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LETTER TO EDITOR

Altered Serum Total Sialic Acid, Lipid Peroxidation, Ceruloplasmin And Glutathione Reductase Levels In Patients With Carcinoma Of Prostate.

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Key Words

Sialic acid, malondialdehyde (MDA), ceruloplasmin, glutathione reductase, Prostate Cancer

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Prostate Cancer is the most prevalent form of cancer found in men above the age of fifty years. It is frequently diagnosed in men between the age of 45 and 89 years, with 72 years of age as the median age of diagnosis. The ages of Indian patients of Prostate Cancer vary from 32 – 86 years with an average age of 43.5 years, which is much lower when compared to the average ages of patients in Western Countries [1]. Sialic Acid is an acetylated derivative of neuraminic acid and it is attached to non reducing residues of carbohydrate chains of glycoproteins and glycolipids. Serum Sialic acid has been reported as a marker of the acute phase response and increased Sialic acid concentrations have been observed in several diseases such as myocardial infarction and diabetes. Serum Sialic acid is also increased during inflammatory processes as a consequence of elevated concentrations of richly sialylated acute phase glycoproteins [2]. On the other hand, some studies have reported that monomeric Sialic acid is a potent defense molecule against oxidative damage and the cell death caused by H₂O₂ [3]. However, its significance has not been discussed in various pathological conditions. Since the oxidative damage caused by free radicals is a pivotal mechanism in the progression of Prostate

Cancer, the relationship between Sialic acid levels and the oxidant – antioxidant status was evaluated. Lipid peroxidation mediated by free radicals is considered to be the major mechanism of cell membrane destruction and cell damage. Alteration in the oxidant – antioxidant profile is known to occur in Prostate Cancer [4]. In our previous study, we showed that erythrocyte lipid peroxidation was significantly increased along with decreased glutathione in patients with prostate cancer, when compared to control subjects [5]. However, the relationship between Sialic acid and antioxidant enzyme status was not assessed. Therefore, in the present study, concentrations of serum Sialic acid, malondialdehyde and ceruloplasmin levels were estimated along with the status of antioxidant enzyme activities in patients with carcinoma of the prostate. The aim of our study was to investigate the changes in the oxidant and the antioxidant status and its relationship with Sialic acid in patients with Prostate Cancer.

The study was conducted in the Department of Biochemistry, Saveetha Medical College and Hospital, Saveetha University, Chennai, T.N, India. Thirty histopathologically proven prostate carcinoma patients from the surgical OPD were chosen for the study. An equal number of age matched healthy subjects were also investigated. The control and patient groups had the same socioeconomic background. Therefore, changes in analytes due to nutritional factors are minimal. Written consents were also taken from the patients prior to the study. Controls and patients were divided into 2 groups.

Group 1: Thirty healthy age matched controls.

Group 2: Thirty patients with histopathologically proven Prostate Cancer.

The venous blood samples obtained from these subjects in the morning after an overnight fasting were used for the analysis. Serum was separated by centrifugation at 1000 g for 15 minutes at +4°C. Separated serum was used for the estimation of Sialic acid, MDA and glutathione reductase. Serum Total Sialic acid levels were determined by using the thiobarbituric acid assay method described by Warren [6]. Serum MDA was determined as the measure of thio barbituric acid reactive substances (TBARS) [7]. The level of Ceruloplasmin which serves as a non enzymatic antioxidant was measured by the method of Ravin [8], and Glutathione reductase activity was measured in the serum by the method described by Goldberg DM [9]. Necessary care was taken during the sample collection, storage and assay.

Statistical analysis between group 1 (controls) and group 2 (patients) was performed by the Mann Whitney U test. The data was expressed as mean ± SD. P values < 0.05 was considered as significant.

The mean ± SD of Total Sialic Acid, Malondialdehyde (MDA), Ceruloplasmin levels and activity of Glutathione Reductase in controls and patients with prostate cancer are described in the [Table/Fig 1]. There was a statistically significant increase in the serum total Sialic acid, Malondialdehyde (MDA) levels and the activity of glutathione reductase in patients with Prostate Cancer as compared to controls.

(Table/Fig1) The mean ± SD values of Total Sialic Acid, Malondialdehyde (MDA), Ceruloplasmin levels and activity of Glutathione Reductase in controls and patients with Prostate Cancer.

Parameter	Group1 (controls) n=30	Group2 (Patients) n=30
Sialic Acid (mg/dl)	28.94 ± 1.13	29.43 ± 0.85 *
MDA (micromoles / L)	8.11 ± 1.26	12.79 ± 1.16 * * *
Ceruloplasmin (mg / dl)	11.69 ± 1.13	4.49 ± 1.36 * * *
Glutathione Reductase (U / L)	29.97 ± 1.18	54.05 ± 1.27 * * *
* P < 0.01 compared to controls * * * P < 0.001 compared to controls		

In the present study, the lipid peroxidation product i.e. MDA levels were found to be increased significantly in the serum of the patients with prostate cancer. The rise in MDA could be due to the 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 elevated MDA levels in erythrocytes have been reported in patients with carcinoma of prostate [4],[5]. In contrast to our findings, no significant change in lipid peroxidation in patients with prostate cancer was reported by Dogru-Abbasoglu S [10].

We observed a significant increase in the serum total Sialic acid levels in patients with prostate cancer as compared to controls. In our study, total serum Sialic acid levels were significantly increased, parallel to oxidative stress. So we suggest that increased levels of Sialic acid levels might be considered as a defense molecule against the increased oxidative stress in prostate cancer. The antioxidant property of Sialic acid as an H₂O₂ scavenger, has been reported by Tanaka et al [11]. Haborth K et al reported increased plasma Sialic acid levels in patients with prostate cancer [12].

We observed a significant decrease in the level of ceruloplasmin (non enzymatic antioxidant defense system) in patients with prostate cancer when compared to controls. The decrease in the levels of these non enzymatic antioxidant parameters may be due to the increased turnover, for preventing oxidative damage in these patients, thus suggesting an increased defense against oxidant damage in prostate cancer. Similar reports of decreased non enzymatic antioxidant levels were reported [13]. In contrast to our results, Nayak SB et al reported significant increased levels of ceruloplasmin in prostate and colon cancer patients [14].

In our study, the erythrocyte antioxidant enzyme, i.e. glutathione reductase activity was found to be increased significantly in patients with prostate cancer. Similar reports of raised antioxidant enzyme activities have been reported in patients with prostate cancer [5]. Glutathione reductase (GR), an oxidative stress inducible enzyme, plays a significant role in the peroxy scavenging mechanism and in maintaining the functional integration of the cell membranes. The rise in the activity of GR could be due to its induction to counter the effect of increased oxidative stress.

In conclusion, oxidative stress may be involved in prostate cancer. There is a shift in the oxidant – antioxidant balance in favour of lipid peroxidation, which could lead to the tissue damage observed in this disease. The results of our study suggest higher oxygen free radical production and decreased ceruloplasmin. A non enzymatic antioxidant level supports the higher oxidative stress hypothesis in prostate cancer. The increased activities of antioxidant enzymes may be a compensatory regulation in response to increased oxidative stress. Furthermore, serum total Sialic acid levels were increased in parallel to oxidative stress, thus supporting the role of Sialic acid as an antioxidant. These results suggest that Sialic acid may be considered as a potent defense molecule against the oxidative damage in prostate cancer.

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