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# VITAMIN D LEVELS IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

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**ABSTRACT**

**Background:** Benign prostatic hyperplasia (BPH) is most commonly encountered non-neoplastic prostatic disease. It is found in approximately 70% of men in their 60s and nearly all men in their 70s. Recently, it was found that low vitamin D level is linked to increase prostate volume and is an independent risk factor for BPH. Prostatic cells possess specific high affinity receptors for 1,25(OH)2D3.

**Aims and Objectives:** To estimate serum Vitamin D [25(OH)D3] levels in patients of BPH and in controls.

**Materials and Methods:** 30 patients (mean age=64.35+9.14 years) of BPH were included along with 30 age-matched controls (mean age=64.35+9.14 years). 5ml of venous blood was collected from subjects in plain vial. It was subjected to centrifugation and serum was separated for analysis of 25(OH)D3 by direct ELISA method.

**Results:** Data was analysed using SPSS (version 12). Independent sample't' test was used for between group comparisons. The mean level of serum vitamin D in cases was 26.8 and it was found to be less as compared to controls (34.1). The level of vitamin D in cases was found to be statistically significant (p value <0.001).

**Conclusion:** Present study observed lower serum Vitamin D levels in patients of BPH. Recently, Vitamin D receptor (VDR) agonists have been shown to be useful in treating BPH patients. Also VDR expression in normal prostate declines with age and prostate hyperplasia is also strongly associated with age. Thus it can be postulated that Vitamin D deficiency could be a risk factor for development of BPH.

**KEYWORDS :** Vitamin D, Benign prostatic Hyperplasia

## Introduction

Benign prostate hyperplasia (BPH), is a non-neoplastic prostatic disease and one of the most common disorder in aging male[1] BPH is a non life-threatening disorder but quality of patients's life is decreased by the symptoms it causes.[2] Prevalence of BPH range from 40-50% at 50 years age, and 80% at the age of 70 years[3,4] and about 90% by the ninth decade.[5] The incidence of BPH is increasing worldwide and is a growing public health concern in Asian countries.[6] The exact etiology of BPH is still difficult to understand.[2] Histologically BPH is defined as hyperproliferation of stromal and epithelial cells of the prostate, caused by complex cellular alterations including changes in proliferation, differentiation, apoptosis and senescence.[7] Enlargement of prostate gland due to overgrowth of prostatic glandular and stromal tissue, obstructs the flow of urine through the urethra.[2] Prostate cell proliferation and apoptosis are regulated by both androgens and intraprostatic growth factors, and increased signaling are supposed to underlie benign prostate hyperplasia,[8] Various sources trigger the initial event, including direct infection, chemical and physical trauma, dietary factors, hormones, exposure to environmental pollutants, genetic predisposition or combination of two or more of these factors cause immune tolerance and the development of an inflammatory reaction to the prostate[9,10] Abdominal obesity is also an established modifiable risk factor.[11] BPH and Prostate Cancer (PC) are chronic diseases that develop from small lesion and require a longer period to become clinical manifestation.[12] There is an imbalance between cell growth and apoptosis in prostate gland which is complex and influenced by many factors like environment around prostate and factors that stimulate proliferation and minimize cell apoptosis.[13,14]

Vitamin D, especially its most active metabolite 1,25-dihydroxyvitamin D3 plays an important role not only in calcium homeostasis and bone remodeling, but also in the control of hormone secretion, immune dysfunction, cell proliferation, differentiation[15,16] and antitumorigenic properties.[17] 7-dehydrocholesterol is the precursor for synthesis of vitamin D and synthesis is catalysed by ultraviolet light present in sunlight, hydroxylation at liver followed by the kidney, resulting in the synthesis of active vitamin D known as 1,25-dihydroxyvitamin D3, or calcitriol.[18] Biologic actions of Vitamin D and its analogues is mediated through the specific vitamin D receptor (VDR)[19,20] which belongs to steroid hormone family of nuclear receptors. Binding of hormone with VDR regulates the transcriptional activity through the vitamin-D response element situated in the promoter region of target genes.[21] The fact that human prostate cell possess VDR was revealed in 1992.[22] Vitamin D receptors also expressed normal as well as malignant prostate cell and also regulated through this receptor.[23,24] A positive correlation exists between VDR gene variants and prostate volume.[25] Investigations of VDR genes on several prostatic diseases have shown an important association with the disease risk. VDR gene Activation may influence androgen receptor (AR) activation leading to the development of BPH[26] and studies reported significant association between risk of BPH with VDR gene polymorphism.[27]

BPH has an inheritable genetic component [28,29] Prostate growth and its stromal and epithelial cells differentiation is actively influenced by the vitamin D.[30] Several studies have suggested that there is a potential role of vitamin D in the development of BPH. Vitamin D3 and few of its analogues have been described as potent regulators and irreversible inhibitors of cell growth and differentiation of prostatic cells, neither cell death nor morphological changes accompanied this antiproliferative effect.[31,32] The aim of the present study is to find Vitamin D3 levels and its analogues in BPH.

## Materials and methods

The present study was conducted in Department of Biochemistry and Urology at Kakatiya Medical College and MGM Hospital, Warangal. 30 patients (mean age=64.35+9.14 years) of BHP were taken from Urology Department and exclusion criteria presented in Table1. and control group (mean age=64.35+9.14 years) containing 30 normal healthy men matched with respect to age. Informed consent was obtained from all study participants and the study protocol was approved by the institutional ethics committee. Patients were included for study based on BPH confirmed by Ultrasonography (USG) and histopathology admitted in Urology department. Blood samples were obtained from all study participants, 5ml of venous blood samples were obtained from both the groups in plain vial. It was subjected to centrifugation and serum was separated. It was analyzed for 25(OH)D3 level by direct ELISA method in both the groups. Normal healthy controls were selected based on who had no history of any voiding symptoms, prostate surgery, family cancer, calcium and/or vitamin D supplements, and suffering from chronic illness. Selection criteria for controls is presented in Table 2.

**Table 1. The exclusion criteria for this study.**

| Exclusion Criteria/Reasons for exclusion |
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| Patients suffering from parathyroid and chronic kidney disease. |
| Patients taking calcium and/or vitamin D supplements. |
| Patients suffering from chronic illness. |

**Table 2. The selection criteria for control group.**

| Exclusion Criteria/Reasons for exclusion |
|---|
| No h/o any voiding symptoms |
| No h/o prostate surgery |
| No h/o family cancer |
| Not any calcium and/or vitamin D supplements |
| Not suffering from chronic illness |

## Results

Data was analysed using SPSS (version 12). Independent sample't' test was used to test between group differences. We evaluated associations between Vitamin D levels in patients of BPH. We found that serum Vitamin D levels are significantly lower in patients of BPH compared with controls. Mean level of serum vitamin D in cases was 26.8 and it was found to be less as compared to controls (34.1). The level of vitamin D in cases was found to be statistically significant (p value <0.001).

## Discussion

In aging male, BPH is relatively common and affects 80% of men at age 80.[33] Schwartz and Hulka proposed that vitamin D and its effect on prostate cancer, and also observed that the epidemiology of prostate cancer, results in adult with vitamin D insufficiency.[34,35] Increased prostate cancer risk is associated with Vitamin D deficiency, it might be due to an altered metabolism or Vitamin D resistance.[36] Vitamin D receptor (VDR) ligands, might be useful in BPH patients for its effect not only on the prostate, but also that on the bladder.[37] Vitamin D3 and its agonist showed a dose dependent inhibition of prostate stromal cells.[38] Studies revealed that vitamin D and vitamin D analogues have antiproliferative and differentiation effects on human prostatic cancer cells in vitro.[22,39] And, preclinical trials have shown that vitamin D and also calcitriol have impact on BPH and prostate cell proliferation, Another study showed that Vitamin D not only decreases cell proliferation alone but also when induced by growth promoting molecules.[40]

Vitamin D analogue has been the recent topic of research interest.[41] In prostate cancers hypercalcemia is the detract factor of vitamin D-based therapies.[34] Bauer and colleagues conducted in vitro studies to determine the impact of the less hypercalcemic vitamin D analog and found that more potent differentiating agent.[41] High dose dietary supplement of vitamin D reduces risk of BPH[40] and decrease prostrate volume[42] in vitro growth of stromal cells is reduced by calcitriol, which derived from the bladder neck of patients, who underwent suprapubic prostatectomy for BPH.

Donna M et al. have reported prostatic epithelial and stromal cells are targets of vitamin D which is also an important inhibitor of prostatic growth.[31] Other studies reported that even at untraditional high doses is potential for BPH treatment with Vitamin D.[43] Administration of active form of vitamin D, may delays the recurrence of prostate cancer after primary therapy.[35] In a beagle model study benign prostatic hyperplasia exhibited spontaneous efficacy by a novel VDR agonist.[11] Geovannin et al in his study concluded that potential for the use of vitamin D in treatment of BPH.[40] These documents suggested that vitamin D had a protective effect on prostate cancer. Also proved by their results indicated that the *Bsm*I polymorphism in the *VDR* gene plays a significant role in protection against prostate cancer and BPH.[27]

Clara Crescioli have reported KGF-effects on BPH cells are opposed by vitamin D3 and its analogues, cell proliferation by KGF-induced is reduced and partially programmed cell death in BPH cells is restored.[8] These observations collectively state that vitamin D may be an important determinant of occurrence and progression of prostate cancer.[27] Therefore, it is hypothesized that vitamin D deficiency is a risk factor for prostate cancer.[44] Also, decreasing availability of UV radiation exposure may be associated with increasing Prostate cancer mortality.

## Conclusion

Present study observed lower serum Vitamin D level in patients of BPH. Recently, Vitamin D receptor (VDR) agonist has been shown to be useful in treating BPH patients.[4] Also, VDR expression in normal prostate declines with age and prostate hyperplasia is also strongly associated with age.[5] Thus it can be postulated that Vitamin D deficiency could be a risk factor for the development of BPH.

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