A study of Vitamin D and parathyroid hormone levels in patients with prostatic cancer

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ABSTRACT

Background: Vitamin D, a key nutrient in the body, has been linked to a decrease in prostate cancer (PCa) morbidity and mortality rates. The study concluded that any compensation mechanism may no longer be adequate for patients with PCa, and further research is needed to understand the mechanisms underlying the relationship between serum Vitamin D and parathyroid hormone (PTH) homeostasis. The findings will help determine cancer prevalence and trends in India and support public health initiatives to control cancer. **Aims and Objectives:** The aim is to assess the mean values of Vitamin D and PTH in patients with PCa and also to compare these levels with that of healthy controls (non-PCa). **Materials and Methods:** One hundred participants in the outpatient department of the Department of Biochemistry were assigned as control subjects, and another 100 participants were participants with PCa. 5 mL of fasting venous blood were drawn into red top vials using a disposable syringe and needle in an aseptic manner. PTH and serum Vitamin D were estimated. **Results:** When comparing PCa patients to healthy controls, the observed Vitamin D level was significantly lower in the former group. Furthermore, a notable distinction in Vitamin D levels was noted between the two groups. Furthermore, we found that PCa patients had higher PTH values than healthy controls. When we compared the PTH values of the two groups, we found a substantial difference. **Conclusion:** The authors conclude from the study that with alterations in the study parameters in patients with PCa, any compensation mechanism may become insufficient.

Key words: Prostate cancer; Vitamin D; Parathyroid hormone; Immunomodulation; Prostate-specific antigen

INTRODUCTION

UV light causes 7-dehydrocholesterol or ergosterol to convert into Vitamin D.[1] Pro-hormone Vitamin D undergoes two hydroxylation reactions at the 1st and 25th positions before becoming the hormone calcitriol.[2] The primary active form, calcitriol, aids in the remodeling of osteoclasts and osteoblasts as well as the absorption of calcium at the intestinal villi, and kidney distal tubular cells.[2]

Prostatic carcinoma has seen a steady increase in morbidity and death rates over the past three decades. The highest rates have been found in Western Europe, Australia, and North America, with variations of up to 30 times between the highest and lowest rates.[3] The idea that sufficient Vitamin D supplementation may lower the incidence of prostate cancer (PCa) and enhance metabolic control in the cancer state is, in fact, supported by a large number of studies.[4-10] The potential role of Vitamin D in PCa has garnered attention due to its potential effects on cancer conditions, and a deeper comprehension of its physiological role is on the horizon.[5] Further research is necessary to determine the precise mechanisms through which Vitamin D and its supplements deliver their health benefits, as they are currently unclear.

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The four parathyroid glands embedded in the thyroid tissue secrete parathyroid hormone (PTH).[2] The PTH primarily affects the kidney, the intestine, and the bone. PTH results in demineralization or decalcification of the bone.[2,11] PTH increases the excretion of phosphates and decreases the renal excretion of calcium in the kidney.[11] PTH causes the kidney to produce calcitriol by stimulating the 1-hydroxylation of 25-hydroxycalciferol.[2] As a result, intestinal absorption is increased indirectly.[12] Numerous studies revealed varying PTH outcomes for participants with PCa.[13-16]

There are no published data regarding PCa patients who reside in the Patna, Bihar region, despite a few studies finding altered levels of Vitamin D and PTH in PCa subjects. Consequently, it is important to evaluate the average Vitamin D and parathyroid hormone levels in PCa patients and to contrast them with those of healthy controls (PCa-free).

Aims and objectives

Aim of the study is to evaluate the Vitamin D and Parathyroid levels in patients with prostatic cancer.

The objective of the study was to use Vitamin D and Parathyroid levels in patients with prostatic cancer and to find out its correlations.

MATERIALS AND METHODS

This case–control study, which complied with the Helsinki Declaration (World Medical Association, 1995), was conducted in the Department of Biochemistry at the Indira Gandhi Institute of Medical Sciences in Patna on 100 patients of prostatic cancer who were attending the Department of Urology and the Regional Cancer Centre (RCC) after obtaining ethical permission from the Institutional Ethical Committee through letter no. 46/Acad. The prostate-specific antigen (PSA), Vitamin D, PTH, calcium, and I. phosphate investigations the research were conducted from January 2019 to August 2020. The goal of the study was to measure PSA levels in patients with PCa and determine how these levels related to Vitamin D, PTH, calcium, and I. phosphate in cases of PCa that had been diagnosed. One hundred healthy individuals were also taken as control. Both cases and control age group were more than 40 years old.

Male patients diagnosed with PCa for the 1st time and older than 40 years were the study's inclusion criteria. The exclusion criteria included undergoing chemotherapy, endocrinopathies, chronic renal disease, chronic infections,

disorders causing abnormal calcium and Vitamin D, and those taking serious medication, as well as being treated with calcium and Vitamin D.

Fasting venous blood (5 mL) were drawn into red top vials with a disposable syringe and needle, under all aseptic conditions. Serum Vitamin D and PTH were estimated.

### Standard procedure of sample collection

After an overnight fasting (at least 8–12 h) blood samples were collected from all the participants in the morning under full aseptic precautions.

Patients were fully explained about the procedure and taken in confidence for drawing their blood samples. Proper aseptic and antiseptic precautions were taken while collecting blood samples to ensure the safety of self and to the participants.

The serum PSA, Vitamin D, PTH, calcium, and I. phosphate levels were collected from patients who presented to the Department of Urology and RCC.

Statistical analysis

The serum levels of PCa patients and control subjects were measured for each of the biochemical parameters mentioned. Every value acquired was presented as mean±standard deviation. An unpaired "t" test was used to analyze the data statistically between the two groups. When analyzing data between more than two groups, one-way analysis of variance (ANOVA), was utilized. The correlation between the two parameters was tested using Pearson correlation. $P < 0.05$ was considered significant.
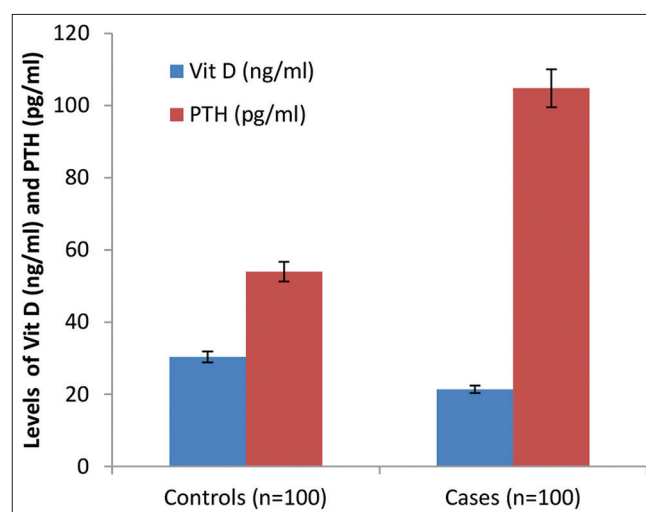
Figure 1: Mean values of Vitamin D and parathyroid hormone in both groups

Table 1: Biochemical parameters of cases and controls				
Biochemical parameters	Case Mean±SD	Control Mean±SD	"t" value	P-value
I. phosphate	4.44±0.400	3.49±0.667	12.014	0.000*
PTH	104.88±14.43	54.08±18.98	23.032	0.000*
Vitamin D	21.38±10.20	30.41±13.08	−5.836	0.000*
PSA	57.83±61.19	0.950±0.858	9.386	0.001*
Calcium	9.14±0.578	9.33±0.575	−2.455	0.016*

P<0.05 is significant. PTH: Parathyroid Hormone, PSA: Prostate-specific antigen

RESULTS

Serum Vitamin D and PTH levels are shown in Figure 1 and Table 1. Vitamin D level was significantly lower (21.4±10.2) in PCa subjects when compared with healthy controls (30.4±13) significant difference (t=5.437, d=198; P<0.001) was observed in Vitamin D levels when both groups mean±SD was compared. On the contrary to the Vitamin D finding, we observed higher PTH values (104.8±14.4) in PCa subjects than healthy controls (54±18.4). Comparison between the two groups in terms of PTH value, we noticed a significant difference (t=21.274, d=198; P<0.001).

In Table 1 and Figures 2 and 3, we have shown the association of Vitamin D and PTH variables in PCa subjects and also in healthy controls, respectively. In the healthy control group, the subjects' levels of Vitamin D showed a moderate positive correlation (R=0.5803). While in the PCa group subjects, we observed a weak negative association (R=−129) in terms of PTH hormone levels.

DISCUSSION

Due to a lack of data, the study's objectives were to evaluate the mean values of Vitamin D and PTH in patients with PCa as well as compare these levels with those of healthy controls (those without PCa) in this specific region.

Research has shown conflicting findings about Vitamin D levels in cancer patients.[4-10] When compared to healthy controls, the Vitamin D level in PCa patients was found to be significantly lower in our study. Furthermore, a notable distinction in Vitamin D levels was noted between the two groups. Moreover, a moderately positive correlation was observed between the levels of Vitamin D in the group of healthy controls. According to a study with results similar to ours, older men may not spend as much time in the sun and are less efficient at producing Vitamin D through the skin than younger men.[6] Similar to our findings, another study has shown that skin with a darker complexion affects the body's Vitamin D levels.[7] Research has demonstrated that PCa mortality varies inversely with ultraviolet light
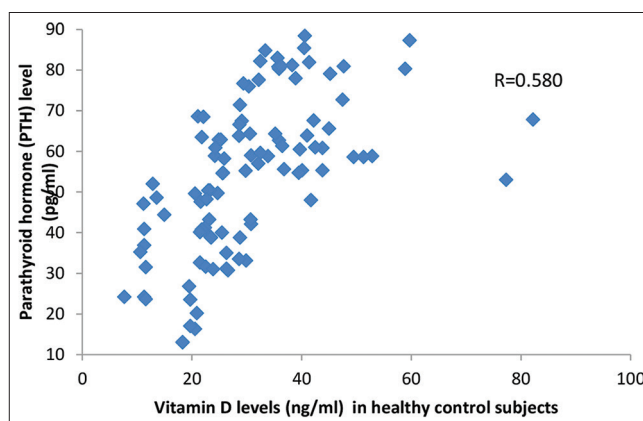
Figure 2: Diagram showing the correlation between Vitamin D and parathyroid hormone in healthy controls
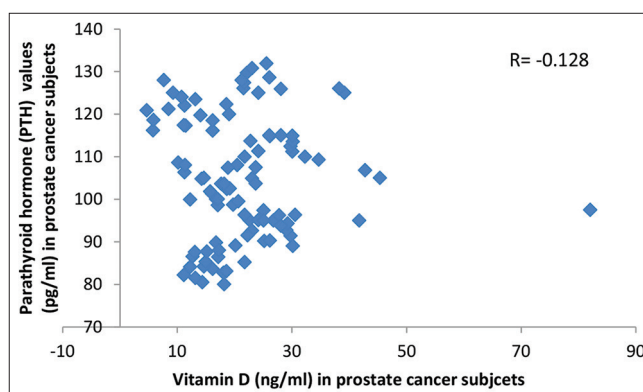
Figure 3: Diagram showing the correlation between Vitamin D and parathyroid hormone in prostate cancer subjects

exposure, which lends support to the current study's findings.[8] Moreover, research[9,10] revealed that individuals with low initial serum Vitamin D levels had a higher chance of developing palpable prostate tumors and were also at a higher risk of developing PCa at an earlier stage. Their tumors also tended to be more aggressive.[10]

In this investigation, we found that subjects with PCa had higher PTH values than subjects in good health. When we compared the PTH values of the two groups, we found a substantial difference. Our findings were supported by studies that revealed changed PTH levels.[13-16] Furthermore, a study has reported no correlation between PTH levels and those of individuals with PCa.[17] Regarding PTH hormone

levels, we have found a slight negative correlation in the subjects in the PCa group.

According to the results of several studies, 1,25(OH)2D causes cell cycle arrest and apoptosis in prostate epithelial cells and PCa cells, which inhibits their growth.[18] Through its effects on the Vitamin D receptor (VDR), Vitamin D prevents the growth of tumor cells and triggers apoptosis.[19] 1,25(OH)2D binds to the VDR, a transcription factor that typically binds to the promoter region of genes that respond to Vitamin D. These Vitamin D-responsive genes are then either activated or repressed by activated VDR interacting with coactivators or corepressors. Prostate epithelium expresses the VDR.[20] By controlling the expression of immune-related genes, such as cytokines, in a variety of intricate ways through VDR activities, Vitamin D modulates the immune response. Nuclear transcription factor VDR modulates the inflammatory response by transcription by interacting with numerous signaling pathways.[21] Studies have also revealed that Vitamin D treatment inhibits proinflammatory molecules in PCa by suppressing the expression of TNFα, IL6, and IL8 in prostate epithelial cells, but not PTGS2 or TNFα in stromal cells.[22] It also suppresses NF-κB signaling, reducing the synthesis of IL-8, a key immune system gene, and reducing the transcription of genes related to inflammation.[22] The implication of these studies can be beneficial in the future as Vitamin D treatment can also be used in the prevention of benign prostate hypertrophy and prostatic cancer and shows promising results as per the previous studies.

Limitations of the study

The study's limitations include the need for additional samples to provide precise findings and the need to clarify the processes by which vitamin D controls immune gene expression in both aggressive and indolent PCa.

CONCLUSION

Based on changes in the study parameters for patients with PCa, the authors draw the conclusion that any compensation mechanism may no longer be adequate. Thus, to fully understand the mechanisms underlying the relationship between serum Vitamin D and PTH homeostasis, extensive additional research is required on a multicountry, multicentric population that should include all ethnic populations. The study's findings will be useful in determining the prevalence and trends of cancer in India. This will support stakeholders at the local and national levels in implementing public health initiatives to control cancer.

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