Research Article

# Study of Serum Calcium Levels among Prostate Cancer Patients in North India

Pankaj Kamble[1*], B. C. Kabi[2], Deepa Haldar[3], Rajesh Jambhulkar[4]

[1,4]Assistant Professor, Department of Biochemistry, Shri Vasantrao Naik Government Medical College, Yavatmal, Maharashtra, INDIA
[2]Director-Professor and Head, [3]Senior Resident, Department of Biochemistry, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, INDIA.
**Email:** pankajkamble32@gmail.com

## Abstract

**Introduction:** A high dietary calcium intake has been associated with increased risk of various cancers in several epidemiological studies. High level of calcium may promote the growth of potentially fatal cancers. There are very few studies which have focussed on the role of serum calcium in this respect. **Materials and Methods:** We assayed total serum calcium in 30 prostate cancer patients and compared with 30 healthy control subjects. **Results:** We observed a statistically significant increase ($p<0.001$) in serum calcium level of prostate cancer patients as compared to controls. A positive correlation was also observed between serum calcium and PSA among cases. **Conclusion:** This study predicted serum calcium as an etiological factor in the etiogenesis of prostate cancer. Further exploration is warranted to substantiate this finding.

**Keywords:** Serum calcium, Prostate cancer, North India

[*]**Address for Correspondence:**
Dr. Pankaj Kamble, Assistant Professor, Department of Biochemistry, Shri Vasantrao Naik Government Medical College, Yavatmal, 445001, Maharashtra, India.
E-mail: pankajkamble32@gmail.com
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## INTRODUCTION

Prostate cancer is the most commonly diagnosed type of cancer in men in industrialized nations. Its incidence is more in Europe and United states as compared to Asian countries. Several risk factors have been proposed including endogenous factors like ethnicity and genes, and exogenous factors like environmental and diet.[1] There are several prospective epidemiological studies which focus on the role of dietary calcium in the etiogenesis of prostate cancer.[2-4] Intracellular calcium level has been shown to control prostate cancer cell growth and susceptibility to apoptosis.[5] Though calcium level is tightly maintained by homeostasis, small alteration could result in increased proliferation, differentiation and apoptosis in prostate cancer cells.[6,7] Calcium homeostasis is maintained by calcium-sensing receptor, a G protein-coupled cell surface glycoprotein, and may play a role in malignant progression of prostate tumors.[8,9] Calcium levels in serum are firmly controlled over a wide range of dietary calcium and generally are not correlated with dietary calcium levels.[10] The recent evidences that suggest the protective role of vitamin D in causation of prostate cancer suggest another possible mechanism, that at high levels, dietary calcium suppresses production of 1,25-dihydroxyvitamin D, thereby increasing risk of prostate cancer.[11] Thus, if the calcium levels in serum are controlled in patients of prostatic tumors, the disease could be less malignant. Till date numerous studies have been carried out in the Western countries focussing calcium intake form diet but the subject of calcium in serum has received sparse attention. The present study was aimed to analyse the association of total serum calcium with prostate cancer risk in North Indian men.

## MATERIAL AND METHODS

The study was conducted in the Department of Biochemistry in association with Department of Urology,

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VardhmanMahavir Medical College and Safdarjang Hospital, New Delhi. 30 cases of prostate cancer and 30 healthy controls were recruited for the study. Baseline diagnostic work-up for the patients of prostate cancer included digital rectal examination, prostate specific antigen level (PSA) and prostate biopsy. Normal healthy controls randomly selected and matched with respect to age and sex. All were screened for normal PSA level. They had no history of any voiding symptom, prostate surgery, family history of cancer and do not suffer from chronic illness. Written informed consent was taken from cases and controls. Clearance from ethical committee of the institute was obtained before proceeding the study. 3ml of blood was collected in plain vials from each subjects and serum was isolated by centrifugation at 5000 rpm for 5 minutes. Serum was stored at -20°C till further analysis. Estimation of PSA level was done by ELISA using the kit provided by DRG International Inc., USA. Total serum calcium was estimated by orthocresolphthaleincomplexone method on spectrophotometer using the kit provided by PZ CORMAY S.A., Poland.

### Statistical Analysis

The data collected was analysed using SPSS version 16.0 (SPSS Inc, Chicago, USA) statistical software package. Unpaired t- test was applied to studythe variation between two groups and the result was expressed in terms of Mean ± S.D.Pearson's coefficient of correlation was calculated to study the significance of correlation between serum calcium and PSA. Level of significance used was $p < 0.05$.

## RESULTS

The mean age of prostate cancer patients was 68 ± 6.7 years and that of controls was 65 ± 5.0 years which was not statistically significant. A statistically significant difference ($p<0.0001$) was observed in total PSA levels between patients (7.9 ± 2.1) and controls (1.8 ± 1.1). Mean value of serum calcium in patients was 12.4 ± 0.7 mg/dl and that in controls was 7.8 ± 0.6 mg/dl. This was statistically significant ($p<0.001$). A statistically significant positive correlation was observed ($r = 0.36$) between serum calcium and PSA which suggest that both tend to decrease or increase together.

**TABLE 1:** Biochemical parameters in study groups (mean ± S.D.)

| | Patients ( n=30) | Controls (n=30) |
|---|---|---|
| Calcium (mg/ml) | 12.4 ± 0.7* | 7.8 ± 0.6 |
| PSA (ng/ml) | 7.9 ± 2.1* | 1.8 ± 1.1 |

*p<0.0001

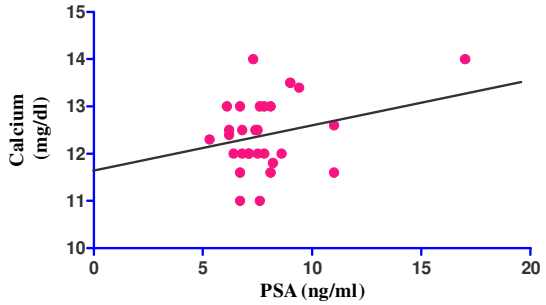


**Figure 1:** Correlation between serum calcium and PSA

## DISCUSSION

Several studies have investigated role of dietary calcium in prostate cancer and found mixed results, [3, 12-13] but few studies focussed on the serum calcium levels, especially in Indian scenario. Our results demonstrated a significantly high level of total serum calcium levels in prostate cancer patients. Also, a positive correlation between serum calcium and PSA levels which suggest that as the prostate cancer advances, the level of serum calcium tend to increase and vice-versa. Thus, it can be proposed that serum calcium can turn out to be a novel biomarker of prostate cancer.Calcium levels in serum generally are not correlated with dietary calcium levels. For example, Mataix et al [14] studies a random subsample of 354 subjects drawn from a cross sectional study of >3400 participants and found no relationship between the measurement of calcium in diet and in serum. Every individual is believed to have his or her own set point for serum calcium that is under genetic control.[15] The concentration of serum ionized calcium normally does not deviate by >2% from its set point. [16] This confers the stability to total serum calcium levels of which 50 % is ionized and physically active. Our observations are consistent with studies that observed elevated risk of prostate cancer with greater calcium.[17-20]The mechanism explaining the association of high serum calcium level and increased risk of prostate cancer remain unclear. High calcium level has been proposed to inhibit the hydroxylation of 25-hydroxyvitamin D to its active form 1,25-dihydroxyvitamin D in kidney.[12] But several studies did not find consistent association between either 25-OHD or 1,25-OHD and prostate cancer risk.[21, 22] Another hypothesis is that increased level of serum calcium affects prostate cancer cells directly. Prostate cancer cells expresses both calcium sensing receptor as well as calcium dependent voltage gated potassium channels.[23, 24] Stimulation of these receptors by extracellular calcium causes decrease in apoptosis and increases prostate cancer cell proliferation *in vitro* and, metastasis *in vivo*. Secondly, calcium had been shown to promote prostate carcinogenesis by affecting insulin-like growth factor

(IGF) system.[25] IGF-I has mitogenic and anti-apoptotic effects on normal and transformed prostate epithelial cells. Since the last decade or so, prostate cancer screening is largely based on the level of PSA. A large randomized clinical trial conducted by Andrioleet al[26] showed that men who are screened for prostate cancer using PSA are not less likely to die of prostate cancer. These findings can questions the usefulness of PSA for population based screening. Most of the men with a positive screening PSA test that is between 4 -10 ng/ml who are referred for prostate biopsy do not have prostate cancer. This leads to unnecessary conduction of prostate biopsies and overtreatment of prostate cancer. This can be avoided if serum calcium is utilized in the setting of prostate cancer screening.

## CONCLUSION

To summarise, our study found an increase levels of serum calcium in patients of prostate cancer. This finding suggests that high level of serum calcium could be an etiological factor in the prostate cancer and it may increase the risk of prostate cancer. It also focuses on the plausible role of serum calcium as a marker of prevalent, clinically significant prostate cancer that could aid in its early detection. On the basis of findings in this study, the mechanism by which calcium may increase prostate cancer risk should be studied further extensively to verify calcium as a risk factor for prostate cancer. Future epidemiologic research is also warranted to study the role of serum calcium in diagnostic setting e.g., in association with PSA. The association between serum calcium levels and prostate cancer should be validated in a large cohort studies in different populations taking into consideration the dietary and hormonal factors so as to confirm the findings of the present study.

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