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RESEARCH ARTICLE

BREAST CANCER PREVENTION AND TREATMENT: THE ROLE OF VITAMIN D

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ABSTRACT

Breast cancer has been considered as the most common type of cancer among the women. The age-adjusted incidence rate is approximately 25.8 per 100,000 women, with a mortality rate of 12.7 per 100,000 women. This means that about 1 in 29 Indian women are at risk of developing breast cancer during their lifetime. Breast cancer happens when cells in the breast start to grow out of control. Physical signs that breast cancer is developing include changes to the skin on the breast, nipple discharge, and a new lump on or around the breast area. Breast cancer is the uncontrolled growth of cells in the breast tissue. It usually begins in the milk ducts or milk-producing glands. Two major etiologic factors in pathogenesis of breast cancer are: Hormonal and genetic. Breast cancer is so prevalent; knowing the steps to help prevent or detect it is important. Vitamin D, a group of fat-soluble vitamins renowned for their role in preserving the balance of calcium and phosphorus. or people with cancer, a form called vitamin D3 (cholecalciferol) is preferred over vitamin D2 (ergocalciferol) as it is better able to raise and sustain vitamin D levels. Some researchers contend that maintaining optimal vitamin D levels may not only prevent breast cancer but also slow disease progression in those with cancer by delaying changes that lead to metastasis.

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INTRODUCTION

Breast Cancer: Breast cancer has been considered as the most common type of cancer among the women within 161 countries, and the most common cause for cancer deaths, within 98 countries.Breast cancer is the type of cancer that mostly affects women in the world, both in developing and developed countries. It is also the leading cause of death by cancer in women worldwide, with an estimated 520,000 deaths annually**.** Breast cancer is the most common cancer among Indian women, accounting for 14% of all cancer cases in this group. The age-adjusted incidence rate is approximately 25.8 per 100,000 women, with a mortality rate of 12.7 per 100,000 women. This means that about 1 in 29 Indian women are at risk of developing breast cancer during their lifetime. Notably, the incidence is higher in urban areas, with 1 in 22 women at risk, compared to rural areas, where the risk is 1 in 60**.** Early detection and awareness are crucial, as more than 50% of Indian women are diagnosed at advanced stages (III and IV), which significantly affects survival rates**.** Known and well-established risk factors for breast cancer include age, family history, and the density of breast tissue, parity, overweight, alcohol intake, and genetic risk factors such as BRCA mutations.(1) Breast cancer happens when cells in the breast start to grow out of control. After skin cancer, it's the most common cancer in people assigned female at birth in the United States.There are different types of breast cancer, and many treatment options are available. Physical signs that breast cancer is developing include changes to the skin on the breast, nipple discharge, and a new lump on or around the breast area.Breast cancer is the uncontrolled growth of cells in the breast tissue. It usually begins in the milk ducts (ductal carcinoma) or milk-producing glands (lobular carcinoma). Over time, it may spread to nearby tissues or distant parts of the body (metastasis).(2)

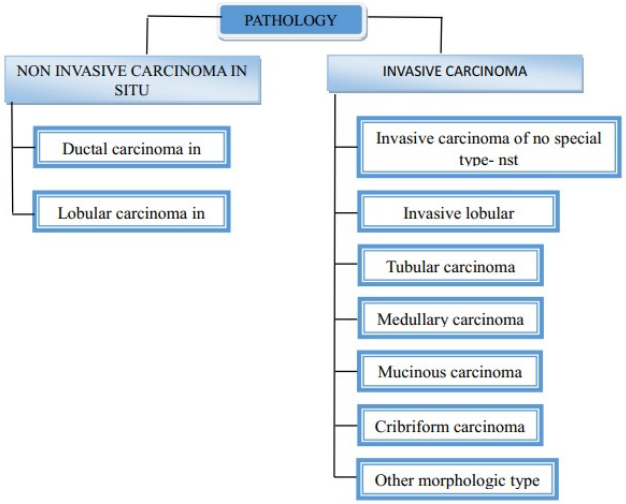
Symptoms: One of the most common breast cancer symptoms is a lump, or mass, on the breast area. Other signs can include:

- Swelling
- Skin dimpling
- Pain
- Swollen lymph nodes
- Changes in the nipple or breast skin
- Nipple turning inward(3)

Early Signs: Subtle breast changes are some of the earliest signs of breast cancer, including: Changes in the look, size, or feel of the breast, changes in the look, size, or feel of the nipple, nipple discharge Early-stage breast cancers aren't always immediately noticeable but can be detected with routine screening and mammograms.(4) There are a couple of ways that breast cancer can spread:

- Through the lymph system
- Through the bloodstream
- Locally (into nearby tissues or organs)

How quickly a particular case of breast cancer will spread depends on several factors, including the type of breast cancer, the stage and grade, and personal factors like your age.[5]



Stages: Stage is based on the size of the primary tumor (T1–4), presence and extent of lymph node involvement (N1–3), and presence or absence of distant metastases (MO–1). Simplistically stated, these stages may be represented as follows:

Early Breast Cancer

- **Stage O:** Carcinoma in situ or disease that has not invaded the basement membrane.
- **Stage I:** Small primary tumor without lymph node involvement.
- **Stage II:** Involvement of regional lymph nodes.

Locally Advanced Breast Cancer

- **Stage III:** Usually, a large tumor with extensive nodal involvement in which the node or tumor is fixed to the chest wall; also includes inflammatory breast cancer, which is rapidly progressive.

Advanced or Metastatic Breast Cancer

- **Stage IV:** Metastases in organs distant from the primary tumor.

The stages of breast cancer describe how much cancer has spread in the body. This helps healthcare providers gauge how serious it is and develop the best treatment plans for your situation.[6]

Etiology and Pathogenesis: Overall, two major etiologic factors in pathogenesis of breast cancer are:Hormonal and genetic.

- Hormonal factors: Breast cancer is a hormone-dependent disease. There is sufficient evidence to suggest that excess endogenous oestrogen or exogenously administered oestrogen for prolonged duration is an important factor in the development of breast cancer.
- Genetic factors: About 10% of breast cancers have been found to have inherited mutations. These mutations include breast cancer (BRCA) susceptibility gene in inherited breast cancer.[7]

Prevention and Early Detection: Because breast cancer is so prevalent, knowing the steps to help prevent or detect it is important. Experts recommend screening and lifestyle changes such as:

- Screening (such as a mammogram) according to recommended guidelines
- Exercising regularly
- Limiting alcohol consumption
- Quitting smoking
- Consuming a low-fat diet
- Breastfeeding, if possible[8]

Vitamin D: Vitamin D is a fat-soluble vitamin essential for maintaining bone health, supporting the immune system, and regulating inflammation. The body produces vitamin D in response to sun exposure, but it can also be obtained through dietary sources and supplements.

Types of Vitamin D

Table 1. Types of Vitamin D

Name	Chemical composition	Uses
Vitamin D_1	Mixture of molecular compounds of ergocalciferol with lumisterol, 1:1	
Vitamin D_2	ergocalciferol (made from ergosterol)	
Vitamin D_3	cholecalciferol (made from 7-dehydrocholesterol in the skin)	
Vitamin D_4	22-Dihydroergocalciferol	
Vitamin D_5	sitocalciferol (made from 7-dehydrositosterol)	

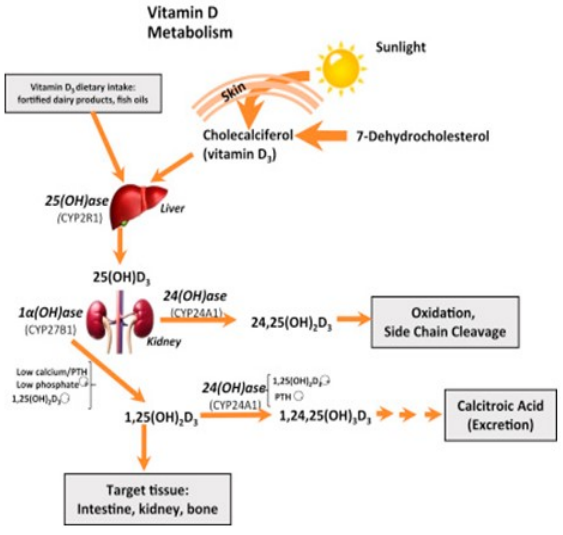


Fig 1. Synthesis and Mechanism of Vitamin D

Recommended Dosage of Vitamin D: Given the relationship between vitamin D and breast cancer, it would seem reasonable to suggest that supplements can lower the risk of cancer and potentially slow the progression of the disease. With respect to disease progression, there is no data to suggest what dose of vitamin D may or may not be therapeutic. Even so, the general aim would be to achieve and maintain optimal vitamin D levels with diet and supplements.

According to the National Institute of Health, the daily vitamin D requirements from all sourcesmeasured in international units (IU) and the equivalent micrograms (mcg) are:

- Adults to age 70: 600 IU/day or 15 mcg
- Adults over 70: 800 IU/day or 20 mcg
- Pregnant and nursing people: 600 IU/day or 15 mcg

For people with cancer, a form called vitamin D3 (cholecalciferol) is preferred over vitamin D2 (ergocalciferol) as it is better able to raise and sustain vitamin D levels. [9] Vitamin D is also beneficial because it helps keep bones strong. This is important because all three aromatase inhibitors used to prevent recurrence and certain chemotherapy drugs used to treat cancer can cause bone loss and weakening. [10]. Regular sun exposure- generally between 10 to 30 minutes, several times per weekcan also bolster vitamin D levels. However, this may not be possible as certain chemotherapy drugs are known to cause photosensitivity. [11]

Food Sources of Vitamin D

Certain foods are rich sources of vitamin D, including:

- Fatty fish, such as trout, salmon, tuna, mackerel, and sardines
- Fish liver oils
- Beef liver
- Egg yolks
- Shrimp
- Mushrooms
- Fortified milk or milk alternatives
- Fortified breakfast cereal
- Fortified orange juice
- Fortified yogurt[11]

VITAMIN D RELATED TO BREAST CANCER: Vitamin D, a group of fat-soluble vitamins renowned for their role in preserving the balance of calcium and phosphorus, is ubiquitous in virtually all tissues and cells of the human body.[12] Its extensive research has been fuelled by its connection to various diseases, including different types of cancer. [13] The significance of the link between vitamin D and cancer, especially in the context of maintaining optimal serum levels for prevention, has grown substantially, given that an estimated 30% of adults grapple with a deficiency in vitamin D (serum 25-hydroxyvitamin D (25(OH)D) < 50 nmol/L), and over 60% exhibit insufficient levels (re-serum 25-hydroxyvitamin D (25(OH)D) 50–75 nmol/L). The root causes are likely multifaceted, encompassing socio-cultural practices that discourage sun exposure, dietary limitations, environmental pollution, a rise in obesity prevalence, and genetic factors.[14] A notable feature is its synthesis through exposure to ultraviolet-B (UVB) radiation from the sun.Using the cholesterol precursor 7-dehydrocholesterol, which absorbs this radiation and transforms it into pre-vitamin D3. Subsequently, it undergoes thermal isomerisation to become vitamin D3.[15] Factors such as different skin types and the place of residence can influence this synthesis process. [16] Additionally, vitamin D is obtained through dietary sources, although the available sources, such as fatty fish or certain fruits, are limited, and through supplements.[17] Regardless of its origin (re-vitamin D2 or vitamin D3), enzymatic hydroxylation in the liver produces 25-hydroxyvitamin D (25(OH)D), followed by further conversion in the kidney to 1, 25-dihydroxyvitamin D2 or D3, known as calcitriol.[18] Calcitriol (1,25(OH)2D) is important for regulating the metabolism of calcium and phosphorus obtained from ingested food and exhibits anticancer effects, influencing various cancer types such as melanoma, colorectal cancer (CRC), and breast cancer (BC).[19]

VITAMIN D AND CANCER PROGRESSION

Some researchers contend that maintaining optimal vitamin D levels may not only prevent breast cancer but also slow disease progression in those with cancer by delaying changes that lead to metastasis (the spread of cancer from the primary tumor).To date, the evidence of this remains mixed. While studies conducted at Stanford University showed that vitamin D deficiency in mice was linked to the rapid onset of metastasis, epidemiologic studies in humans have not been so cut and dry.[20] This is due in part to the fact that vitamin D deficiency is extremely common in women with breast cancer, affecting as many as 94% to varying degrees at the time of diagnosis.It is hard, therefore, to determine the exact role that vitamin D plays in the onset of metastatic breast cancer and at what level vitamin D supplementation may or not be therapeutic.[21]

TREATMENT

Supportive and Palliative Care: In advanced or metastatic breast cancer, supportive care focuses on symptom relief and quality of life improvement. Palliative interventions may include pain management, psychological support, and nutritional counselling. It is recommended that average-risk women get a mammogram every two years from age 40 to 74. Those at high risk of breast cancer (such as those with a genetic risk factor) may need to be screened earlier and more often.[22]

CONCLUSION

While research suggests a potential link between vitamin D levels and breast cancer risk, the exact nature and strength of this association remain unclear. Observational studies have shown an inverse relationship, with lower vitamin D levels associated with increased breast cancer risk. However, randomized controlled trials have yielded inconsistent results. Maintaining optimal vitamin D levels through sun exposure, diet, and supplementation may offer some protection against breast cancer. Vitamin D deficiency is common and may contribute to increased breast cancer risk. More research is needed to definitively establish the role of vitamin D in breast cancer prevention and treatment.

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