Correlation Of Total Prostate Specific Antigen With Levels Of Prolactin In Indian Patients With Prostate Cancer: A Preliminary Report

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**ABSTRACT**

**Introduction:** Prostate Specific antigen (PSA) is a sensitive tumour marker in prostate cancer. Available results suggest that increased circulating prolactin promote prostate growth and induce prostate tumour growth. However, epidemiological data concerning the association between prolactin and prostate cancer are sparse and inconclusive. Several case-control and prospective cohort studies have not shown any association. We tested the hypothesis that elevated circulating prolactin are associated with increase in prostate cancer risk.

**Methods:** Serum Total PSA and Serum Prolactin levels were measured with an electro chemiluminescent (ECLIA) assay.

**Results & Discussion:** A significant correlation may exist between Prolactin and Total PSA in prostate carcinoma. Further studies with larger sample size would be required to establish whether prolactin could be a diagnostic / prognostic marker for prostate carcinoma.
INTRODUCTION:
Prostate cancer is a hormone-sensitive malignancy affecting millions of men. Among all types of tumors in men, prostate cancer is the second most common worldwide; and is among the top ten leading sites of cancers in India.[1] Previously it was thought, that prevalence of prostate cancer in India is far lower as compared to the western countries. However, with the increased migration of rural population to the urban areas, changing life styles, increased awareness, and easy access to medical facility, more cases of prostate cancer are being diagnosed and it is evident that we are not very far behind as compared to the western countries.[2] The cancer projection data in India shows that the number of cases will become doubled by 2020.[3]
Prostate Specific antigen (PSA) is the most sensitive, useful tumour marker in screening, staging and follow-up of prostate cancer patients. The diagnosis of prostate cancer has relied heavily on the use of PSA, for over 20 years.[4] Serum PSA levels are influenced by the age of the patient, the stage and grade of the tumour, procedures such as digital rectal examination and biopsy and the volume of the prostate gland. Literature regarding the influence of all these factors on serum PSA levels are available.[5] However, whether serum hormone levels can influence serum PSA levels has not yet been studied extensively. Since both prostate glandular cells and prostate cancer cells are hormone dependent, a strong influence between the serum PSA levels and hormones are likely to occur.[6]
Prolactin hormone, though associated with stimulation of the growth and function of the mammary gland or milk production, it has various roles in the male body too. Receptors for prolactin are found on the prostate cells.[7] Prolactin acts as an additional local growth factor in the prostate gland.[8] It regulates prostate development, growth and differentiation.[9]
Prolactin is synthesized in the anterior pituitary lactotroph cells[10] and is secreted in episodes. In humans, prolactin is produced atleast in the anterior pituitary, decidua, myometrium, breast, lymphocytes, leukocytes and prostate.[7]
Local production of prolactin (Prolactin produced locally in the prostate, though it is also produced and released into the circulation from the anterior pituitary gland of the brain) has also been demonstrated in the prostate. Thus, local activity is not dependent on the endocrine system (acting at a distance), but may occur entirely within the cell (autocrine) or between local cells (paracrine) (prostate cancer and hormones).
Prolactin hormone is made up of 198 amino acids, with molecular weight of 22 – 23 kD. The target organ for prolactin is the mammary gland, the development and differentiation of which is promoted by prolactin.[11] Plasma prolactin rises sharply at puberty. It continues to increase in parallel with the age-related increase, as seen in the incidence of benign prostatic hyperplasia and prostate cancer.[7]
The receptors for prolactin are expressed in the prostate, and the expression is highly elevated in high-grade prostate intra-epithelial cell neoplasia (PIN), a precursor of prostate cancer. This suggests that prolactin could be involved in prostate cancer development.
The available experimental and chronobiological results suggests that increased levels of circulating prolactin induce prostate growth and possibly prostate tumour growth. However, epidemiological data concerning prolactin and prostate cancer are sparse and inconclusive. Limited data is available with respect to the specific and direct effects of prolactin on human prostate. Also, the mechanisms underlying the responses of prostate cells to prolactin is still unclear. There has been limited literature on the role of human prolactin in normal prostate function or prostatic disease. There has been no demonstration of a consistent association between circulating prolactin concentrations and risk of prostate cancer.[7]
In this study, we tested the hypothesis that elevated levels of circulating prolactin are associated with an increase in prostate cancer risk. We conducted a case-control study, using serum samples collected from Prostate carcinoma patients, along with age-matched controls.
MATERIALS AND METHODS

Subjects: A total of 48 Prostate cancer patients diagnosed in our Institute were included in this study. The average age of the patients was 65 years. Fifty healthy individuals (average age: 65 years) served as controls for the study. The study was approved by the Institutional Review Board. Informed consent was obtained from all the subjects and Controls.

Methods:
Serum Total PSA and Serum Prolactin levels were measured with an electrochemiluminescent (ECLIA) assay on Cobas e411, Roche Diagnostics, Mannheim, Germany. The reference values are 0 – 4.0 ng/ml for Total PSA and 4.04 – 15.2 ng/mL for Prolactin.

RESULTS
Abnormally high levels of serum Total PSA were observed in all patients included in the study. The average serum Total PSA levels observed was 1011 ng/mL (Table 1). Higher levels of prolactin were seen in 48% (23 / 48) of the patients. The average prolactin level in the patients was observed to be 22 ng/mL. Whereas, the prolactin levels in the control group was observed to be <15.0 ng/ml (Table 1).

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<th>Table I: Details of patients / controls</th>
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This shows that a significant correlation may exist between the serum levels of Prolactin and serum Total PSA in carcinoma prostate patients. The t test was performed to determine the exact statistical difference between the control and patient groups. The comparison of controls with the prostate carcinoma patients showed a statistically significant difference with p<0.05.

DISCUSSION AND CONCLUSION
The findings obtained during this preliminary study demonstrates a significant correlation between prostate cancer risk and circulating prolactin, as 48% of the patients with abnormally higher levels of serum Total PSA showed elevated serum prolactin levels. While prolactin levels in the control group was within the normal limits.

According to Harper et al, the role of prolactin in prostatic cancer still remains unclear, as there is no clear association between hormone levels (e.g. prolactin) and tumour grade. However, this does not entirely rule out the possibility that prolactin may be involved in prostate cancer pathogenesis. According to Srinivasan Vijayakumar, a large scale study on men above 40 years old without prostate cancer may provide a clear understanding about the influence of serum prolactin levels on prostatic physiology.

Thus, given the influence of prolactin on prostate tissue, studies with a larger sample size would be required so to detect any minor influence. The present study shows that there may be a direct correlation between the serum PSA and serum Prolactin levels. Further studies with a larger sample size would be required to establish whether prolactin could be used as a prognostic tool or marker for diagnosis / prognosis of prostate carcinoma patients.

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