

## LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN PATIENTS WITH CARCINOMA OF PROSTATE

KRISHNA MOHAN SURAPANENI\* AND VENKATA RAMANA G.

*Department of Biochemistry,  
Dr. Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation,  
Chinoutpally, Gannavaram (Mandal) – 521 286 (A.P.)*

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**Abstract :** Prostate cancer is the most prevalent cancer found in men above the age of fifty years and is frequently diagnosed in men between 45 and 89 years of age with a median age of 72 years. This work was undertaken to assess oxidative stress and anti oxidant status in patients with carcinoma of prostate. Glutathione (GSH), Malondialdehyde (MDA), Super Oxide Dismutase (SOD) levels in Erythrocytes and plasma Glutathione-S-Transferase (GST) levels were estimated in patients with carcinoma of prostate and compared to controls. It was observed that Erythrocyte GSH levels were significantly lower and Erythrocyte MDA & SOD levels were significantly higher in patients with carcinoma of prostate compared to controls. No significant change was observed in case of GST compared to controls. Oxidative stress may be involved in prostate cancer as evidenced by the higher MDA levels and lower GSH levels. The increased activity of antioxidant enzyme may be a compensatory regulation in response to oxidative stress.

**Key words :** Glutathione (GSH) Malondialdehyde (MDA)  
Super Oxide Dismutase (SOD) prostate cancer  
Glutathione-S-Transferase (GST)

### INTRODUCTION

Prostate cancer is the most prevalent cancer found in men above the age of fifty years and is frequently diagnosed in men between 45 and 89 years of age with a median age of 72 years. The age of Indian patients of prostate cancer varies from 32–86 years with an average age of 43.5 years, which is much lower when compared to the average of patients in Western Countries (1).

Prostate cancer is the third most common cancer in men and number two cancer killer above the age of seventy years. Individuals with positive family history are likely to develop disease at a younger age compared to the people without family history of cancer (2, 3). Alteration in the oxidant-antioxidant profile is known to occur in cancer (4, 5).

In the present study, the following parameters were assessed in the

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\*Corresponding Author : Email: krishnamohan\_surapaneni@yahoo.com

erythrocytes and plasma to elucidate the oxidant-antioxidant status in patients with carcinoma of prostate. Erythrocyte Glutathione (GSH) levels were estimated as an index of antioxidant status. Erythrocyte Malondialdehyde (MDA) levels were measured as Thiobarbituric Acid Reacting Substances (TBARS) which served as an Index of extent of lipid peroxidation. The antioxidant enzymes Super Oxide Dismutase (SOD) in Erythrocytes and Glutathione-S-Transferase (GST) levels in plasma were estimated. GST is an enzyme involved in antioxidant defense and also involved in detoxification. It is used as a tumor marker in certain cancers such as oral cancer. Alterations in GST levels in tumor tissue have been reported by various studies (4, 5).

#### METHODS

The study was conducted in Department of Biochemistry, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutpally, Gannavaram (Mandal), A.P, INDIA. Thirty histopathologically proven prostate carcinoma patients from surgical OPD of Dr. Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation General Hospital, Chinoutpally, were chosen for the study. An equal number of age matched healthy subjects were also investigated. Due permission was obtained from the ethical committee of the Dr. PSIMS & RF General Hospital, Chinoutpally before the start of the work. The written consents were also taken from the patients prior to study.

The controls and patients were divided into 2 groups.

Group 1: Thirty healthy age matched controls.

Group 2: Thirty patients with histologically proven prostate cancer.

The venous blood samples obtained from these subjects were used for the estimation of GSH, MDA, SOD in Erythrocytes and GST in plasma. GSH was estimated by the method of Beutler et al using Di Thio Bis Nitro Benzoic acid (DTNB) (6). MDA was determined as the measure of TBARS (7). SOD (EC 1.15.1.1) levels were estimated in the hemolysate by the method of Misra and Fridovich based on the inhibition of auto oxidation of epinephrine to adrenochrome at  $P^H$  10.2 (8) and GST (EC 2.5.1.18) was measured by using 1-Chloro-2, 4-Di Nitro Benzene (CDNB) (9). All reagents used were of analytical reagent grade. DTNB, CDNB and Thiobarbituric acid were obtained from Sigma chemicals, St. Louis, MO. Statistical Analysis between Group 1 (Controls) and Group 2 (patients) was performed by unpaired t-test using the stat-view package.

#### RESULTS AND DISCUSSION

The mean  $\pm$  SD of Erythrocyte GSH, MDA, SOD and plasma GST are indicated in Table I. There was a statistically significant lower GSH levels in patients with carcinoma of prostate compared to controls. The MDA & SOD levels were significantly higher in group 2 compared to group 1. The levels of plasma GST did not show any significant change between controls and patients ( $P > 0.05$ ).

In the present study GSH an antioxidant was significantly lower in patients with carcinoma of prostate, when compared to

TABLE I: The mean $\pm$ SD values of Glutathione (GSH), Malondialdehyde (MDA), Superoxide Dismutase (SOD) and Glutathione-S-transferase (GST) in controls and patients with carcinoma of prostate.

Parameter	Group 1 (controls) n=30	Group 2 (patients) n=30
GSH (mg/gm of Hb)	16.69 $\pm$ 3.48	8.19 $\pm$ 2.24*
MDA (nmoles/gm of Hb)	8.91 $\pm$ 3.94	13.23 $\pm$ 2.54*
SOD (EU/gm of Hb)	1688.80 $\pm$ 532.87	2523 $\pm$ 497.99**
GST (Micromoles/dl of serum)	8.57 $\pm$ 1.06	9.94 $\pm$ 0.88 <sup>NS</sup>

\*P<0.01 compared to controls

\*\*P<0.001 compared to controls

NS-Not significant when compared to controls (P>0.05)

controls. The lower GSH levels may be due to the increased turnover of GSH for preventing oxidative damage in these patients. Similar reports of lower GSH levels in cancers have been reported earlier by Ahmed et al (10) in patients with cervical cancer. They have observed that GSH levels were mainly reduced in poorly differentiated tumours than in well and moderately differentiated tumours. Reduced glutathione levels in cancer were also reported by Bhuvanamurthy et al (5) and Faber et al (11). GSH depletion is reported in hepatoma at an advanced stage (12). An increase in tumour tissue glutathione levels in oral squamous cell carcinoma has been reported by Subapriya et al (13).

In our study lipid peroxidation product i.e. Malondialdehyde (MDA) levels were significantly higher in the Erythrocytes of patients with carcinoma of prostate. Rise in MDA could be due to increased generation of Reactive Oxygen Species (ROS) due to the excessive oxidative damage generated in these patients. These oxygen species in

turn can oxidize many other important biomolecules including membrane lipids. Similar reports of higher MDA levels in prostate cancer were observed by Aydin A et al (14). Elevated MDA levels have been reported in patients with Malignant breast tumour (15, 16), colorectal cancer tissue (17) and in erythrocytes of rats with hepatoma (12). Gerber et al (18) and Saintot et al (19) have been reported diminished MDA levels in patients with breast cancer.

In our study antioxidant enzyme i.e. Super Oxide Dismutase (SOD) levels in hemolysate have been significantly higher in patients with carcinoma of prostate. Similar reports of elevated SOD levels in cancers were obtained by Yeh et al (20). The rise in the levels of SOD could be due to its induction to counter the effect of increased oxidative stress. Skrzydelwska et al have reported increased activities of SOD, Glutathione peroxidase and glutathione reductase (enzymatic antioxidant defense system) and a decrease in GSH content (Non enzymatic antioxidant parameters) in cancer tissue suggesting an increased defense against oxidant damage in cancer (21).

The Glutathione-S-Transferases are a group of multifunctional proteins, which play a central role in detoxification of electrophilic chemicals and the hepatic removal of potentially harmful hydrophobic compounds from blood (22). We have observed no significant difference in the levels of GST in controls and patients with carcinoma of prostate. Similar reports of unchanged GST levels in cancers have been reported (17). No significant difference in activity of GST was observed in human breast cancer tumour cell line and adriamycin

resistant cell line. This indicates that GST may not appear to play a role in drug resistance (23). GST levels were found to be decreased in uterine cervical carcinoma (5, 24) and in fibro adenoma and adeno carcinoma of breast (16). An increase in GST in oral tumour tissue has been reported by Saroja et al (4, 13).

#### In conclusion

Oxidative stress may be involved in

prostate cancer. The results of our study have shown higher oxygen free radical production which is evidenced by higher MDA levels supports the oxidative stress hypothesis in prostate carcinoma. Moreover the Body's defense mechanisms would play an important role in the form of antioxidants and try to minimize the damage, adapting itself to the above stressful situation. The increased activity of antioxidant enzyme may be a compensatory regulation in response to oxidative stress.

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