cancer patients and in 54% (27) of the control group (P value 0.011)

Table- 1 vitamin D levels among cases and controls.

	VIT D LEVEL <20ng/mL	VIT D LEVEL ≥20ng/mL	TOTAL
CASES	39 (78%)	11 (22%)	50 (100%)
CONTROL	27 (54%)	23 (46%)	50 (100%)
TOTAL	66 (66%)	34 (34%)	100 (100%)

CHI-SQUARE(χ^2)=6.417, p value=0.011 (significant)

Table -2 Age wise distribution of vitamin D level among study groups:

AGE GROUP	VIT D LEVEL <20ng/mL	VIT D LEVEL ≥20ng/mL	TOTAL
<40 YRS	11 (64.7%)	6 (35.3%)	17 (100%)
41-50 YRS	25 (54.3%)	21 (45.7%)	46 (100%)
51-60 YRS	30 (81.1%)	7 (18.9%)	37 (100%)
TOTAL	66 (66%)	34 (34%)	100 (100%)

Chi square test(χ^2)=6.546, p value=0.038 (significant)

Among age group <40 yrs 11 cases out of 17 patients show vit D deficiency.

Among age group 41-50 yrs, 25 out of 46 patients show vit D deficiency.

Among age group 51-60 yrs, 30 out of 37 patients show vit D deficiency.

Table-3 Distribution of cases and controls on the basis of vit D level

VIT D LEVEL	CASES	CONTROL
<20ng/mL	39 (78%)	27 (54%)
20-30ng/mL	9 (18%)	21 (42%)
>30ng/mL	2 (4%)	2 (4%)

p value=0.030 (significant)

Table shows that 78% of breast cancer patients were vit D deficient while 18% were vit D insufficient. 42% of healthy control were vit D insufficient while 54% were vit D deficient.

Among the breast cancer patients the tumor characteristics (histology, grade, stage, and receptor status) did not show any significant associations with serum levels of vitamin D.

DISCUSSION:

The present study was conducted over the period of one and half year from May 2014 to October 2015. The study included 100 subjects comprising 50 cases of breast cancer presented to the oncology department and equal number of age and sex matched healthy persons were included in the control group.

The result of our study showed that 78% breast cancer females and 54% healthy females were vitamin D deficient. Serum vitamin D levels were significantly lower in patients with breast cancer when compared to the control group. This is almost correlating with the findings of the

study by Suma et al in Mysuru, India, Imtiaz et al in Pakistan and Crew et al in US. In their study, Suma et al reported vitamin D deficiency in 64% of breast cancer patients while Imtiaz et al and Crew et al reported in 95.6% and 74% of breast cancer patients respectively. [13,14,15]. Our finding is also well supported by study of Bidgoli et al. They studied serum 25(OH)D levels in Iran among newly diagnosed premenopausal women with breast cancer and showed more than 50% of analyzed individuals had very severe or severe vitamin D deficiency. The 25-hydroxyvitamin D deficiency caused 7.5-fold greater risk among postmenopausal breast cancer women compared with control. [16]

Few studies have examined the association between 25(OH) D levels at diagnosis and subsequent breast cancer outcome. Goodwin and colleagues followed a cohort of 522 early stage breast cancer patients and reported that women with deficient 25(OH) D levels (<20 ng/ml), compared with those women with sufficient levels (>30 ng/ml), had a higher risk of distant recurrence and of death. [17] In another similar study by Mohr et al, reported that higher serum 25(OH)D concentrations were associated with lower fatality rates in patients with breast cancer. Patients with the highest concentration of 25(OH)D had approximately half the fatality rate compared to those with the lowest concentration and suggested that serum 25(OH)D in all patients with breast cancer should be restored to the normal range (30- 80 ng/ml), with appropriate monitoring. [18] A recent study by Thanasiithichai et al showed that a concentration of 25(OH)D below 16 ng/ml was found to be independently associated with poor survival in breast cancer patients, regardless of age, lymph node status, stage or breast cancer subtype. [19] These studies showed that serum 25(OH)D level at the time of diagnosis in breast cancer patients has prognostic value. Several studies have shown a negative relationship between sunlight exposure and breast cancer risk. Proposed mechanism for this negative association is sunlight induced dermal synthesis of vitamin D, which evidence suggests, can reduce the risk of breast cancer. [20]

Vitamin D may play a number of roles in the prevention of breast cancer development and progression. The biologically active form of vitamin D, 1,25(OH)2D3, binds to the vitamin D receptor (VDR) in normal breast epithelium and this complex regulates the cell cycle, promotes differentiation, increases cell-to-cell adhesion, protects cells from DNA damage, regulates cytokines, activates immune cells, and suppresses inflammation, all of which may act to reduce malignant transformations. In breast cancer cells, this complex also activates apoptosis and other mechanisms to suppress tumor growth. Additionally, other vitamin D metabolites from recently discovered alternative pathways, such as 20(OH)D3 from the CYP11A1-mediated metabolism of vitamin D, have been found to have preventive effects similar to 1,25(OH)2D3 [21]. Decrease serum 25(OH)D level may result in impaired generation of 1,25(OH)2D3 within the breast tissue, might increase the risk of tumor development.

CONCLUSION:

Our study concluded that there is inverse relationship between serum vitamin D levels and breast cancer. Among the breast cancer patients the tumor characteristics (histology, grade, stage, and receptor status) did not show any significant associations with serum levels of vitamin D. There is an urgent need for better designed and randomized clinical trials that will address the association of vitamin D level with breast cancer risk, breast cancer development, recurrence, and survival at different breast cancer stages. As vitamin D deficiency is very common in Indian women, raising and maintaining serum vitamin D at population level is a safe and affordable strategy. It may play a role in reducing the incidence of both vitamin D deficiency and breast cancer, particularly among poor women where the breast cancer mortality is highest due to limited resources for early detection, diagnosis, and treatment

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