

## A Comparative Study of Serum Phosphorus and Serum Calcium in Disorders of Prostate at SMS Hospital, Jaipur

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### Abstract

**Background:** Benign prostatic hyperplasia (BPH) and prostate cancer are the most common disorders of prostate gland. Prostate cancer is the second most frequent malignancy (after lung cancer) in men worldwide. Calcium and phosphorus ions are essential for cell growth, proliferation and differentiation as their signaling is essential for regulating these physiological functions. The present study was thus undertaken with the main aim of comparing serum phosphorus and serum calcium level in patients suffering from disorders of prostate (BPH and Prostate cancer) with age matched healthy controls.

**Materials & Methods:** After taking necessary permissions, a cross sectional study was conducted at Department of Biochemistry and Department of Urology, SMS Hospital, Jaipur. This study includes 35 patients suffering from BPH and Prostatic Cancer aged 40-75 years compared with 35 matched controls. Serum levels of phosphorus and calcium was measured by Spectrophotometry in fully Automated chemistry analyzer AU680 (BECKMEN COULTER).

**Results:** Results were analyzed statistically by ANOVA test and Student's t-test. Mean serum calcium level in cases was low ( $8.1 \pm 0.64$  mg/dl) compared to controls ( $10.0 \pm 0.72$  mg/dl). Comparison between prostatic disorders, serum calcium was high in BPH ( $8.6 \pm 0.44$  mg/dl) compared to Prostate Cancer ( $7.7 \pm 0.42$  mg/dl). Mean serum phosphorus level in cases was low ( $2.7 \pm 0.43$  mg/dl) compared to controls ( $3.7 \pm 0.45$  mg/dl). Comparison between prostatic disorders, serum phosphorus was high in BPH ( $3.0 \pm 0.30$  mg/dl) compared to prostate Cancer ( $2.5 \pm 0.39$  mg/dl). The difference observed in results above was statistically highly significant ( $p < 0.001$ ).

**Conclusion:** The findings of this study conclude that there is biologic plausibility for a role of phosphorus and calcium in prostate carcinogenesis. Decreased serum calcium and phosphorus levels correlate with the severity of prostate cancer. Hence, it can be concluded that estimation of serum phosphorus and calcium levels can be used for early screening and diagnosis of disorders of prostate.

**Keywords:** Benign prostatic hyperplasia (BPH), Prostatic Cancer, Calcium, Phosphorus

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## Introduction

Benign prostatic hyperplasia (BPH) and prostate cancer are the most common disorders of prostate gland. The incidence rates of this cancer are constantly and rapidly increasing and the cancer projection data shows that the number of cases will double by the end of 2020. [1]

In India BPH is a common geriatric problem with an incidence of 92.97% (n=185) & 93.3% (n=200). [2] Current estimates are that the number of individuals 80 years and older in the US will rise from 9.3 million in 2000 to 19.5 million in 2030, an increase of over 100%. [3] In observance of Prostate Cancer Awareness month i.e. September, Indian Council of Medical Research (ICMR) has released data on the incidence rate of prostate cancer in India. It states that the incidence rate of prostate cancer is 9-10/100000 population, higher compared to countries like Asia and Africa, but lower compared to the US and Europe. [3]

The exact etiology of prostate cancer is still not known, although a number of factors can increase the risk of developing the condition includes increasing age, ethnic group, family history, obesity and diet. Many recent studies have reported that the chronic inflammatory process plays an important role in the development of Prostate Carcinoma. [4] The disrupted oxidant/antioxidant balance in favor of oxidants in this process may contribute to this pathological process. [5]

The second most important disorder of the prostate includes benign prostatic hyperplasia (BPH) is characterized by the non-malignant overgrowth of prostatic tissue surrounding the urethra, ultimately constricting the urethral opening giving rise to symptoms associated to lower urinary tracts obstruction. It is caused by accumulation of dihydrotestosterone with aging that leads to enlargement of prostate. [6] BPH is not linked to cancer and does not increase your risk of getting prostate

cancer—yet the symptoms for BPH and prostate cancer can be similar. Family history, diabetes mellitus, heart disease and obesity also consider as risk factor for BPH. [7]

Screening for carcinoma prostate includes serum PSA level and digital rectal examination (DRE). Biopsy is required in susceptible cases to diagnose or confirm prostate cancer. [8] The major limitation for using PSA, as a screening prostate cancer biomarker, is that it increase in many other benign condition like BPH and prostatitis. [9] It is thought that many factors form the basis for the correlation between inflammation and cancer. For example, inflammatory compounds such as free oxygen radicals and cytokines released in this environment cause DNA damage and may affect the process of cancer development. [10]

The effect of serum level of calcium and phosphorus in carcinoma prostate is poorly defined. Calcium and phosphorus ions are essential for cell growth, proliferation and differentiation as their signaling is essential for regulating these physiological functions. There is biologic plausibility for a role of serum phosphorus and calcium in prostate carcinogenesis. [11]

In the present study we have tried to categorize the patients in to prostatic carcinoma or benign prostatic hyperplasia based on their serum prostate specific antigen, calcium and phosphorus level and their comparison with healthy controls.

### Materials and Methods:

After taking Necessary permission from the institute ethical committee and Department of Urology, the study was conducted at Central Lab, Department of Biochemistry and Urology OPD, SMS Medical College and hospital, Jaipur. This study was a Hospital based comparative Cross sectional study and sampling for the

study was done from the period of July 2020 to November 2020.

Diagnosed cases of benign prostatic hyperplasia and prostate cancer in the age group of 40–75 years, with PSA levels more than normal value (i.e. >4 ng/mL) and who had given written informed consent were included in the study. Age matched healthy individuals (relatives/attendants of patient and hospital staff) who were willing to participate in the study giving written consent were taken as controls. An informed written consent was obtained from the patients and controls. Patients with the following conditions: Advanced cases of Prostate Cancer, prostatitis, or history of previous biopsy or urological procedure, Lympho - myeloproliferative and hemolytic diseases, Gout, Chronic kidney disease. Chronic liver diseases, history of drugs affecting calcium level were excluded from the study.

Selection of subject was based on inclusion and exclusion criteria, age and sex matched controls and cases were included in the present study after obtaining informed consent. A proforma

was used to record relevant information and patient's data. 4 mL of venous blood was collected in plain vacutainer and analysed. Serum PSA level was analysed by chemiluminescence in Advia centaur analyser (immunoassay lab) while Serum levels of phosphorus and calcium was measured by Spectrophotometer in fully Automated chemistry analyzer AU680 (BECKMEN COULTER).

All the relevant Demographic, clinical and laboratory data was entered into Microsoft office excel sheet, and thereafter, the data was collected on primer software for Statistical analysis. The association between continuous and categorical variables was assessed by comparisons of means using Anova Test and Student T-test. Statistical significance was set by using p value less than 0.05.

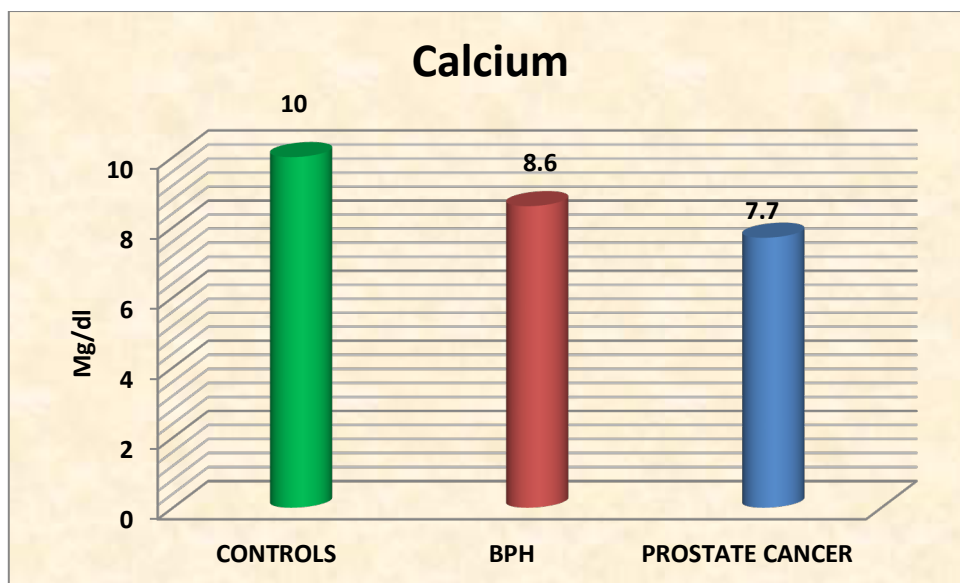
## Results

The characteristics of the studied population, including age, the mean levels of PSA, serum phosphorus and serum calcium on comparison between controls, BPH and Prostatic cancer are shown in Table 1.

**Table 1: Statistical Indices of the study (\*P-value as obtained on applying ANOVA test)**

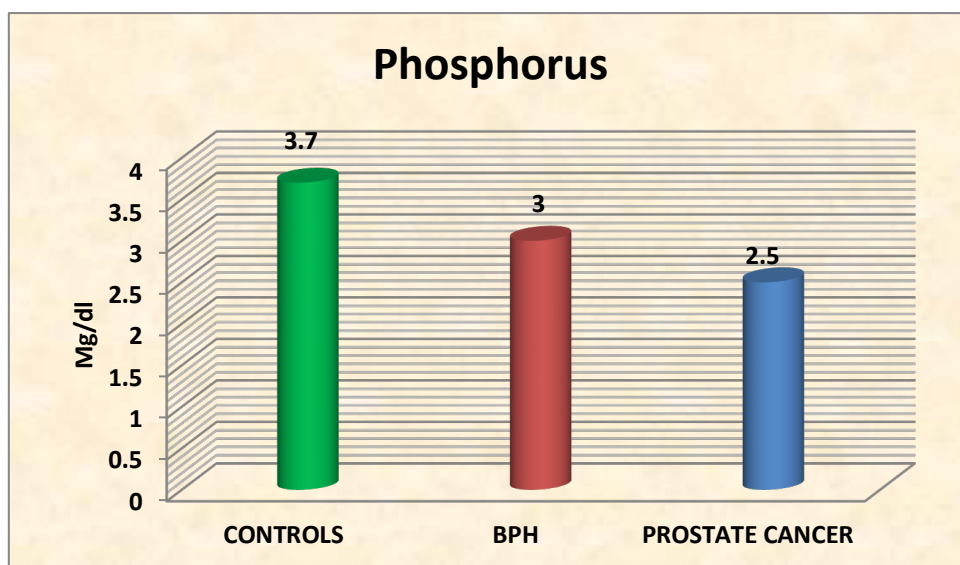
Test/ Parameters	Controls (n=35)	BPH (n=35)	Prostate cancer (n= 35)	P value
Age (years)	63.1 ± 7.75	62.1 ± 7.67	63.5 ± 7.75	0.723 (NS)
PSA (ng/ml)	2.2 ± 1.09	10.4 ± 3.18	65.7 ± 12.22	<0.01 (S)
Calcium (mg/dl)	10.0 ± 0.72	8.6 ± 0.44	7.7 ± 0.42	<0.01 (S)
Phosphorus (mg/dl)	3.7 ± 0.45	3.0 ± 0.30	2.5 ± 0.39	<0.01 (S)
FBS (mg/dl)	93.3 ± 14.08	91.2 ± 12.62	89.7 ± 15.92	0.570 (NS)
Urea (mg/dl)	26.0 ± 7.52	26.8 ± 7.45	26.6 ± 8.96	0.905 (NS)
Creatinine (mg/dl)	0.78 ± 0.11	0.76 ± 0.11	0.80 ± 0.11	0.344 (NS)

**Serum Calcium:** This table shows mean calcium level in controls is (10.0 ± 0.72 mg/dl), in BPH is (8.6 ± 0.44 mg/dl) and in Prostate cancer is (7.7 ± 0.42 mg/dl). P value is statistically significant < 0.01 as shown in Table 1 and Figure 1.



**Figure 1: Comparison of Serum Calcium between Controls, BPH & Prostatic cancer cases**

**Serum Phosphorus:** This table also shows mean phosphorus level in controls is (3.7 ± 0.45mg/dl), in BPH is (3.0 ± 0.30 mg/dl) and in Prostate cancer is (2.5 ± 0.39 mg/dl). P value is statistically significant < 0.01 as shown in Table 1 and Figure 2.



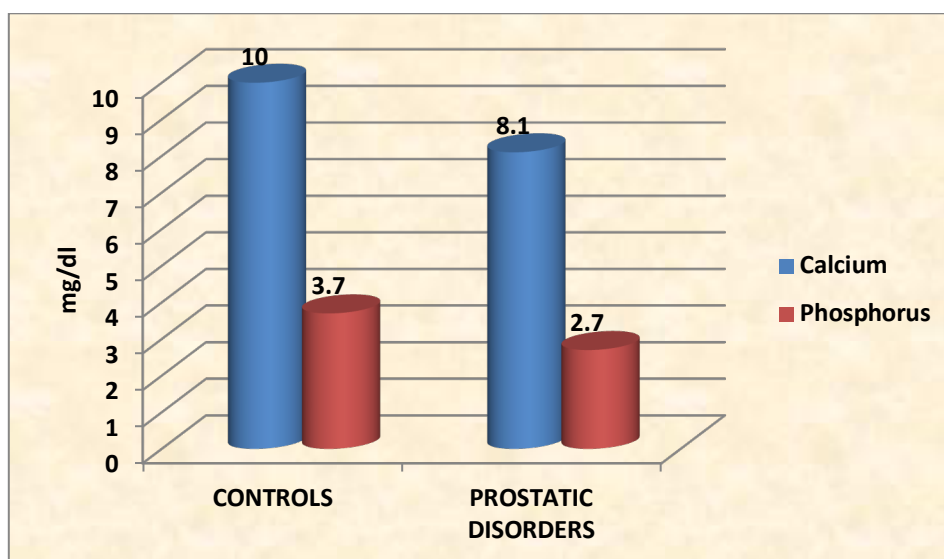
**Figure 2: Comparison of S. Phosphorus between Controls, BPH & Prostatic cancer cases**

**Comparison of Mean Serum Calcium and Phosphorus levels between controls and Prostatic disorders**

**Table 2: Data analysis using Student T-test**

Test/ Parameters	Controls	Prostatic Disorders	P value
N	35	70	
Calcium (mg/dl)	10.0 ± 0.72	8.1 ± 0.64	<0.01 (S)
Phosphorus	3.7 ± 0.45	2.7 ± 0.43	<0.01 (S)

Table 2 and Figure 3 shows mean Calcium level in controls is ( $10.0 \pm 0.72$  mg/dl) and in prostate disorders is ( $8.1 \pm 0.64$  mg/dl). P value is statistically significant  $< 0.01$ . This table also shows mean phosphorus level in controls is ( $3.7 \pm 0.45$  mg/dl) and in prostate disorders was ( $2.7 \pm 0.43$ mg/dl). P value is statistically significant  $< 0.01$ .



**Figure 3: Comparison of Mean Serum Calcium and Phosphorus levels between controls and Prostatic disorders**

## Discussion

Prostate cancer and BPH are the most frequent pathologies of the prostate gland, whose management strategies are totally different. Prostate Cancer is the most frequently diagnosed malignancy in men and the second leading cause of cancer deaths especially in Western countries. [12] On the other hand, BPH is the second most frequent pathology of prostate gland that clinically/ symptomatically mimic prostate cancer. There is an urgent need for appropriate diagnostic and prognostic markers to detect Prostate Cancer and to differentiate it from other pathologies of prostate gland. The present study was undertaken to assess the levels of PSA, calcium, and phosphorus in different pathologies of prostate gland, in an attempt to use a combination of markers to differentiate the above conditions to avoid the use of unnecessary biopsies.

In our study it is shown that mean age group of BPH ( $62.1 \pm 7.67$  years) was slightly less than the controls group ( $63.1 \pm 7.75$  years) and Prostate Cancer ( $63.5 \pm$

$7.75$  years) However, p value was non-significant ( $p=0.723$ ) as the cases and controls were matched for age. Our observations revealed that Mean serum PSA level in control was ( $2.2 \pm 1.09$  ng/ml), in BPH was ( $10.4 \pm 3.18$  ng/ml) and in prostate carcinoma was ( $65.7 \pm 12.22$  ng/ml). This shows serum PSA level increases with disease severity. The discovery of PSA as a biomarker and demonstration of its utility in early diagnosis and monitoring of Prostate Cancer dates back to the early 1980s. These findings correlated with the studies by Jung et al (2004) [13] and Anim et al (2006) [14] confirming the increased levels of PSA in different pathologies of prostate gland.

In the current study serum calcium and phosphorus levels ( $8.1 \pm 0.64$ mg/dl) and ( $2.7 \pm 0.43$ mg/dl) respectively are decreased in prostatic disorders compared to healthy controls ( $10.0 \pm 0.72$ mg/dl) and ( $3.7 \pm 0.45$ mg/dl) respectively ( $p$  value  $< .01$ ). Calcium and phosphorus ions are essential for cell growth, proliferation and differentiation as their signaling is

essential for regulating these physiological functions. Low serum levels of these ions shows consumption of these ions in cell growth and proliferation.

More decrease of serum calcium ( $7.7 \pm 0.42$ mg/dl) and serum phosphorus ( $2.5 \pm 0.39$ mg/dl) level in carcinoma patients compared to BPH (calcium  $-8.6 \pm 0.44$  mg/dl) and ( phosphorus  $-3.0 \pm 0.30$ mg/dl) (p value < .01) patients may be due to extensive accretion of these ions into bones. Serum total calcium was significantly lower in patients with bone metastasis than those without. A decrease in serum calcium is indicative of advanced disease in prostate cancer.

Raskin et al performed a retrospective analysis in of serum calcium levels in patients with metastatic bone disease and reported a 33% prevalence of hypocalcaemia in patients with prostate cancer. [15] This is in accordance with the findings of Kukreja et al. which show a significant decrease in serum calcium in Prostate carcinoma in 1988. [16] According to them, in patients with solid tumors like prostate, breast, or lung cancer, hypocalcaemia develops due to extensive osteoblastic metastases. This is also in accordance with study by Szentirmai et al. in 1995 which revealed that few patients with prostate cancer and bone metastases have a low serum calcium concentration, and some have severe hypocalcaemia. [17]

Elevated extracellular calcium is thought to prevent apoptosis via the Calcium-sensing receptor. [18] A weak negative association has been shown between serum Calcium and the incidence of fatal prostate cancer in Swedish men. [19] Furthermore, the association between serum Calcium levels and aggressive lesions or fatal prostate cancer has been observed in some studies. [20] It has been previously hypothesized in 2009 that high serum Calcium or PTH increase, is a risk factor for fatal prostate cancer. [21]

Blood Calcium levels are tightly regulated and only moderately affected by dietary intake of Calcium and absorption rates. [22] A case study (1995) showing hypophosphatemia and hyper phosphaturia in a 65 year old man with prostate cancer has been reported in Prostate cancer induced oncogenic hypophosphatemic osteomalacia. [23] These finding are also supported by one recent study done by Shahana et al. in 2017 [9 ]They also found low serum calcium and phosphorus level in Prostate cancer patients. [24]

### Conclusion

In our study, Serum phosphorus and calcium levels were low in prostate disorders compared to controls. Hence, altered level of these parameters can be an indicator of prostate disorders. Additionally Serum phosphorus and serum calcium levels were found to be raised in BPH compared to Carcinoma prostate. So, these parameters can give additional benefits along with PSA for screening and diagnosis of prostate cancer. Decreased serum calcium and phosphorus levels may correlate with the severity of prostate cancer. Hence, it can be concluded that estimation of serum phosphorus and calcium levels can be used for early screening and diagnosis of disorders of prostate.

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