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# The Association between Oxidative Stress and One Carbon Metabolism in Prostate Neoplasm in a Tertiary Care Hospital

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## ABSTRACT:

Carcinoma of the prostate is the most common malignant tumour in men over the age of 65 years with peak age of incidence between 70 and 74 years. Oxidative stress and one carbon metabolism are important contributory factors in etiopathogenesis in Prostate Neoplasm. Significant increase in oxidative stress and serum homocysteine level and no difference of serum vitamin B12 was found in BPH and prostate cancer cases compared to control group. Following study was conducted to compare level of Oxidative Stress Marker and One Carbon Metabolism markers between Prostate neoplasm patients and control Group. We concluded that Homocystine and Vitamin B12 were high in patients with prostate cancer as well as BPH patients when compared with age matched healthy controls.

**Keywords:** prostate cancer ,redox potential, one carbon metabolism.

## INTRODUCTION:

Carcinoma of the prostate is the most common malignant tumor in men over the age of 65 years with peak age of incidence between 70 and 74 years. [1] In 2017, ~161, 360 prostate cancer cases were diagnosed and 26, 730 men died from prostate cancer in the United States. The disease is more common in countries with higher proportions of elderly men in their population. However, the paradox of management is that although 1 in 6 men will eventually

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be diagnosed with prostate cancer, and the disease remains the second leading cause of cancer deaths in men, only 1 man in 30 with prostate cancer will die of his disease.[2]

In Prostate Cancer, one- carbon metabolism pathway is modulated by the Androgen Receptor. This pathway is comprised of a number of connected pathways that promote the folate - mediated transfer of one- carbon units which are necessary for essential cellular processes, including DNA synthesis, repair and the maintenance of redox status. [3,4,5]

"Oxidative stress" is t he state of a cell, characterized by excess production of reactive oxygen species ( ROS) and/or a reduction in antioxidant defenses mechanism responsible for metabolism. ROS are formed as a natural by- product of the normal oxygen metabolism. Under normal circumstances, a cell is able to maintain an adequate homeostas is between the formation of ROS and its removal through enzymatic pathways or via antioxidants. [Z]

Folate is necessary for DNA synthesis, repair and methylation, and biological reactions involving folate require vitamins B6 and B12 as cofactors. Low concentrations of these vitamins can impair one- carbon metabolism pathways, [7] leading to homocysteine accumulation, insufficient methyl groups for DNA methylation or depletion of DNA synthesis and repair precursors, thus, potentially promoting carcinogenesis. [8]

Keeping above background, parameters like MDA ( for oxidative stress), Vitamin B 12 and homocysteine ( for status of the one carbon metabolism) were selected for the present study to investigate some of the multifactorial etiology of prostate neoplasms. Studies on these parameters in prostate neoplasms are very few in number and the results are also far from any definite conclusion. Hence, present study aims to compare serum level of these parameters between control, and prostate neoplasm cases to find any association.

## MATERIAL AND METHOD:

The following study was conducted in Department of Biochemistry in Santosh Medical College, Ghaziabad. Total 195 individuals were included in this study.

- Group 1 (Patients with BPH): Group 1 includes 65 patients with Benign Prostatic Hyperplasia (BPH) of the age group between 50 years – 90 years.
- Group 2 (Patients with Prostate Neoplasm): Group 2 includes 65 patients with Prostate Neoplasm of the age group between 50 years – 90 years.
- Group 3 (Normal Healthy Individuals): Group 3 includes 65 Normal Healthy Individuals of the age group between 50 years – 90 years.

Patients with Prostate Neoplasm of age group between 50-90 years were included in the study. Female patients, Histologically confirmed cases of BHP or Prostate Cancer, Patients with other cancers, patients with liver diseases, Patients on anti-oxidants or multi-vitamin

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medications, Patients who have altered PSA level for any other prostrate pathology like prostatitis were excluded from the study.

## RESULT:

| Condition | Age (years) | MDA (nmol/mL) | Homosystine (µmol/L) | Vitamin B12 (ng/mL) | PSA (ng/mL) | AST Levels | ALT (U/L) | ALP(U/L) |
|---|---|---|---|---|---|---|---|---|
| Prostate Cancer | 70.55 ± 9.32 | 37.78±5.13 | 55.26±6.27 | 314.22±44.95 | 44.32±5.92 | 44.80±9.54 | 23.89±4.39 | 10.26±2.49 |
| BPH | 70.57±9.19 | 5.69±1.13 | 28.06±2.56 | 295.58±18.96 | 6.18±1.44 | 39.49±10.23 | 25.55±7.71 | 11.40±2.67 |
| Control | 69.86±9.88 | 3.19±0.81 | 9.46±1.65 | 268.00±57.1 | 1.80±2.33 | 37.57±11.75 | 23.75±3.85 | 10.12±3.33 |

The Mean ± SD of different parameter in Prostate cancer, BPH and healthy controls were compared in the following table. The difference in MDA, homocysteine, vitamin b12, PSA, ALT, AST, ALP levels in different groups was found to be statistically significant (p value < 0.05).

## DISCUSSION:

In our study, the mean age of Prostate Cancer, BPH and Control was 70.55 ± 9.32, 70.57 ± 9.19 and 69.86 ± 9.88 respectively. In a study conducted by Srivastava et al.[9] mean age of Prostate cancer patients were found to be 61.9 ± 11.4 and mean age of patients with BPH was 59.6 ± 8.4. In a study conducted by Sannigrahi S et al.[10] Mean age of control, BPH and Prostate cancer cases was 67.83±7.3, 69.55±7.6 and 66.00±9.4 years, respectively which is similar to our study. Thus, it is seen that older men are more likely to be diagnosed with high-risk Prostate Cancer and have lower overall survival.

Similarly, the Mean ± SD of MDA in Prostate cancer, BPH and healthy controls was found to be 37.78 ± 5.13, 5.69 ± 1.13 and 3.19 ± 0.81 respectively ($p<0.05$). In a study conducted by Arif M et al.[11] on BPH patients, mean value of MDA was 19.27 ± 4.84 µg/ml in BPH patients and normal control was 0.72 ± 0.02 µg/ml and Homocysteine in Prostate cancer, BPH and healthy controls was found to be 55.26 ± 6.27, 28.06 ± 2.56 and 9.46 ± 1.65 respectively ($p<0.05$) In a study conducted by Sannigrahi S et al.[10] the levels of Homocysteine in BPH, Prostate cancer and controls was found to be was found to be 27.9 ± 4.86, 54.2 ± 11.9 and 9.51±3.03 respectively. Vitamin B12 in Prostate cancer, BPH and healthy controls was found to be 314.22 ± 44.95, 295.58 ± 18.96 and 268.0 ± 57.1 respectively ($p<0.05$). This is similar to a study conducted by Price AJ et al.[12]where they found that circulating concentrations of both folate and vitamin B12 were positively associated with risk of Prostate Cancer. PSA in Prostate cancer, BPH and healthy controls was found to be 44.32 ± 5.92, 6.18 ± 1.44 and 1.80 ± 2.33 respectively ($p<0.05$) In a study conducted by Malati T et al.[13] they found that among BPH group the mean PSA concentration was 3.6 ng/ml.

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Mean AST level was found to be 44.80 ± 9.54, 39.49 ± 10.23 and 37.57 ±11.75 in Prostate cancer, BPH and healthy controls respectively. The difference in different groups was found to be statistically significant (p value < 0.05). Mean ALT level was found to be 23.89 ± 4.39, 25.55 ± 7.71 and 23.75 ± 3.85 in Prostate cancer, BPH and healthy controls respectively. However, this difference in ALT level in different groups was not found to be statistically significant (p value > 0.05).Mean ALP level was found to be 10.26 ± 2.49, 11.40 ± 2.67 and 10.12 ± 3.33in Prostate cancer, BPH and healthy controls respectively.

## CONCLUSION:

From the present study "The association between Oxidative Stress and One Carbon Metabolism in Prostate Neoplasm in a tertiary care Hospital in North India" conducted in 195 patients and controls, it was observed that MDA levels were elevated in prostate cancer patients and BPH patients as compared to normal healthy individuals. This is suggestive of high level of oxidative stress associated with prostate cancer and BPH. Detailed exploration by extensive studies may help to find out possible role of antioxidants in modulating outcome of such patients.

In addition, it was observed that Homocystine and Vitamin B12 were high in patients with prostate cancer as well as BPH patients when compared with age matched healthy controls. The finding of present study, i.e. association of hyperhomocystinemia with carcinoma and benign hyperplasia of prostate needs to be validated by large prospective studies. This may help to establish the role of homocysteine as a novel marker for prostate neoplasm in addition to prostate specific antigen.

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