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SERUM VITAMIN D AND BREAST CANCER: A CASE CONTROL STUDY AMONG WOMEN IN MARATHWADA, INDIA

Clinical Biochemistry

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ABSTRACT

Background: Vitamin D (Vit. D) is closely linked to various diseased conditions including malignancy. It is an environmental and dietary agent with known anticarcinogenic effects. Deficiency of Vit. D is highly frequent in the world which is an important warning to human health. **Objective:** We evaluated the association between serum Vit.D and breast cancer (BC). **Material and Methods:** Present case control study was carried out on 104 breast cancer women and 104 healthy controls at SRTRGMC, Ambajogai. Serum Vit.D was measured by Enzyme linked Immunosorbent assay (ELISA). The difference in serum levels was evaluated by using statistical methods.**Results:** Serum levels of Vit. D were significantly high in BC patients than the healthy controls. (171.74 ±101.53 Pg/ml Vs 77.96 ± 29.2 Pg/ml respectively. P<0.001) **Conclusion:** Our study results suggest that, increased Vit.D levels may be associated with BC.

KEYWORDS

Breast cancer, Vit.D, Elisa, Steroid hormone, BMI, UV exposure.

INTRODUCTION:

Cancer results from uncontrolled cell growth and proliferation caused by mutations in DNA by the process of carcinogenesis, carried out by carcinogenic (drugs and chemicals), biological (viruses), or physical (radiation) agents. Mutations in DNA converts proto-oncogenes into oncogenes.1 In 2025, 2,041,910 new cases and 618,120 cancer deaths are projected to occur in the US, Younger women less than 50 years have 82% higher incidence rate than their male partners.[2]

Female breast cancer (BC) incidence and mortality vary significantly across countries. GLOBOCON 2022 reported 2.3 million new BC cases and 666000 BC related deaths occurred globally reporting 23.8% cases and 15.4% deaths in all cancer cases. It is noted that, increased early onset BC cases are only observed in developing countries while decreased cases are seen in developed countries.[3]

In India BC trend is in premenopausal women and 29% to 52% are diagnosed with stage III. Mortality of BC patient is increasing in India.[4]

Global Breast Initiative in early 2021, a program has been launched by WHO and international partners to achieve the final goal that includes concentrating attention on health promotion and early detection, timely diagnosis, high quality treatment and wide BC management.[3]

Vitamin D is a steroid hormone plays an important role in the body in maintaining calcium and phosphorus homeostasis. There are two major forms of vit. D. D2 is ergocalciferol which is of plant origin and D3 cholecalciferol which is of animal origin. In humans Vit. D is synthesized from 7-dehydrocholesterol in the skin when exposed to the sun light mainly ultraviolet B-light. (Wave length 280-315mm). and it is the main source. Additional source of Vit.D is diet rich in fish oils, eggs, fortified foods such as cereals and fruit juices. The two forms D2 and D3 differ primarily in their side chain structure., however they are converted to the same biologically active compound calcitriol (1,25, (OH)2D3).[5]

Vit.D is closely linked to various diseased conditions including malignancy. Deficiency of Vit.D is highly frequent in the world which is an important warning to human health. Serum levels of Vit.D drastically changes during the treatment of BC with decreased concentrations specially during chemotherapy. In addition to dietary intake, Vit.D supplements used for cancer prevention and a helping treatment to chemotherapy in malignancies.[6]

Vit.D provides a new awareness into BC, therefore to explore the emerging roles of vit.D in patients with BC, we investigated the serum levels of Vit.D in BC women.[6]

Material and Methods:

One hundred and four BC patients at SRTR Govt, medical college and hospital, Ambajogai, Marathwada, Maharashtra, were included as cases in the study and compared with one hundred and four healthy controls. The age of the cases and controls were between 20 to 70 years. Information form regarding age, the menstrual status, family history of malignancy, oral contraceptives, BMI was filled along with written informed consent was taken. Controls were closely matched to BC cases. The study was approved by the Medical Ethics Committee of research centre.

Blood sample collection:

3 ml blood was collected from each individual in a plain vacutainer without anticoagulant. Kept in aside for 1-2 hours or centrifuged after an hour for serum separation. Samples were processed for Vit.D estimation.

Vit.D was measured by using enzyme linked immunosorbent assay (ELISA) based on biotin double antibody sandwich technique according to manufacturer's instructions. (KRISHGEN Biosystems)

Reference range :

Statistical analysis:

All the data were analysed by OpenEpi version 2.3, a statistical software. P<0.05 was considered as statistical significance. During the evaluation of study variables, descriptive statistical methods (mean, SD) were used. For a comparison of variables of normal distribution, t-test for independent samples was used and Chi square test for categorial variables.

RESULTS:

Table 1 Demographic and Biochemical Data

Subjects	Control Mean ±(SD)	Cases Mean ±(SD)	P value
NO. of Cases	n=104	n=104	----
Age in years	41.7 ± (10.2)	46.49 ± (10.82)	P<0.05
Sr. Vit.D3 (ng/ml)	38.28 ± (96.15)	20.23± (5.88)	P<0.05

Table 2

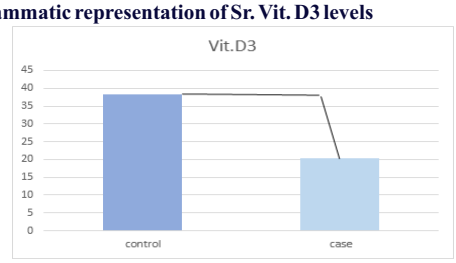
Subject		Controls n (%)	Cases n (%)	P value	OR (95%CI)
Premenopausal		28 (53.8%)	16(30.8%)	P<0.05	OR=0.38
Postmenopausal	24(46.2%)	36 (69.2%)	P<0.05		OR=2.63
BMI	Normal	92(88.5%)	75(72.1%)	P<0.05	OR=2.96
	High	12(11.5%)	29(27.9%)		

Age showed statistically significant difference in cases and controls. There was a statistically Significant increase in serum MDA levels in BC cases than in controls. (Table 1)

Similarly, it was seen that, Among premenopausal women 30.8% cases and 53.8% controls. Premenopausal status showed significantly lower odds ratio compared to controls (x2=5.6, OR=0.38; p=0.02). Among postmenopausal women 69.2% BC cases and 46.2% healthy controls (x2=5.6, OR=2.63;95%CI:1.17-5.87; P=0.02). The association between menopausal status and BC is statistically significant. There is a significant difference between cases and controls about the distribution of BMI (X2=8.77, p=0.003). Women with higher BMI were frequently observed in cases (27.9%) than in controls. (11.5%).

Women with high BMI showed increased chances of developing BC compared to women with normal BMI (OR=2.96;95%CI:0.1.42-6.20). (Table 2)

Diagrammatic representation of Sr. Vit. D3 levels



DISCUSSION:

Vit. D may inhibit growth of BC cells through down regulation of ER expression and alterations of estrogen signalling and synthesis.[7] Low dietary intake of Vit. D, older age, obesity, skin pigmentation, sun exposure, physical activity, education, socioeconomic status are risk factors for vit. D deficiency.[8]

In the present study, we observed, significant decrease in the levels of Vit. D in BC cases when compared with healthy controls. Results of many studies correlate with our study.[9,10,11,12,]

Fransisca Sperati found no association with a reduced risk of BC development and Vit.D use in postmenopausal women.

Elizabeth Jacob conducted randomized double-blind clinical trials and failed to support inverse relationship of Vit.D and BC progression and /or mortality.

UV exposure is very important to maintain the normal levels of Vit. D. Women are not exposed to the sun due to sociocultural practises related to dress. Lifestyle choices and housing designs helps to avoid sun exposure and may create Vit. D deficiency.[9] In menopausal women, the ability of the skin and kidneys to produce 1,25, (OH)2D3 is reduced thereby intestinal absorption is reduced. Results in lower levels of Vit. Vit. D deficiency promotes tumorigenesis, oxidative stress, DNA damage of malignant cells. It activates oncogenesis and inactivates tumour suppressor genes, and therefore enhancing cancer cells proliferation.[13] Melanin is extremely efficient at absorption of UVB radiation, causing increased skin pigmentation which reduces vit. D photosynthesis.[8] Vit. D deficiency is also associated with secondary elevation in serum PTH levels which has carcinogenic and tumour promoting effects, may lead to an increased risk of BC.[12] Insulin-like growth factor (IGF-1) is a mitogenic and antiapoptotic peptide that can stimulate proliferation of breast epithelial cells, The active Vit. D metabolite is able to block the mitogenic effects of IGF-1, leading to a decrease in proliferation and increase in apoptosis. With aging there is a physiological decline in the IGF-1.[13]

In the present study, Postmenopausal status was significantly associated with increased BC risk (OR=2.63;95%CI:1.17-5.87; P<0.05). This may be because of prolonged exposure to environmental carcinogens.[14]Vit. D deficiency in postmenopausal women increases susceptibility towards BC. In the present study we observed a significant association between higher BMI and BC which suggest that higher BMI is an important risk factor for BC. In premenopausal women estrogens are not influenced by aromatization, so higher BMI or obesity does not play a significant role in carcinogenesis but postmenopausal women have high activity of aromatase in adipose tissue results in higher estrogen levels and thereby increased chances to develop BC.[15] Similarly many studies showed clear inverse association between BC and Vit.D levels. Insufficiency of Vit.D can result in an increase in fat mass by activation of lipogenesis. It was found that, obese and elderly women have less sunlight exposure, Volumetric dilution of Vit.D, decrease in 1α-hydroxylase enzyme in adipose tissue of obese people may contribute to increase the susceptibility to BC.[16]

CONCLUSION:

Our results suggest that significantly deficient levels of Vit.D may contribute to develop breast cancer in women of Marathwada, Maharashtra, India.

Limitations of study:

There are some limitations of this study. The sample size was multicentric. Other demographic parameters such as Diet, Smoking, alcohol intake were not included. Larger study may be needed for more precise results.

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Conflicts of interest…. There are no conflicts of interest.

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