ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 8, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

PREVALENCE OF SERUM SUBOPTIMAL VITAMIN D3 LEVELS AND ITS CORRELATION WITH TREATMENT OUTCOME, SOCIODEMOGRAPHIC PROFILE AMONG CANCER PATIENTS: A RETROSPECTIVE ANALYSIS

ANJAN BERA[1], SHATARUPA DUTTA[2], CHANDRIMA BANERJEE[1], SAPTARSHI BANERJEE[3]*

[1]Department of Radiotherapy, NRS Medical College and Hospital, Kolkata, West Bengal, India. [2]Department of Radiotherapy, RG KAR Medical College and Hospital, Kolkata, West Bengal, India. [3]Department of Radiotherapy, Medical College and Hospital, Kolkata, West Bengal, India. Corresponding author: saptarshi Banerjee, Email: dr.saptarshibghs@gmail.com

Received: 03 May 2022, Revised and Accepted: 15 June 2022

ABSTRACT

Objectives: In areas of etiology and prevention of cancer research, Vitamin D3 is currently one of the most promising agents. By virtue of anti-inflammatory, immunomodulatory, antiangiogenic, and proapoptotic effects, Vitamin D3 may inhibit carcinogenesis, cancer cell proliferation, and tumor progression. We wanted to study the prevalence of Vitamin D3 deficiency among cancer patients and whether there is any correlation between this Vitamin D3 level with response to the treatment of cancer and survival.

Methods: Between, January 2014 and December 2017, 199 patients, who completed treatment at our radiotherapy department, were included in this study. In a non-fasting state, a venous blood sample was obtained during the follow-up period, and the serum level of Vitamin D3 was determined by chemiluminescence immunoassay method.

Results: A higher prevalence of suboptimal D3 concentration was seen in patients with stable or progressive disease (PD) than in those patients cured, this was statistically significant. The complete response versus partial response and PD p-values are 0.0001 and 0.0008, respectively. Overall survival (OS) difference between D3 sufficiency and insufficiency is not statistically significant (p-0.4422). However, OS difference between D3 sufficiency and deficiency is statistically significant (p-0.0001). Similarly, the OS difference between D3 insufficiency and deficiency is statistically significant (p-0.0001).

Conclusions: Vitamin D3 level is significantly associated with response and there is also a positive correlation with OS. Statistically significant (p-0.0001) OS difference between D3 insufficiency and deficiency is present. Statistically significant higher prevalence of suboptimal D3 concentration was seen in patients with stable or PD than in those patients cured.

Keywords: Vitamin D3, Deficiency, Cancer, Overall survival.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i8.45104. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Worldwide, non-communicable disease (NCD) is responsible for 63% of death in the year 2008 and India's NCD accounts for 53% of deaths. Among NCDs, cancer is one of the leading causes of death in India and accounts for 6% of mortality in the year 2008 [1]. It is now well recognized that Vitamin D3 deficiency is associated not only with rickets and fractures of bone; but also, with the increased risk of other NCD s, namely, cancer and cardiovascular disease and diabetes mellitus. In the year way back 1980, Garland and Garland first hypothesized that Vitamin D and sunlight may reduce the risk of colon cancer [2]. Since then, in this area, substantial research has been made. With anti-inflammatory, immunomodulatory, antiangiogenic, and proapoptotic effects, Vitamin D3 may inhibit carcinogenesis, cancer cell proliferation, and tumor progression (Fig. 1) [3]. Vitamin D3 may also reduce death from cancer by decreasing the metastatic potential of carcinoma. When serum Vitamin D3 level is low, the risk of bladder cancer goes up, and at the same time, patients with high Vitamin D3 levels correlated with better survival and outcome [3]. The best functional indicator of Vitamin D3 status in the human body is circulating 25 (OH) D and this circulating Vitamin D3 also reflects the sum of oral intake and synthesis of Vitamin D3 from the skin. Irrespective of age, gender, and geographical location, despite adequate exposure to sunlight throughout the year, Vitamin D3 deficiency is common in the Indian population [4,5]. In a study among the ethnic population from northeastern India, the prevalence of Vitamin D deficiency was seen in 65% population [6]. In another population-based cross-sectional study among multi-ethnic Asian adults, 75% population had suboptimal Vitamin D3 levels [4]. Low serum levels of Vitamin D3 are associated with an increased risk of cancer and cardiovascular disease. The region with greater sun exposure is associated with a lower rate of death from cancer and cardiovascular disease [4]. Many studies reported the prevalence of Vitamin D3 deficiency and its causal relationship with cancer [4-6]. In this context, we wanted to study the prevalence of Vitamin D3 deficiency among cancer patients and whether there is any correlation between this Vitamin D3 level with response to the treatment of cancer and survival.

METHODS

Between, January 2014 and December 2017, 199 patients, who previously completed treatment for malignancy, at our radiotherapy department, were included in this study. Patients on anti-psychotic, anti-tubercular, and steroid medication were excluded from analysis as these agents may affect blood levels of Vitamin D3. A venous blood sample, in a non-fasting state, was obtained and serum level of Vitamin D3 was determined by chemiluminescence immunoassay method. According to clinical practice guidelines by the Endocrine Society in the year 2011, Vitamin D3 concentration is optimal when the value is more than 30 ng/ml; insufficiency when the value is between 21 and 29 ng/ml, and deficient when leveling below 20 ng/ml. Lifestyle and sociodemographic factors including age, gender, education level, body mass index (BMI), and income level were obtained. We have also estimated the prevalence of Vitamin D3 insufficiency and deficiency among cancer patients and the correlation between Vitamin D3 level with response to anticancer therapy and overall survival (OS).

All the data were collected from the record section of the department of radiotherapy after obtaining ethical clearance from the Institutional Ethical Committee and before collection of data, we have taken the informed consent of the patient and/or patients relatives, stating the nature of this study and no herm and no financial burden would occur, and further, management of the patients would not be hampered.

RESULTS

A total of 199 patients with different types of cancer, who completed treatment in the department of radiotherapy in the NRS medical college Kolkata, were analyzed for Vitamin D3 levels. Among them, 59 had sufficient Vitamin D3, 80 had insufficiency, and 60 patients (30.15%) had Vitamin D3 deficiency. The mean Vitamin The D3 level of the study population was 24.85 ng/ml. In the study population, 82 were male and 117 were female. Mean Vitamin D3 level in female population (23.56±7.26 ng/ml) was significantly lower than male (26.7±9.21 ng/ml) (p=0.008). It was found that Vitamin D3 level was not associated with the age of the patient (linear regression p=0.59). Association of Vitamin D3 level with BMI was assessed. This association was not statistically significant (linear regression p=0.054). The mean Vitamin D3 levels of literate and illiterate patients were almost similar, 24.89±8.54 ng/ml for literate and 24.83±7.66 ng/ml for illiterate patients (p=0.96). Mean Vitamin D3 level was not significantly associated with income. For Above Poverty Line (APL) patients, mean Vitamin D was 25.55 ng/ml, and for Below Poverty Line (BPL) patients, it was 24.33 ng/ml (p=0.3) (Table 1).

The Association of the response of the patients with mean Vitamin D levels was analyzed. It was found that, the mean Vitamin D3 level of patients who achieved Complete Response (CR) (26.47±7.86 ng/ml) was significantly higher than patients with Partial Response or Stable Disease (PR or SD) (18.88±6.22 ng/ml) (p<0.0001). The mean Vitamin D3 of patients having Progressive Disease (PD) (20.39±8.31 ng/ml) was also significantly less than patients with CR (p=0.0008). There was no significant difference in Vitamin D level between patients with PR or SD and patients with PD (p=0.48) (Table 2).

During analyzing the relation of OS with Vitamin D level, it was found that OS was positively associated with Vitamin D level. Linear regression p-value is 0.0001 (Table 3 and Fig. 2). Differences in mean OS were compared between patients having Vitamin D sufficiency (>30 ng/ml), insufficiency (21–30 ng/ml), and the deficiency (upto 20 ng/ml). It was found that the mean OS of patients with sufficient Vitamin D (51.47±25.52 months) was significantly higher than the mean OS of patients with Vitamin D deficiency (29.95±20.26 months) (p<0.0001). The mean OS of patients having Vitamin D insufficiency (48.09±25.67 months) was also significantly higher than patients with Vitamin D deficiency (p<0.0001). The mean OS of patients with Vitamin D sufficiency and insufficiency was almost similar (p=0.44) (Table 4).

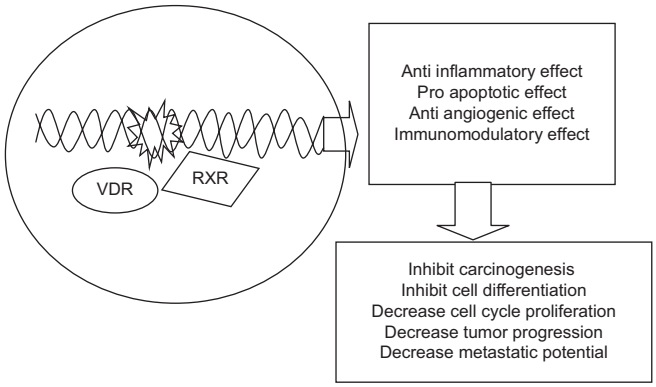

Fig. 1: Mechanism of action Vitamin D3

DISCUSSION

In our study, women are more likely to be insufficiency in vitamin D3 than men, that is, gender discrepancy is evident in our study. The mean Vitamin D3 level is significantly lower in female patients (p=0.0008). This is explained by the fact that the woman tends to avoid sunlight exposure and believes that "fairer is beautiful." Moreover, traditional attire that blocks ambient sunlight leads to decreased Vitamin D3 production in the and consequently lower serum Vitamin D3 concentration compared to men. Furthermore, those, who, to avoid skin cancer or sunburn, cover up or use sunscreen lotion with high SPF factor or cover up their body, because cultural reasons stay out of the sun to keep skin pale are at risk of Vitamin D3 insufficiency.

With increasing age, cutaneous production of Vitamin D3 decreases. At the same time, in a person with a darker complexion, due to reflection by skin melanin and absorption of the ultraviolet ray is decreased; cutaneous Vitamin D synthesis is inhibited. In this context, in India, a substantial proportion of the population has a darker complexion and due to rapid economic development, many young adults are subject to indoor jobs, thereby limiting Sun exposure and consequently, the synthesis of Vitamin D3 further decreased [4,5].

In our study, BMI and age of the patient are not associated with both insufficiency and deficiency with a linear regression p=0.054 and 0.59, respectively. A study by Man *et al.*, reported, that an Indian ethnicity, age <65 years, female sex, and higher BMI levels were associated with a lower level of Vitamin D3 [4]. No association was seen with family income level

Table 1: Relation of Vitamin D level (ng/ml) with various demographic factors

Relation of Vitamin D with Gender						
Test	Group	N	Mean	SD	SEM	p-value
t-test	Male	82	26.70	9.21	1.02	0.008
	Female	117	23.56	7.26	0.67	
Relation of Vitamin D with Age						
Test	Number of XY pairs	R square	Equation	Deviation from horizontal	F	p-value
Linear Regression	199	0.00144	Y= −0.02568*X+26.16	Not Significant	0.284	0.595
Relation of Vitamin D with BMI						
Test	Number of XY pairs	R square	Equation	Deviation from horizontal	F	P-value
Linear Regression	199	0.0187	Y=0.2963*X+17.98	Not Significant	3.762	0.054
Relation of Vitamin D with Literacy						
Test	Group	N	Mean	SD	SEM	p-Value
t-Test	Literate	139	24.89	8.54	0.72	0.96
	Illiterate	60	24.83	7.66	0.99	
Relation of Vitamin D with Income						
Test	Group	N	Mean	SD	SEM	P-VALUE
t-Test	APL	85	25.55	9.25	1.00	0.303
	BPL	114	24.33	7.41	0.69	

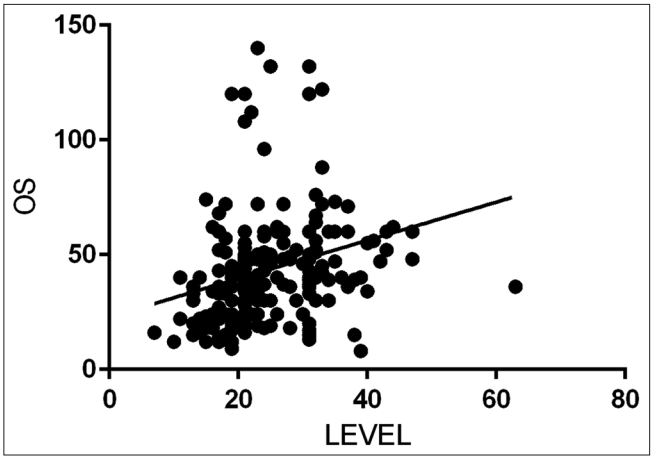

Fig. 2: Linear regression between OS and Vitamin D3 level

Table 2: Comparison of Vitamin D levels (ng/ml) in different Response groups

Group	n	Mean±SD	p-value
CR	152	26.47±7.86	<0.0001
PR or SD	24	18.88±6.22	
CR	152	26.47±7.86	0.0008
PD	23	20.39±8.31	
PR or SD	24	18.88±6.22	0.483
PD	23	20.39±8.31	

Table 3: Relation of Overall Survival (OS) with Vitamin D by Linear Regression; Y=OS, X=Vitamin D Level

Best-fit values	
Slope	0.833±0.214
Y-Intercept	22.91±5.596
X-Intercept	−27.49
1/Slope	1.20
95% Confidence Interval	
Slope	0.414–1.252
Y-Intercept	11.94–33.88
X-Intercept	−80.73–−9.66
Goodness of Fit	
R Square	0.072
Significance	
F	15.20
p-value	0.0001
Deviation from horizontal	Significant
Equation	Y=0.8333*X+22.91

Table 4: OS Differences in different Vitamin D level groups

Group	n	Mean±SD	p-value
Sufficiency	59	51.47±25.52	<0.0001
Deficiency	60	29.95±20.26	
Insufficiency	80	48.09±25.67	<0.0001
Deficiency	60	29.95±20.26	
Sufficiency	59	51.47±25.52	0.44
Insufficiency	80	48.09±25.67	

(APL and BPL) or education level (literate and illiterate) in our study. Few studies reported higher Vitamin D3 levels seen in patients presented with earlier stage than those with stage III or IV diseases, that is, an inverse correlation between carcinoma stage and serum Vitamin D3 level [7-9]. Inone study by Antunac Golubic *et al*., Vitamin D3 insufficient patients' anticancer therapy with or without Vitamin D3 supplement reported no difference in OS or progression-free survival [10]. The author concluded that no beneficial effect may be due to poor compliance. Another study reported prolonged disease-free survival along with improved quality of life, social, and physical functioning despite low dose Vitamin D3 supplementation (200–400 IU/day for 1 year) [11]. In an updated meta-analysis of randomized control trials (RCT), by Keum *et al*., Vitamin D3 supplementation reduces total cancer mortality, but total cancer incidence is not decreased [12].

Another RCT reported supplementation with Vitamin D reduced the incidence of both metastatic and fatal cancer with normal weight subjects showing the strongest risk reduction [13]. In our study, positive correlation with Vitamin D3 level and OS and response to therapy, that is, CR and PR.

Our study has much strength, including a large number of patients with geographic diversity, long follow-up, and baseline Vitamin D3 estimation in so many patients. We have used clearly defined clinical tests in our study. Our study also has limitations. One limitation of our study is single institutional.

CONCLUSIONS

Vitamin D3 level is significantly associated with response and there is also a positive correlation with OS. Statistically significant (p-0.0001) OS difference between D3 insufficiency and deficiency is present. Statistically significant higher prevalence of suboptimal D3 concentration was seen in patients with stable or PD than in those patients cured. The CR versus PR and PD p-values are 0.0001 and 0.0008, respectively. OS difference between D3 sufficiency and insufficiency is not statistically significant (p-0.4422). However, OS difference between D3 sufficiency and deficiency is statistically significant (p-0.0001).

Vitamin D3 deficiency is a widespread public health problem and is linked to many health-related issues including cancer. Therefore, during anticancer therapy, it is better to estimate serum Vitamin D3 level and correct the deficiency and insufficiency by oral supplementation.

ACKNOWLEDGMENT

The authors express their appreciation to Prof. Srikrishna Mandal, Head of the Radiotherapy Dept. for reviewing our manuscript. We likewise acknowledge the contributions of Government West Bengal for supplying all treatment including chemotherapeutics free of cost and to their work by all Junior residents, medical physicists, and all radiation technologists of our radiotherapy department.

CREDIT AUTHORSHIP CONTRIBUTIONS STATEMENTS

DR. Anjan Bera-conceptualization, methodology, data collection, data interpretation, review of statistical analysis, and writing of the manuscript.

Dr. Shatarupa Dutta and Dr. Chandrima Banerjee-methodology, data collection, data interpretation, and review of the manuscript.

Dr. Saptarshi Banerjee-methodology, data collection, data interpretation, statistical analysis, and review of the manuscript.

CONFLICTS OF INTEREST

All authors declare no conflicts of interest in publishing this article.

AUTHORS FUNDING

This research did not receive a grant of any type from funding agencies in the public, commercial, or not from sectors. As a government policy, "cancer treatment free of cost to all," treatments including all investigations and chemotherapeutics supplied free of cost by Govt. of West Bengal, India.

REFERENCES

1. Sharma K. Burden of non-communicable diseases in India: Setting priority for action. Int J Med Sci Public Health 2013;2:7-11.

doi: 10.5455/ijmsph.2013.2.7-11
2. Garland CF, Garland FC. Do sunlight and Vitamin D reduce the likelihood of colon cancer? Int J Epidemiol 1980;9:227-31. doi: 10.1093/ije/9.3.227, PMID 7440046
3. Dalhoff K, Dancey J, Astrup L, Skovsgaard T, Hamberg KJ, Lofts FJ, *et al*. A phase II study of the Vitamin D analogue Seocalcitol in patients with inoperable hepatocellular carcinoma. Br J Cancer 2003;89:252-7. doi: 10.1038/sj.bjc.6601104, PMID 12865912
4. Man RE, Li LJ, Cheng CY, Wong TY, Lamoureux E, Sabanayagam C. Prevalence and determinants of suboptimal Vitamin D levels in a multiethnic Asian population. Nutrients 2017;9:1-12. doi: 10.3390/nu9030313, PMID 28327512
5. Asegaonkar SB. Vitamin D and Type 2 diabetes mellitus: Indian perspectives. J Diabet Complicat Med 2016;30:110-6.
6. Goswami B, Sarkar S, Reang T, Reang S, Sengupta S, Bhattacharjee B. Prevalence of vitamin D3 insufficiency among the rural ethnic population of Tripura and its association with Type-2 diabetes mellitus. Int J Med Sci Public Health. 2019;8:806-10. doi: 10.5455/ijmsph.2019.0514112072019
7. Palmieri C, MacGregor T, Girgis S, Vigushin D. Serum 25-hydroxyvitamin D levels in early and advanced breast cancer. J Clin Pathol 2006;59:1334-6. doi: 10.1136/jcp.2006.042747, PMID 17046848
8. Fakih MG, Trump DL, Johnson CS, Tian L, Muindi J, Sunga AY. Chemotherapy is linked to severe vitamin D deficiency in patients with colorectal cancer. Int J Colorectal Dis 2009;24:219-24. doi: 10.1007/s00384-008-0593-y, PMID 18830610
9. Niv Y, Sperber AD, Figer A, Igael D, Shany S, Fraser G, *et al*. In colorectal carcinoma patients, serum Vitamin D levels vary according to the stage of the carcinoma. Cancer 1999;86:391-7. doi: 10.1002/(sici)1097-0142(19990801)86:3<391:aid-cncr5>3.0.co;2-a, PMID 10430245
10. Golubić ZA, Baršić I, Librenjak N, Pleština S. Vitamin D supplementation and survival in metastatic colorectal cancer. Nutr Cancer 2018;70:413-7. doi: 10.1080/01635581.2018.1445766, PMID 29533115
11. Wang L, Wang C, Wang J, Huang X, Cheng Y. Longitudinal, observational study on associations between postoperative nutritional Vitamin D supplementation and clinical outcomes in esophageal cancer patients undergoing esophagectomy. Sci Rep 2016;6:38962. doi: 10.1038/srep38962, PMID 27958342
12. Keum N, Lee DH, Greenwood DC, Manson JE, Giovannucci E. Vitamin D supplementation and total cancer incidence and mortality: A meta-analysis of randomized controlled trials. Ann Oncol 2019;30:733-43. doi: 10.1093/annonc/mdz059, PMID 30796437
13. Chandler PD, Chen WY, Ajala ON, Hazra A, Cook N, Bubes V, *et al*. Effect of Vitamin D3 supplements on development of advanced cancer: A secondary analysis of the VITAL randomized clinical trial. JAMA Network Open 2020;3:e2025850. doi: 10.1001/jamanetworkopen.2020.25850, PMID 33206192