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A Prognostic Study of MDA, SOD and Catalase in Breast Cancer Patients

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Abstract: ***Breast cancer is one of the most commonest cancer after the cervical cancer in Indian women. The balance between oxidant and antioxidant has been suggested as an important factor for initiation and progression of breast cancer. The aim of the study is to determine erythrocyte superoxide dismutase (SOD), catalase (CAT) activities as antioxidant enzymes and malondialdehyde (MDA) levels in women having breast cancer and compared it with age matched healthy control women. Superoxide Dismutase (SOD), Catalase, malondialdehyde (MDA) were assayed in 300 subject, in which 150 Breast Cancer patients and 150 healthy control. BMI was also measured in each of the patients and control groups. In this study, we found the SOD and CAT activities in breast cancer patients were significantly lower than control groups. Activities of malondialdehyde (MDA) was greater in patients compared with the control group which may reflect increased oxidative stress in the patient of breast cancer. The results of this study have shown a higher reactive oxygen species (ROS) production and decreased SOD and CAT activities, which support the oxidative stress hypothesis in carcinogenesis. This study was considered these enzymes as biomarker for early detection of recurrent the disease.***

Keyword: Malondialdehyde (MDA), Superoxide Dismutase (SOD), Catalase (CAT), Reactive Oxygen Species (ROS), Breast Cancer

1. Introduction

Cancer is a major public health problem worldwide with millions of new cancer patients diagnosed each year and many deaths resulting from this disease (1, 2). Breast cancer is one of the most frequent disease in Indian women. Reporting of variation in incidence of breast cancer in different population of different parts of Asian continent may be due to multiple factors, including geographic variation, racial/ethnic background, genetic variation, lifestyle, environmental factors, the presence of known risk factors, and utilization of screening mammography, stage of disease at diagnosis, and the availability of appropriate care (3,4). Oxidative stress occurs when there is an imbalance between reactive oxygen species (ROS) and antioxidants reaction capacity which stimulate the development of a disease such as breast cancer (5, 6). Antioxidant defenses protect against free radicals, but these defenses are not completely adequate and systems that repair damage by ROS are also necessary (7). While some ROS are necessary and play important physiological roles, ROS can also cause harm. Excess oxidative species can directly damage DNA, proteins and lipids. Furthermore, reactive oxygen species (ROS), such as superoxide anions and hydrogen peroxide induced lipid peroxidation, play a major role in malignant transformation and tumor cell proliferation and invasion (8). Antioxidants can be divided into two systems: enzymatic and non-enzymatic. The enzymatic system involves enzymes produced by the organism itself, as superoxide dismutase (SOD), catalase (CAT). The enzyme SOD acts as a defense against superoxide, while the enzyme catalase act on H_2O_2 (9). Free radicals, primarily the reactive oxygen species, superoxide and hydroxyl radicals which are highly reactive having an unpaired electron in an atomic or molecular orbit are generated under physiological conditions during aerobic metabolism and can damage the almost all kind of molecules in living cells. As free radicals are potentially toxic, they are usually inactivated or scavenged by antioxidants before they can inflict damage to lipids, proteins or nucleic acids. The human body has a complex antioxidant defense system that includes the antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GSHPx), and catalase (CAT). These block the initiation of free radical chain reactions (10). When free radicals are generated in excess or when the cellular antioxidant defense system is defective, they can stimulate chain reactions by interacting with proteins, lipids and nucleic acids causing cellular dysfunction and even death. Enzymes SOD and CAT have a vital role in the follow up of breast cancer disease. These enzymes counteracts the deleterious action of Reactive Oxygen Metabolites (ROMs) such as singlet oxygen ($^1O_2$), super oxide anions (O_2^-), Hydroxyl radical (^0OH) hydrogen peroxide (H_2O_2) (11, 12) .

The present study aimed to determine changes in the levels of malondialdehyde (MDA), superoxide dismutase (SOD) and catalase in serum of breast cancer patients and healthy control.

2. Material and Methods

The study was conducted in Department of Biochemistry at Sri Aurobindo Institute of Medical Sciences and PG Institute, Indore (MP). Study was approved by the Ethical committee of the institute. Informed consent was taken from patients before drawing blood. Study population comprised 150 breast cancer patients who were consecutively recruited from the oncology clinic of the hospital between 1st March 2014 to 31st December 2015. Breast cancer patients suffering from any other medical problems were excluded from the study. All participants had completed radiation and/or chemotherapy treatments were taken. 5ml blood sample was collected from each patient in plain tube and EDTA tube taking aseptic precautions. The tube was centrifuged at 3000 rpm for 10 minutes. Plasma was collected carefully and used for the assay of lipid peroxidation. RBCs were mixed with 0.9% saline and centrifuged. Supernatant was removed. The process was repeated 3 times to prepare RBC suspension, which was used for the assay of SOD and CAT. BMI was measured in each of the patients and control. Serum super

oxide dismutase (SOD) activity was estimated by the method of **Marklund and Marklund (1988).**The absorbance was measured at 560 nm. The values were expressed in Units/GmHb (13). Serum catalase activity was assayed by the method of **Aebi (1984)**. The absorbance was measured at 420 nm and values were expressed as Units/ GmHb (14). Plasma Malondialdehyde (MDA) was estimated by **Jean CD** at 530 nm (15).

Statistical analysis: The data for biochemical analyses are expressed as mean and standard deviation (SD). Statistical comparisons were performed by Student's t-test using the SPSS version 17.

3. Result

Table 1 shows demographic data of BMI level of Breast Cancer patients. Body mass index (BMI) was found significantly increased when compared with control.

Table 1: BMI level of Breast Cancer patients and controls

Subjects	Age (mean±SD)	BMI (kg/m^2) (Mean±SD)
Control (n = 150)	47±13	24.2 ± 1.7
BC Patients (n = 150)	45±15	29.3 ± 2.1 *

* p<0.01 significantly raised activity. BC: Breast Cancer.

Table 2 showed antioxidant profile of Breast Cancer patients compared with control. Group 1st and group 2nd showed significantly low level of SOD and Catalase activity and significantly high level of MDA in comparison to normal subjects. Breast Cancer group showed higher activity in MDA and lower activity in SOD and Catalase compare with control group.

Table 2: Oxidative stress in patients suffering from Breast Cancer

Parameter	SOD activity Unit/g Hb (mean±SD)	Catalase activity Unit/g Hb (mean±SD)	Plasma MDA nmol/ml (mean±SD)
Control (n = 150)	6.1±1	7.1±0.9	1.9±0.28
BC Patients (n = 150)	3.1±0.6*	4.1± 0.5*	5.8±3.2*

* p<0.01 significantly raised activity. BC: Breast Cancer.

4. Discussion

This analysis shows the significant high BMI of breast cancer patients compared to healthy person. It is generally recognized that the risk of post menopausal breast cancer increases with increasing BMI (16, 17). Increased body mass index (BMI) is a risk factor for developing adult malignancy (16). Excess body weight has been linked to an increase risk of postmenopausal breast cancer and growing evidence also suggest that obesity is associated with poor prognosis in women diagnosed with early stage breast cancer (17,18,19).

Oxygen free radicals which were generated through several enzymatic and non enzymatic biological reactions in aerobic organisms have the ability to attack a wide variety of macromolecules such as lipid, protein, carbohydrate and DNA (10). **Batra *et al.*** (20), demonstrates that there were increases of reactive oxygen metabolites (ROMs) production in various path physiological conditions (8). In addition, **Negahdar *et al.*, (2005)** (11), hypothesized that mutagenecity of oxygen led to chromosomal damage resulting from an increase in the free radical production.

MDA is a low molecular weight aldehyde that can be produced from free radical attack on poly unsaturated fatty acids. The process of lipid peroxidation is one of the oxidative conversions of polyunsaturated fatty acids to MDA, the main sensitive parameter of lipid peroxidation. Increased plasma MDA levels have been reported in breast cancer (21). Several reports present evidence that reactive oxygen species (ROS) are involved in the etiology and progression of breast cancer because certain markers of oxidative stress, including DNA adducts and lipid peroxidation products, such as malondialdehyde (22). This result showed increase in MDA level in breast cancer as compared to control.

The antioxidant enzyme Superoxide dismutase and catalase are the backbone of the cellular antioxidant defense system (23). The low activity of these antioxidant enzymes might be due to depletion of antioxidant defense system. The activity of the hydrogen peroxide detoxifying enzymes catalase was significantly decreased in the more metastatic line. (24). Several researches were considered SOD and CAT enzymes acts as anti carcinogens, antitoxins and inhibitors at initiation, promotion and transformation of carcinogenesis (26, 27, 28, and 29). In the present study, SOD and CAT activities were significantly decreased in the sera and/or plasma of Breast Cancer patients than healthy controls, thus occurred due to high production of free radicals that leaded to accumulation of ROMs (26) that it observed the role of antioxidants to lower incidence of various human morbidities or mortalities molecules as ROMs.

5. Conclusion

From the above study and its discussion, the elevated BMI level is the common feature of the breast cancer. It is highly recommended that people should reduce weight and control obesity in order to reduce risk of breast cancer. it was found that the antioxidant level decreased in breast cancer patient due to increased Reactive Oxygen Species. It is concluded that the biochemical changes of Superoxide Dismutase, catalase and malondialdehyde may be considered enzymes as biomarker for early detection of recurrent disease and also monitoring the effective therapeutic follow up of the patients. These are the best biomarker for diagnosis, prognosis, and treatment of breast cancer.

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