

REVIEW ARTICLE

Impact of vitamin D deficiency on cancer incidence and mortality among the elderly population: A systematic review

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Abstract

Vitamin D plays a vital role in calcium and phosphate balance and bone structure. In recent times vitamin D deficiency has become a well-known epidemic. The current study shows vitamin D deficiency causes various types of cancer along with heart disease. The current diet has removed most of the best sources of vitamin D. Healthy bones and teeth need vitamin D. Most of the low-fat diets have removed vitamin D from the diet. Vitamin D has to be consumed with fatty meal. Food items such as dairy products are hardly fortified with vitamin D in India. Subclinical vitamin D deficiency is extremely prevalent in both urban and rural settings. In USA and Canada, in spite of having food fortification techniques still vitamin D deficiency prevails. In this paper various case studies related to vitamin D deficiency in relation to cancer have been reviewed. A proper diet to overcome this problem have been suggested along with some preventive measures.

Keywords

Vitamin D; Cancer; Vitamin D Deficiency; Breast Cancer

Introduction

Vitamin D is a fat-soluble vitamin that helps in increasing the intestinal absorption of calcium, magnesium, and phosphate. It helps to absorb Calcium, which helps to make strong bones. It is found in two forms namely ergocalciferol and cholecalciferol. Sufficient consumption of Vitamin D is necessary to provide protection from the development of osteoporosis, hypertension, cancer, and several autoimmune diseases.

Apart from this, Vitamin D reduces the risk of influenza. Many medical cases have shown an inverse relationship between blood concentrations of Vitamin D and risk of type 2 diabetes. Insufficient

Vitamin D levels in type 2 people may affect insulin secretion and glucose tolerance. Anti-inflammatory impacts of glucocorticoids along with along with vitamin D supports people with steroid-resistant asthma. Calcitriol minimizes cancer progression by decelerating the growth and evolution of new blood vessels in cancerous tissue, increasing cancer cell death and minimizing cell multiplication and metastases.

Foods such as fatty fish like tuna, salmon, mackerel along with dairy products, orange juice, soy milk and cereals, beef liver, cheese, and egg yolks are a good source of vitamin D. Salmon is an excellent source of lean protein and omega-3 fatty acids and one small piece provides recommended doses of vitamin D

intake. Apart from these ones can get nutrients from orange juice and yogurt in the grocery store. Mushrooms such as chanterelle, morel, shiitake or portobello provide low-calorie vitamin D intake. Two large eggs provide one-tenth of regular vitamin D dosage. Apart from these canned light tuna provides the most vitamin D about 150 IUs per 4 ounces. Ricotta cheese is the best source of natural cheese source of vitamin D with IUs of the nutrients. It along with fruits mostly antioxidants serves as a healthy breakfast. Beef liver provides notable amounts of protein, amino acids, minerals, and vitamin D. Milk contains small amounts of vitamin D. Soya milk has 300 IUs per cup.

In spite of being able to create vitamin D, often human body has a high risk of vitamin D deficiency. People including elderly, obese individuals, exclusively breastfed infants and those who have limited sun exposure often are prone to face vitamin D deficiency. Apart from these people having fat malabsorption syndromes like cystic fibrosis, Crohn's disease has a high risk to become vitamin D deficient. Several studies have reviewed the hypothesis which is a part of Harvard cohort studies and the latest perception of the vitamin D-induced distinction of neoplastic cells which produced cells which could achieve near-normal and matured phenotype (1, 2). A research examined the relationship between consumption of dairy products, calcium or lactose and nutrients and risk of ovarian cancer among 31,925 subjects in Breast Cancer Detection Demonstration Project (BCDDP) follow-up cohort (3). A study evaluated the positive and negative effects of vitamin D supplementation to prevent mortality in adults (4). A survey was conducted to find the frequency of vitamin D deficiency and its correlation with hypothesis test which showed commonness of vitamin D deficiency in the US population (5). The epidemiologic studies showed low incidence and mortality rates from various cancers in areas with a higher rate of UV-B exposure (6). A study summarized the total status of trials involved in calcitriol and its analogs either individually or combining with known anti-cancer agents (7). The vitamin D status, decided by 25-OH vitamin D levels among women suffering from breast cancer and bone mineral density (BMD) is a concern of many studies (8). Also, vitamin D in a cohort of 89 French MCC patients to evaluate the relationship between vitamin D and MCC features and result. 65.1 % patients shows vitamin D deficiency (9). A case study

evaluated the effect of 25 D concentrations on the health of 18 years or older (10). A study analysed the investigation on the controlled trials of vitamin D supplements, with or without calcium to see the probable effects of the trials (11). A researcher performed a review and analysis to the phase where there was an association between circulating biomarker and supplements of vitamin D with mortality from cardiovascular, cancer etc (12). The breadth, validity, and presence of biases of the relationships of vitamin D with various outcomes has been evaluated by many researchers (13). A group of researchers assessed the entire data not only on one particular part of the data (14). The relationship between Vitamin D status and path of change in section of cognitive function in a cohort of ethnically diverse older adults has been evaluated in many studies (15). The vitamin D levels and occurrence of vitamin D deficiency among Korean cancer survivors in comparison to non-cancer measures suggested the factors related to vitamin D deficiency (16). An analysis gathered separate participant data from three big European population-based cohort studies and got the best-limited support for a hypothesis that vitamin D had a major role in cancer expansion and avoidance among European older adults (17). An observational study determined the frequency of vitamin D deficiency in patients with breast, lung and colorectal cancer (18). The associations of dairy products, lactose, calcium and vitamin D with ovarian cancer risk has been tested by several studies (19).

The relationship between consumption of total, dietary and supplemental vitamin D and skin cancer risk depending on 63,760 women in Nurses' Health has also been assessed. (20).

The prospect whether dietary supplementation along with vitamin D3 and calcium could reduce cancer risk among older woman has been studied (21). Researchers have evaluated pre-treatment vitamin D deficiency in relation to breast cancer auguring characteristic in Brazilian postmenopausal women (22). A study on 50 women with primary invasive, on-metastatic breast cancer was performed to find the frequency and importance of vitamin D deficiency in Egyptian women (23). As per the reports of the National Institute of Mental Health, Schizophrenia is a brain disorder affecting 1.1 percent of American adults.

A review published in October 2014 in the Journal of Clinical Endocrinology & Metabolism suggests that

vitamin D deficient people have twice the chance to be diagnosed with schizophrenia in comparison to sufficient vitamin D levels.

In the year 2018, 18 million cancer cases were estimated around the world. Out these, 9.5 million cases were of men and 8.5 million were of women. The most common cancers globally are listed in [\(Table-1\)](#)

Material & Methods

This study has used the questionnaires from the previous works to explore the relationship between vitamin D deficiency and cancer development risk. The questionnaire was developed from the earlier literature review of vitamin D and cancer using distinct case studies. The original questionnaire involved a major role of vitamin D and how its deficiency acts as a threat to cancer. Data were collected from several case studies from several medical colleges. The researcher summarized the objectives of this study prior to the distribution of questionnaires. [\(Table-2\)](#) presents the various effects of Vitamin D deficiency in relation to cancer

Results

There is vulnerability regarding whether nutrient D with or without calcium lessens the danger of death (38 preliminaries, 81 173 preliminaries, 46 237 patients). This study gives a brief idea about the deficiency of vitamin D and its association with cancer. Maintaining a proper diet is necessary to ensure the body is never a deficit of vitamin. Vitamin D is essential for healthy bones. Apart from this, foods such as fortified milk, eggs, mushrooms, and fish (especially wild salmon, tuna, and mackerel) are a prime source of vitamin. Additional food items that are significant sources of calcium, including broccoli and leafy green vegetables, were also included in the FFQ. For colorectal neoplasia, interacting effects of hormonal replacement in postmenopausal women should be evaluated. Vitamin D supplementation alone did not diminish hip crack by 15% or more (12 preliminaries, 27 834 patients). Nutrient D co-regulated with calcium diminished hip crack in standardized people (two preliminaries, 3853 patients) however did not adjust the overall danger of hip break by 15% or more in network abiding people (seven)

Discussion

The study has combined all the case studies to bring out the impact of vitamin D deficiency in distinct

demographics. Analyses in the HPFS suggest that vitamin D deficiency may contribute to the higher risk of some cancers, especially those of the digestive system, in African-Americans. Every one of the 4,275 ladies who had been determined to have breast cancer growth during the BCDDP, each of the 25,114 ladies who experienced bosom medical procedure yet had no proof of dangerous ailment. Nutrient contents were estimated using a nutrient database derived from the National Health and Nutrition Examination Survey (NHANES) II. The Block/NCI FFQ has been validated previously in similar populations (20,21). The 2005 to 2006 NHANES oversampled certain subgroups of the US populace, counting low-salary people, more seasoned grown-ups matured 60 years or on the other hand more seasoned, African Americans, and Mexican Americans, to give a more top to a bottom depiction of these populace gatherings. An aggregate of 12 862 people was examined into the 2005 to 2006 NHANES. Among the inspected people, 10 348 (80.5%) partook in the meeting, 9950 (77.4%) were associated with the examination, and 8306 (65%) gave legitimate information on nutrient D estimation. VDR was observed to be emphatically =expressed in every one of the 28 MCC tumor examples researched. Vitamin D supplementation alone did not diminish hip crack by 15% or more (12 preliminaries, 27 834 patients). A cohort study was done on 382 members in an outpatient facility selected between February 2002 and August 2010 with gauge appraisal and yearly follow-up visits. 25-hydroxyvitamin D (25-OHD) was estimated, with VitD status characterized as the accompanying: inadequate, under 12 ng/mL; lacking, 12 to under 20 ng/mL; adequate, 20 to under 50 ng/mL; or high, 50 ng/mL or higher. Of the 382 people, a subset (n = 318 [83.2%]) had somewhere around 2 intellectual assessments (run, 2-11) considering longitudinal assessment. The general example included 113 African American members (29.6%), 96 Hispanic members (25.1%), 158 white members (41.4%), and 15 members from other racial/ethnic gatherings (3.9%; 6 Asian, 6 Filipino, 3 other). Members (N = 382 at the pattern) had a mean (SD) time of 75.5 (7.0) years; 61.8% were ladies; and 41.4% were white, 29.6% African American, 25.1% Hispanic, and 3.9% other race/ethnicity. A determination at enlistment included 17.5% with dementia, 32.7% with gentle psychological weakness, and 49.5% cognitively typical. The mean (SD) 25-OHD levels were essentially lower for African

American and Hispanic members contrasted and white members (17.9 [15.8] and 17.2 [8.4] versus 21.7 [10.0] ng/mL, individually; $P < .001$ for both). Utilizing the Korea National Health and Nutrition Examination Survey (KNHANES), 915 malignancy survivors and 29,694 controls were chosen. Serum 25(OH)D dimensions were estimated; nutrient D inadequacy was characterized as 25(OH)D dimensions under 20ng/mL.

(Figure 1) shows the Year wise total cancer prevalence in India [ICMR, 2006; ICMR, 2009]

Conclusion

The prospective studies have shown the importance of vitamin D in cancer prevention. The results which we obtain from the case studies give a brief idea about the importance of a nutritional approach for cancer prevention. Nutrient contents were estimated using a nutrient database derived from the National Health and Nutrition Examination Survey (NHANES) II. Flowing 25(OH)D is viewed as the best marker of nutrient D status since it mirrors the nutrient D got from both eating regimen/enhancements and sun introduction and has a more extended half-life when contrasted with 1,25-dihydroxy nutrient D3 [1,25(OH)2D]. The Institute of Health Metrics and Evaluation (IHME) reported that India ranked tenth among the countries with the lowest rate of cancer incidence in the world - with only 106.6 new cancer cases in 2016 for 100,000 members of its population. From the territorial spread point of view, Bargarh district has the maximum incidence with 25.37% followed by Sambalpur with 24.36%. Total six districts of Western Odisha account for more than 83% of the incidence. Different territories of neighboring Chhattisgarh have the incidence of 4.87%. Even though located at an urban site, yet the population served by our center caters to mainly the rural population of western Odisha as well as neighboring states of Chhattisgarh and Jharkhand. This is important to note because about three-quarters of Indians reside in rural areas. Yet, mortality for specific cancers is estimated mostly with data from India's 24 urban population-based cancer registries, with only two registries representing rural areas. Diets high in a natural product may bring down the danger of stomach and lung cancer growth. Eating salmon, cremini mushroom, fortified milk, fortified orange juice, raisin bran cereal, mackerel fish, tuna fish, Sardine canned in oil, swiss cheese may decrease the

danger of lung, mouth, pharynx, and larynx diseases. Diets high in non-boring vegetables, for example, broccoli, spinach, and beans may help secure against stomach and esophageal disease. Eating oranges, berries, peas, ringer peppers, dim verdant greens and different nourishments high in nutrient C may likewise secure against esophageal malignant growth.

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Tables

TABLE 1 LIST OF MOST COMMON CANCERS OF 2018

Rank	Cancer	New cases diagnosed in 2018	% of all cancers (excl. non-melanoma of skin)
1	Lung	2,093,876	12.3
2	Breast	2,088,849	12.3
3	Colorectal	1,800,977	10.6
4	Prostate	1,276,106	7.5
5	Stomach	1,033,701	6.1
6	Liver	841,080	5.0
7	Oesophagus	572,034	3.4
8	Cervix uteri	569,847	3.3
9	Thyroid	567,233	3.3
10	Bladder	549,393	3.2
11	Non-Hodgkin lymphoma	509,590	3.0
12	Pancreas	458,918	2.7
13	Leukaemia	437,033	2.6
14	Kidney	403,262	2.4
15	Corpus uteri	382,069	2.2
16	Lip, oral cavity	354,864	2.1

17	Brain, central nervous system	296,851	1.7
18	Ovary	295,414	1.7
19	Melanoma of skin	287,723	1.7
20	Gallbladder	219,420	1.3
21	Larynx	177,422	1.0
22	Multiple myeloma	159,985	0.9
23	Nasopharynx	129,079	0.8
24	Oropharynx	92,887	0.5
25	Hypopharynx	80,608	0.5
26	Hodgkin lymphoma	79,990	0.5
27	Testis	71,105	0.4
28	Salivary glands	52,799	0.3
29	Anus	48,541	0.3
30	Vulva	44,235	0.3
31	Kaposi sarcoma	41,799	0.2
32	Penis	34,475	0.2
33	Mesothelioma	30,443	0.2
34	Vagina	17,600	0.1

TABLE 2 CASE STUDIES OF DIFFERENT CANCERS

Author's Name	Methodology	Paper Title	Outcomes	Research gap
Glovannucci	Methodologies include the investigation of flowing 25(OH)D dimension, dietary and valuable admission, and utilization of anticipated 25(OH)D.	Vitamin D and Cancer Incidence in the Harvard Cohorts	Investigations in the HPFS propose that nutrient D inadequacy may contribute to the higher danger of a few malignant growths, particularly those of the stomach related framework, in African-Americans	Hormonal replacement in postmenopausal women for colorectal neoplasia is to be evaluated in future.
Gocek & P.Studzinski	The flagging pathways used here controls the movement of a few interpretation factors, and the genealogy deciding C/EBP group of translation factors.	Vitamin D and Differentiation in Cancer	Nutrient D, 1., 25-dihydroxy vitamin D3 (1,25D), is one. D3 offers the possibility to be an option too, or to give an adjunctive mediation to, the treatment, as well as to act in the avoidance of neoplastic ailments.	Broad extra examinations are justified to give a premise to the plan of enhanced treatments of leukemia and strong tumors.
Koralek et al.	Respondents were also asked to list the frequency of consumption of each food item in terms of the number of servings consumed per day, week, month, or year.	Relationship between Calcium, Lactose, Vitamin D, and Dairy Products and Ovarian Cancer	The visit dairy utilization isn't related to an expanded danger of ovarian malignant growth and might be related to the lower danger of ovarian disease.	The likelihood of a diminished danger of ovarian malignant growth for dietary calcium justifies further assessment in forthcoming investigations.
Bjelakoviet al.	The study was done based on the type of studies,type of participants,type of interventions,type of outcome measures.	Vitamin D supplementation for prevention of mortality in adults(Protocol)	-----	Vitamin D supplementation in a roundabout way can be done by lessening breaks or irresistible maladies in a more seasoned populace.
Forrest et al.	The study consolidates interviews and physical	Prevalence and correlates of vitamin D deficiency in US adults	-----	The NHANES was affirmed by its institutional survey board, and examining the open space information

	examinations. The meeting incorporates statistic, financial, dietary, and well-being related inquiries.			from NHANES does not require extra-institutional survey board endorsement.
Krishnan et al.	The Women's Health Initiative (WHI) randomized preliminary presumed that simultaneous estrogen treatment altered the impact of calcium and vitamin D supplementation on CRC hazard	The Role of Vitamin D in Cancer Prevention and Treatment	Higher dietary admission of nutrient D has been related to a lower rate of pancreatic malignant growth.	-----
Krishnan & Feldman	Clinical preliminaries have been completed in patients to test the impacts of nutrient D3 [the dietary enhancement.	Mechanisms Of the Anti-Cancer and Anti-Inflammatory Actions of Vitamin D	Numerous epidemiologic investigations show that nutrient D inadequacy builds the danger of an assortment of tumors and that larger amounts of nutrient D are related with a better guess and enhanced results.	Calcitriol has remedial and disease preventive impacts in some cancers.
Peppone et al.	Concentrate included 224 ladies determined to have Stage 0-III bosom disease who got treatment at the James P. Wilmot Cancer Center.	The Effect of Various Vitamin D Supplementation Regimens in Breast Cancer Patients	Breast cancer patients with inadequate/deficient 25-OH nutrient D levels had essentially brought down lumbar BMD (p=0.03).	-----
Samimi et al.	Clinical discoveries, Merkel cell polyomavirus markers and nutrient D status were surveyed in a partner of French MCC patients.	Vitamin D deficiency is associated with greater tumor size and poorer outcome in Merkel cell carcinoma patients	Vitamin D inadequacy was noted in 65.1% of the patients and was autonomously connected with more noteworthy tumor measure at a conclusion (P0.006) and with metastasis repeat (HR, 2.89; 95% CI, 1.03 to 8.13; P0.043).	The relationship between nutrient D inadequacy and MCC qualities and result, together with the discovery of the VDR in MCC cells, propose that nutrient D could impact the science of MCC.
Autier et al.	The authors had concentrated on people matured 18 years or more established.	Vitamin D status and ill health: a systematic review	-----	-----
Bolland et al.	The authors completed a preliminary successive meta-examination of existing randomized controlled preliminaries of nutrient D supplements	The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis	Nutrient D co-regulated with calcium diminished hip crack in standardized people (two preliminaries, 3853 patients) however did not adjust the overall danger of hip break by 15% or more in network abiding people (seven preliminaries)	-----
Chowdhury et al.	The author needed to condense the accessible observational and interventional proof	Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies	The inquiry procedure recognized 2704 extraordinary references. After beginning screening dependent on titles and edited compositions, 320	-----

	in one refreshed deliberate survey		articles stayed for further assessment.	
Feldman et al.	The authors talk about the studies that look at this speculation, with an accentuation on breast, prostate and colon diseases, for which the most information have been collected.	The role of vitamin D in reducing cancer risk and progression	Calcitriol maintains molecular pathways.	Vitamin D metabolites or analogs may likewise be useful in the treatment of malignancy, particularly when added to existing treatments.
Theodoratou et al.	Three sorts of studies were qualified for the umbrella survey: efficient reviews and meta-examinations that analyzed observational relationship between flowing nutrient D fixations and any clinical result	Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials	The study builds a relationship between vitamin D focuses and birth weight, dental caries in kids, maternal vitamin D fixations at term, and parathyroid hormone which focuses in patients with interminable kidney malady requiring dialysis is plausible.	-----
Miller et al.	A cohort study was done on 382 members in an outpatient facility selected between February 2002 and August 2010	Vitamin D Status and Rates of Cognitive Decline in a Multiethnic Cohort of Older Adults	-----	-----
Oh et al.	Utilizing the Korea National Health and Nutrition Examination Survey (KNHANES), 915 malignancy survivors and 29,694 controls were chosen.	The Prevalence of Vitamin D Deficiency among Cancer Survivors in a Nationwide Survey of the Korean Population	Nutrient D lack was seen in 62.7% of disease survivors and 67.1%of controls.	Nutrient D lack was predominant among both cancer survivors and controls in Korea.
Mena et al.	Three European partner considers (EPIC-Elderly, ESTHER and TROMSØ), had accessible plasma or serum 25(OH)D estimations and finish follow-up for cancer incidence.	Pre-diagnostic vitamin D concentrations and cancer risks in older individuals: an analysis of cohorts participating in the CHANCES consortium(2015)	The results do not support that vitamin D has a huge effect on cancer growth improvement and we propose sitting tight for the consequences of RCTs before planning proposals with respect to nutrient D supplementation for disease aversion.	-----
Aguirre et al.	A planned observational investigation was intended for disease patients admitted to the general ward in 2014, suffering from breast, lung, and colorectal malignant growth.	Vitamin D deficiency in patients admitted to the general ward with breast, lung, and colorectal cancer in Buenos Aires, Argentina	The study found a high commonness of nutrient D insufficiency in hospitalized malignant growth patients under dynamic treatment.	Numerous authors have suggested dosing nutrient D levels in this populace; normalizing serum levels is troublesome.
Qin et al.	Associations were assessed among 490 ovarian malignancy cases and 656 age- and site-coordinated	Dairy, calcium, vitamin D and ovarian cancer risk in African–American women	The study enlisted a vast example of AA ovarian cancer growth cases and controls from different geographic areas and with	The sun introduction in summer months and high calcium, low-lactose diet may profit ovarian disease avoidance in AA ladies.

	controls of African–American plummet of African American Cancer Epidemiology Study		assorted financial and way of life attributes, which grants our capacity, to sum up, the outcomes to the AA populace.	
Park et al.	The study is divided into four parts: study of the population, evaluation of vitamin D consumption, evaluation of covariates, evaluation of BCC, SCC and other melases, and statistical assessment.	Vitamin D Intake and Risk of Skin Cancer in US Women and Men	No proof was discovered that orally taken nutrient D plays an imperative defensive job against the rate of KC and cutaneous melanoma.	Future research is justified to affirm the discoveries and distinguish the potential instruments fundamental these associations.
Lappe et al.	This study utilizes the preliminary protocol and statistical assessment.	Effect of Vitamin D and Calcium Supplementation on Cancer Incidence in Older Women	The essential result was the first finding of a disease (barring non-melanoma skin malignancies), and every member with another malignant growth was checked just once.	-----
Filho et al.	The populace amass contained 192 Brazilian postmenopausal ladies as of late determined to have breast cancer growth, matured 45 to 75 years.	Vitamin D deficiency is associated with poor breast cancer prognostic features in postmenopausal women	In Brazilian postmenopausal ladies with breast cancer, there was a relationship between nutrient D inadequacy or insufficiency and tumors with more regrettable prognostic highlights.	-----
Ismail et al.	The serum dimension of 25-hydroxy nutrient D [25(OH)D] was estimated by ELISA at finding, before any malignancy treatment.	Prognostic Significance of Serum Vitamin D Levels in Egyptian Females with Breast Cancer	The authors found that the disease freely predicts serum 25(OH)D; confined and territorial BC were related with lower serum 25(OH)D contrasted with in situ disease (Neuhouse et al., 2008).	-----

Figures

FIGURE 1 YEAR WISE TOTAL CANCER PREVALENCE IN INDIA

