

Evaluation of Vitamin D in Breast Cancer in a Tertiary Care Hospital

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ABSTRACT

Introduction: Vitamin D has been implicated to play a very important role in different types of cancers due to its pleiotropic effects such as cell proliferation, cell differentiation, apoptosis etc. The implications of vitamin D deficiency are more evident in breast, prostate and colorectal cancer. Studies have revealed vitamin D supplementation reduces the risk of Breast cancer.

Aim: The main objective of our study was to find out whether low serum 25-hydroxy vitamin D levels was associated with breast cancer.

Materials and Methods: Study group included 25 diagnosed cases of breast cancer. Equal number of age and sex matched

healthy persons were included in the control group. Serum 25-hydroxy vitamin D was estimated by electrochemiluminescence immunoassay.

Results: Mean vitamin D levels were low in breast cancer patients, when compared to controls (p -value < 0.05), which shows that low vitamin D levels are associated with increased risk of breast cancer.

Conclusion: Our study showed that low levels of vitamin D are associated with breast cancer when compared to apparently healthy controls. Estimation of serum vitamin D in patients with breast cancer might help in the early diagnosis and treatment of breast cancer.

Keywords: Colorectal cancer, Supplementation, Vitamin D deficiency

INTRODUCTION

Vitamin D and its role in various cancers, has gained much attention in the recent years. Growing body of evidences has shown that low vitamin D levels are associated with different types of cancers. Among the various cancers, the implications of vitamin D deficiency are more evident in breast, prostate and colorectal cancer [1-3].

Breast cancer has been found to be the most prevalent malignancy in women in India and throughout the world. Globally, about 1.8 million individuals with breast cancer were reported during the year 2013 and 464,000 died of breast cancer. Prevalence of female breast cancer has been rising steadily with a moderate increment since 2000. Breast cancer has replaced cervical cancer as the leading cause of cancer deaths in females in India [2,4].

Recent studies have shown that vitamin D supplementation along with moderate sun exposure was associated with reduction in the incidence of breast cancer as well as mortality in patients with breast cancer [5,6]. It was observed that breast cancer patients with low serum vitamin D levels were more susceptible to fractures of spine due to loss of Bone Mineral Density (BMD) [7,8]. Another study showed that women having both low and high pre-diagnostic serum 25-hydroxy vitamin D levels are at higher risk of breast cancer specific mortality [9]. However, not many studies have been

done to evaluate the correlation between serum vitamin D and the incidence of breast cancer.

In this pilot study, we tried to elucidate the association between serum vitamin D levels in breast cancer patients.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry, in a Tertiary Care Hospital in Mysuru, India, after obtaining institutional ethical committee clearance. Duration of the study was 1 year (February 2015 to January 2016). Considering maximum prevalence of vitamin D deficiency in breast cancer as 50%, 25 diagnosed cases of breast cancer were included in this pilot study. Equal number of age and sex matched apparently healthy individuals were included in the control group. Breast cancer was diagnosed by clinical history, clinical examination and FNAC (Fine Needle Aspiration Cytology)/biopsy of breast tissue.

Patients with bone disorders, renal disorders and patients on vitamin-D supplementation were excluded from the study.

After obtaining written informed consent from all the participants prior to blood collection, about 3 mL of venous blood was collected under aseptic precautions, which was then subjected to centrifugation at a speed of 5000 rpm for 15 minutes and serum separated. The serum samples were stored in vials at -80°C . The samples were thawed only at

the time of vitamin D estimation. Quantification of vitamin D was performed in Roche-Cobas e411 immunoassay analyzer which is based on electro-chemiluminescence technology.

STATISTICAL ANALYSIS

Data collected was entered in MS Excel 2010 and analyzed using SPSS version 23. Descriptive statistical analysis measures like mean, standard deviation, percentage were applied. Other inferential statistical tests like unpaired T test, Pearson's correlation were utilized for assessing relation between serum 25-hydroxy vitamin D levels in breast cancer. The differences were interpreted as statistically significant when $p < 0.05$.

RESULTS

In this study, association between vitamin D levels in diagnosed cases of breast cancer was assessed. In the breast cancer group, the mean age of the cases was 49.28 ± 10.55 years and the mean age of the controls was 48.76 ± 10.23 years. The mean vitamin D levels were significantly lower (p value < 0.05) in breast cancer patients when compared to controls [Table/Fig-1]. There was no significant variation in the mean vitamin D levels in different age groups, both in cases and controls.

Subjects were further sub-classified based on the vitamin D reference ranges: < 20 ng/mL-deficient; $20-30$ ng/mL-insufficient; and > 30 ng/mL-sufficient [10,11] [Table/Fig-2].

Study Groups	Mean \pm SD	p-value
Cases	16.66 \pm 8.101	0.001
Controls	23.75 \pm 6.293	

[Table/Fig-1]: Mean vitamin D levels in patients with breast cancer.

Vitamin D Cut-off	Cases	Controls
< 20 ng/mL	16 (64%)	7 (28%)
$20-30$ ng/mL	5 (20%)	13 (52%)
> 30 ng/mL	4 (16%)	5 (20%)

[Table/Fig-2]: Distribution of subjects with breast cancer based on vitamin D cut-off values.

We observed that 64% of the cases were in the vitamin D deficient range (< 20 ng/mL) which further substantiates our findings that vitamin D deficiency is positively correlated with breast cancer.

There was no statistically significant correlation between vitamin D levels and education status, occupation, marital status, and socioeconomic status in both cases and controls.

DISCUSSION

Apart from its role in calcium homeostasis, vitamin D has been implicated to play a very significant role in cancer, diabetes, bone cell proliferation, immune responses etc. Our study showed an inverse relationship between serum vitamin D levels and breast cancer. Serum vitamin D levels

were significantly lower in patients with breast cancer when compared to the control group.

Our findings are in line with few studies, one prognostic study on breast cancer, found an association between serum vitamin D levels and prognosis of breast cancer. Mohr SB et al., reported that high serum levels of 25-hydroxy vitamin D can decrease the mortality from breast cancer and suggested that normal serum 25-hydroxy vitamin D should be restored in breast cancer patients in order to decrease the mortality [6,12].

In our study, vitamin D levels were lower in the breast cancer patients when compared to the control group and the difference was statistically significant. However, considering the reference ranges of western population, vitamin D levels were lower even in the control group. Since, reference range for vitamin D in Indian population has not been established, vitamin D levels in the control group could be optimal for this population.

Majority of actions of vitamin D are said to be mediated by ligand-regulated transcription receptor, the Vitamin D Receptor (VDR). The VDR is an intracellular hormone receptor that specifically binds the active form of vitamin D and interacts with target-cell nuclei to produce a variety of biological effects [13,14]. The involvement of $1\alpha,25$ -dihydroxy vitamin D in extra skeletal physiological function is said to be mediated through the expression of VDR in many types of cancer cells, including cells derived from tumors of the breast, prostate, pancreas, colon, cervix, etc., [14].

Studies have demonstrated that vitamin D and its analogues have inhibitory effect on breast cancer cell growth by regulating cell cycle. The effects of vitamin D on breast cancer cells has been attributed to the arrest of G0/G1 phase of cell cycle, suppression of growth stimulatory signals and potentiating the growth inhibitory signals, as well as induction of apoptosis [15,16].

Low circulating concentrations of 25-hydroxy vitamin D either due to reduced UV exposure or due to less in take of vitamin D may result in impaired generation of $1,25$ -dihydroxy vitamin D within the breast tissue, might increase the risk of tumour development [17,18].

LIMITATION

Our study has tried to provide an insight into the role of serum vitamin D in early diagnosis and also the utility of vitamin as a novel treatment option in reducing the risk of breast cancer. Since, the sample size is less, we could not evaluate the vitamin D in different stages/grades of breast cancer. Future large scale studies might throw light on the role of serum vitamin D in breast cancer.

Future prospectives: Further studies needs to be done on-

1. Correlation between serum vitamin D in different stages of breast cancer
2. Effect of vitamin D supplementation in breast cancer patients.

3. Study of polymorphisms of VDR gene in these patients.

CONCLUSION

Our study showed that low levels of vitamin D were associated with breast cancer when compared to apparently normal healthy controls. Estimation of serum vitamin D in patients with breast cancer might help in the early diagnosis and treatment of breast cancer.

Future large scale studies on vitamin D levels in patients with breast cancer may further substantiate the role of vitamin D as a dietary supplement to improve the prognosis of these patients.

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