A Study of Vitamin D Levels in Patients of Prostate Cancer

Pankaj R Kambale[1,*], Deepa Haldar[2], B.C. Kabi[3], Kalpana P. Kambale[4]

[1]Assistant Professor, Dept. of Biochemistry, SMBT Institute of Medical Sciences & Research, Nasik, Maharashtra [4]Senior Lecturer, Dept. of Periodontology, SMBT Institute of Dental Sciences & Research, Nasik, Maharashtra, [2]Senior Resident, [3]Director-Professor & HOD, Dept. of Biochemistry, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi

***Corresponding Author:**
Email: pankajkamble32@gmail.com

Abstract

Background: Prostate cancer is the second most common cancer among men worldwide contributing to three fourth of the registered cases across the globe. Although it is more common in western countries, its incidence is rising in India due to demographic and epidemiological transitions. Some epidemiological studies have suggested that vitamin D has anticancer properties. But the data on vitamin D deficiency and prostate cancer is inconsistent, particularly in Indian population.

Materials and Methods: In this case control study, we compared Vitamin D levels in 120 subjects with prostate cancer with those of 120 age-matched healthy controls. 25(OH) vitamin D levels in were estimated by ELISA. Data was collected and analysed by suitable statistical methods.

Result: Levels of 25 (OH) vitamin D were 11.7±1.06 ng/ml in cases as compared to 24.3±1.54 ng/ml in controls (p value <0.0001)

Conclusion: There is a strong inverse association between 25(OH) vitamin D serum levels and prostate cancer risk. Keywords: vitamin D, prostate cancer, vitamin D receptor

Keywords: Vitamin D, Prostate Cancer, Vitamin D Receptor

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-6377.2016.00033.2

Introduction

Prostate cancer has become a major health problem globally during the last few decades. It is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide. The worldwide prostate cancer burden is expected to grow to 1.7 million new cases and 499,000 new deaths by 2030. It is simply due to the growth and aging of the global population.(1) Although incidence rates of prostate cancer are considered low in Asian and North African countries, ranging from 1 to 9/100,000 persons(2), demographic and epidemiological transitions in developing countries like India have shown an increasing trend in the burden of various cancer cases including prostate cancer. The data shows that almost all regions of India are equally affected by this cancer. The cancer projection data shows that the number of cases will become doubled by 2020.(3)

Vitamin D, the sunshine vitamin, plays a pivotal role in bone and calcium metabolism. However, apart from these traditional calcium-related actions, it is being increasingly recognized for its role in immune system, central nervous system, epithelial cells and various endocrine processes.(4) Vitamin D exerts its biological effects through binding and activating the intracellular Vitamin D receptor (VDR), which acts as a ligand dependent transcriptional factor in many types of tissues, including the prostate.(5) Prostate cells contain vitamin D receptors and also the enzymes necessary for vitamin D metabolism. Vitamin D promotes cell differentiation, apoptosis, inhibition of cellular proliferation, angiogenesis and tumor cell invasion.(6,7) Studies done so far to explore the association between vitamin D deficiency and prostate cancer have yielded conflicting results. Some epidemiological studies have shown inverse associations of circulating total 25-hydroxyvitamin D [25(OH)D], with prostate cancer risk at the individual level.(8-10) Overall, however, the evidence is inconsistent, with one meta-analysis finding little evidence that circulating concentrations of total 25(OH)D are associated with prostate cancer.(11-13) Few studies have supported for a protective role of 25(OH)D in advanced prostate cancers(14-16) In India, scenario is not yet clear. Thus, in the present study, we investigated associations of circulating total 25(OH)D levels with prostate cancer.

Materials and Methods

The study was conducted in the Department of Biochemistry in collaboration with Department of Urology, Vardhman Mahavir Medical College and Safdarjang Hospital, New Delhi. Clearance from institutional ethical committee was obtained before preceding the study. Cases included 120 newly diagnosed patients of prostate cancer which were histologically confirmed. Patients suffering from any parathyroid disorder and chronic kidney disease as well

as those taking calcium and/or vitamin D supplements were excluded. Control groups consists of 120 normal age and sex matched healthy subjects. All normal healthy controls were screened for prostatic specific antigen (PSA) level (normal <4.0 ng/ml). Selected controls did not have any history of cancer and/or prostate surgery and not on calcium and/or vitamin D supplements. Written informed consent was taken from all subjects.

3ml of blood was collected in plain vial. Serum was separated within one hour of collection and stored at -80°C for vitamin D estimation. The estimation of serum vitamin D was performed by competitive ELISA technique. The kit was procured from DLD Diagnostika GMBH, Germany.

Statistical Analysis: Data was analysed using Graph Pad Prism 5.0 version. The data is presented as Mean±SEM. A p value of <0.05 is considered significant. The difference in vitamin D levels in subjects with prostate cancer compared to age-matched control subjects without prostate cancer was evaluated by the unpaired ***t***-test. The association between vitamin D level and prostate cancer risk was evaluated by calculating odd ratios (OR) and 95% confidence intervals (CI).

Results

In the present study, all the patients of prostate cancer were above the age of 50 years and they were age matched with healthy controls (p value = 0.51). The levels of serum vitamin D in patients of prostate cancer were very low as compared to that in healthy controls (Table 1). The level in prostate cancer patients (11.7±1.06 ng/ml) when compared to that in healthy controls (24.3±1.54 ng/ml) show statistically significant association (p < 0.0001).

Table 1: Serum 25(OH)D mean levels among cases and controls

	Mean±SEM (ng/ml)	p value
Prostate cancer patients (n=120)	11.7±1.06	<0.0001***
Controls (n=120)	24.3±1.54	

Vitamin D deficiency is defined as 25(OH)D < 20 ng/mL, insufficiency as 20–30 ng/mL and sufficiency as ≥30 ng/mL[17]. By evaluating association between 25(OH)D level and prostate cancer risk, it was observed that 66.7% of prostate cancer patients were deficient as compared to 41.7% of healthy controls (Table 2).

Table 2: Serum 25(OH) levels and prostate cancer risk

25(OH)D level (ng/ml)	Cases (n=120)	Controls (n=120)	OR	95% CI
Less than 20	80 (66.7%)	50 (41.7%)	2.80	1.66-4.73
20-30	28 (23.3%)	22 (18.3%)	1.36	0.72-2.53
More than 30	12 (10%)	48 (40%)	0.17	0.08-0.33

Discussion

Vitamin D deficiency is on the verge to become a major public health problem in India. There is widespread prevalence of varying degrees (50- 90%) of Vitamin D deficiency in Indian population.[18] Incidence of prostate cancer is increasing in India. Although this rate is less than that seen in Western countries, changes in lifestyle and increase in life expectancy is presently increasing this rate in India. The etiology of prostate cancer is still unclear. However several potential risk factors have been suggested that may change incidence rates of this cancer which includes ethnicity, diet/nutrition, environment, and genetics.[19,20] This study evaluated the role of vitamin D as a possible etiological agent of prostate cancer.

The value of serum 25(OH)D level in prostate cancer patients was significantly low as compared to healthy age matched controls. Similar observations were made by several studies.[21-23] In a Fannish study, the authors found that low serum 25(OH)D concentrations were associated with high risk prostate cancer.[21] In addition, there are two more reports[22,23] suggesting that circulating 25(OH)D at median or higher than median levels have lower risk for prostate cancer progression. Fang et al[24] also found that prostate cancer patients with lower 25(OH)D had a higher risk of developing metastatic or fatal prostate cancer. In a study by Varsavsky and associates in Spain[25] which included 91 patients of prostate cancer, 78% of the total prostate cancer patients were deficient and insufficient in vitamin D level. In another cross sectional study by Choo et al, sixty four patients (60.4%) were found to be insufficient in vitamin D.[26] Shui and associates conducted a study and found that men with the highest quartile of plasma 25(OH)D levels had less than half the risk of lethal prostate cancer compared with men who were in the lowest quartile of plasma 25(OH)D levels.[27]

This study also showed that 40% of the healthy controls were sufficient in vitamin D level as compared to only 10% of the patients (Table 2). Another interesting finding in the present study was that patients deficient in vitamin D (less than 20 ng/ml) had nearly 3 fold increased prostate cancer risk compared to controls. These results can be explained by the fact that 25(OH)D gets converted to the active form of vitamin

D, calcitriol [1,25(OH)2D], by the action of enzyme 1-α hydroxylase which is expressed by the prostatic cells. Calcitriol has been shown to have an antiproliferative, prodifferentiation and proapoptotic properties and acts as an inhibitor of cell migration.[28] Prostate cancer cells have reduced 1-alpha-hydroxylase activity as compared to normal prostate epithelial cells, and thus have a reduced ability to locally convert 25(OH)D to 1,25(OH)2D.[29] Thus, this study shows that vitamin D could be one of the possible etiological agents in causation of prostate cancer. Further studies consisting large number of sample population from different parts of India are required to emphasize vitamin D deficiency in prostatic diseases.

References

1. Ferlay, J., Shin, H.R., Bray, F., et al., 2010. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10. International Agency for Research on Cancer, Lyon, France.
2. Perin, N.N. Global variation in cancer incidence and mortality. Curr. Sci. 2001;81:465- 474.
3. Shalu Jain, Sunita Saxena, Anup Kumar. Epidemiology of prostate cancer in India. Meta Gene.2014;2:596–605.
4. Haussler MR, Whitfield GK, Haussler CA, et al. The nuclear vitamin D receptor: biological and molecular regulatory properties revealed. J Bone Miner Res.1998;13:325-49.
5. Miller GJ, Stapleton GE, Ferrara JA, et al. The human prostatic carcinoma cell line lncap expresses biologically active, specific receptors for 1 alpha,25-dihydroxyvitamin D3. Cancer Res. 1992;52:515-20.
6. Luong, KV and Nguyen LT. The beneficial role of vitamin D and its analogs in cancer treatment and prevention. Crit Rev Oncol Hematol. 2010;73:192-201.
7. Holt SK, Kwon EM, Peters U, Ostrander EA, Stanford JL. Vitamin D pathway gene variants and prostate cancer risk. Cancer Epidemiol Biomarkers Prev, 2009;18:1929-33.
8. Schwartz GG. Vitamin D and the epidemiology of prostate cancer. Seminars in Dialysis. 2005;18:276–89.
9. Polek TC, Weigel NL. Vitamin D and prostate cancer. Journal of Andrology. 2002;23:9 17.
10. Giovannucci E. The epidemiology of vitamin D and cancer incidence and mortality: A review (United States). Cancer Causes and Control. 2005;16:83–95.
11. Gilbert R, Metcalfe C, Oliver SE, Whiteman DC, Bain C, Ness AR, Donovan J, Hamdy F, Neal DE, Lane JA, Martin RM. Life course sun exposure and risk of prostate cancer: population-based nested case-control study and meta-analysis. International Journal of Cancer. 2009;125:1414–23.
12. World Cancer Research Fund / American Institute for Cancer R. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspectiveed. AICR; Washington DC:2007.
13. Gilbert R, Martin RM, Beynon R, Harris R, Savovic J, Zuccolo L, Bekkering GE, Fraser WD, Sterne JAC, Metcalfe C. Associations of circulating and dietary vitamin D with prostate cancer risk: a systematic review and dose-response meta-analysis. Cancer Causes and Control. 2011:319–40.
14. Willis MS, Wians FH. The role of nutrition in preventing prostate cancer: a review of the proposed mechanism of action of various dietary substances. Clinica Chimica Acta. 2003;330:57–83.
15. Lokeshwar BL, Schwartz GG, Selzer MG, Burnstein KL, Zhuang SH, Block NL, Binderup L. Inhibition of Prostate Cancer Metastasis in Vivo: A Comparison of 1,25-Dihydroxyvitamin D (Calcitriol) and EB1089. Cancer Epidemiology Biomarkers Prevention. 1999;8:241–48.
16. Ahonen MH, Tenkanen L, Teppo L, Hakama M, Tuohimaa P. Prostate cancer risk and prediagnostic serum 25-hydroxyvitamin D levels (Finland). Cancer Causes and Control. 2000;11:847–52.
17. Ritu G., Ajay Gupta. Vitamin D Deficiency in India: Prevalence, Causalities and Interventions. Nutrients 2014; 6: 729-775.
18. Harinarayan CV and Joshi SR. Vitamin D status in India-Its implications and remedial measures, J Assoc Physicians India. 2009; 57:40-48.
19. Lichtenstein P, Holm NV, Verkasalo PK, et al. Environmental and heritable factors in the causation of cancer--analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med. 2000;343:78-85.
20. Tzonou A, Signorello LB, Lagiou P, et al. Diet and cancer of the prostate: a case-control study in Greece. Int J Cancer. 1999;80:704-8.
21. M. H. Ahonen, L. Tenkanen, L. Teppo, M. Hakama, and P. Tuohimaa. Prostate cancer risk and prediagnostic serum 25-hydroxyvitamin D levels (Finland). Cancer Causes and Control. 2000;11:847–852.
22. H. Li, M. J. Stampfer, J. B. Hollis et al. A prospective study of plasma vitamin D metabolites, vitamin D receptor polymorphisms, and prostate cancer. PLoS Medicine 2007, vol. 4, no. 3, article e103.
23. S. Tretli, E. Hernes, J. P. Berg, U. E. Hestvik, and T. E. Robsahm. Association between serum 25(OH)D and death from prostate cancer. British Journal of Cancer 2009;100:450–454.
24. Fang F, Kasperzyk JL, Shui I, Hendrickson W, Hollis BW, Fall K, Ma J, Gaziano JM, Stampfer MJ, Mucci LA, Giovannucci E. Prediagnostic Plasma Vitamin D Metabolites and Mortality among Patients with Prostate Cancer. PLoS ONE [Electronic Resource]. 2011; 6:e18625.
25. Varsavsky M, Reyes-García R, Cortés-Berdonces M, García-Martin A, Rozas-Moreno P, Muñoz-Torres M. Serum 25 OH vitamin D concentrations and calcium intake are low in patients with prostate cancer. Endocrinol Nutr. 2011 Nov;58(9):487-91.
26. Choo CS, Mamedov A, Chung M, Choo R, Kiss A, Danjoux C. Vitamin D insufficiency is common in patients with nonmetastatic prostate cancer. Nutr Res.2011 Jan;31(1):21-26.
27. Irene M. Shui, Lorelei A. Mucci, Peter Kraft, et al. Vitamin D–Related Genetic Variation, Plasma Vitamin D, and Risk of Lethal Prostate Cancer: A Prospective Nested Case–Control Study. J Natl Cancer Inst 2012;104:690–699.
28. Donkena KV, Young C. Vitamin D, sunlight and prostate cancer risk. Adv Prev Med. 2011;281863:13.
29. Chen TC, Wang L, Whitlatch LW, Flanagan JN, Holick MF. Prostatic 25-hydroxyvitamin
30. D-1alpha-hydroxylase and its implication in prostate cancer. Journal of Cellular Biochemistry. 2003;88:315–22.