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## **Effects of chemotherapy on antioxidant enzymes activities and lipid peroxide levels in the blood of women with breast cancer**

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**Abstract**---Breast cancer is the most frequent cancer among women around the world. Various studies have looked into the causes of that cancer in order to find a technique to diagnose it early and treat it effectively. The current study investigated the relationship between the decrease of an antioxidant enzyme among breast cancer patients and the effect of chemotherapy on it. This study investigated the relationship between the reduction of antioxidant enzymes and the effect of chemotherapy in breast cancer patients. The survey was conducted on 70 histopathologically diagnosed breast cancer patients (all women) from the Babylon Mirjan Medical City Oncology Centre, with 30 apparently healthy women serving as controls. The current study found differences in some biochemical markers between controls and cases with breast cancer. The Superoxide dismutase (SOD) activity in the control was (64.4023.76) U/ml, while its activity in the case was significantly decreased to reach (9.516.59) U/ml in the first group (1–5 doses) and (9.254.62) U/ml in the second group (6–10), and the GSH concentration in the control was (17.579.09), whereas its activity in the case was significantly reduced to reach (2.070.88)  $\mu\text{mol/ml}$  in the first group (1–5), (2.341.65)  $\mu\text{mol/ml}$  in the second group (6–10), and (1.280.18)  $\mu\text{mol/ml}$  in the third group (> 10 doses). The study demonstrated that the frequency of significant

association was reported between the decrease in antioxidant enzyme activity when using chemotherapy and breast cancer risk.

**Keywords**---Breast Cancer, Antioxidant Enzyme, Chemotherapy.

## Introduction

According to the latest global cancer statistics, breast cancer (BC) is one of the most important cancers in women worldwide and was the second leading cause of cancer-related death in 2018 [1]. Chemotherapy is rarely used to treat BC, but it may be necessary in some cases [2]. Chemotherapy is an option for some molecular subtypes of breast cancer, with chemotherapy being an option for others. Triple-negative breast cancer is regarded to be one of the most aggressive molecular subtypes, with a higher treatment response rate than other subtypes. Despite adjuvant treatment, these patients' overall survival remained dismal [3]. New methods and molecular prognostic markers are needed to improve patient outcomes because chemotherapy is routinely utilized in triple-negative, inflammatory, and advanced BC [4]. Oxidative stress occurs when the reactive oxygen species (ROS) and antioxidant response are out of balance, promoting the progression of illnesses such as breast cancer [5], [6]. Antioxidant defences are efficient against free radicals, but they are insufficient in isolation [7]. While certain ROS are required for physiological function, others can be detrimental. Reactive species in excess can cause direct damage to DNA, proteins, and lipids. Furthermore, ROS like superoxide anion and hydrogen peroxide-induced lipid peroxidation are important in malignant transformation, tumour cell proliferation, and invasion [8]. Antioxidants are divided into two categories: enzymatic and non-enzymatic. For example, the enzymes superoxide dismutase (SOD) and catalase are created by the body (CAT). Superoxide dismutase is a type of enzyme that breaks down superoxide. Catalase protects against H<sub>2</sub>O<sub>2</sub> while superoxide dismutase protects against superoxide [9]. Free radicals such as reactive oxygen species, superoxide, and hydroxyl radicals, which have unpaired electrons in atomic or molecular orbitals, are created under physiological conditions. During aerobic metabolism, almost all molecules in living cells can be removed. Due to their potentially harmful nature, free radicals are usually inactivated or scavenged by antioxidants before they affect lipids, proteins, or nucleic acids. Superoxide dismutase, glutathione peroxidase, and catalase are antioxidant enzymes that are part of the human body's sophisticated antioxidant defense system. These inhibit the initiation of free radical chain reactions [10].

When free radicals are created in excess of the cellular antioxidant defense mechanism is compromised, they trigger a chain reaction by interacting with proteins, lipids, and nucleic acids, causing cellular malfunction and even death. The enzymes superoxide dismutase and catalase are essential in the treatment of breast cancer. Reactive oxygen species metabolites (ROM) such as singlet oxygen (1O<sub>2</sub>), superoxide anion (O<sub>2</sub><sup>-</sup>), hydroxyl radical (OH<sup>•</sup>), and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) are neutralized by these enzymes [11], [12]. The researchers aimed to investigate the effects of chemotherapy on malondialdehyde (MDA), superoxide dismutase (SOD), and catalase levels in breast cancer patients and healthy controls.

## 2 Materials and Methods

### 2.1 Study Subjects

The study was conducted between September 2020 and April 2021. Seventy breast cancer patients, 70 breast cancer patients and 30 healthy individuals were adopted from the Oncology Centre in the Medical City of Mirjan, Babylon. Collect peripheral blood anticoagulant (EDTA) tubes for DNA isolation.

### 2.2 Measurement of serum antioxidant enzymes (SOD, CAT, GSH) and Malonaldehyde

The activities of superoxide dismutase were determined by autoxidation of Pyragallol according to [13]. Catalase assay was measured according to procedures of [14] and [15]. Glutathione activity was determined according to the method of [16] and [17]. Lipid peroxidation has been estimated by the Thiobarbituric acid assay for malondialdehyde (MDA) concentration according to [18], [19], and [20]. The serum lipid peroxidation was determined by [21].

## 3 Results and Discussion

### Superoxide dismutase (SOD) activity

The superoxide dismutase (SOD) activity in the control group was (64.4023.76) U/ml, whereas its activity in the case group was significantly reduced to (40.8928.55) U/ml in the first group (1–5 doses), (40.5127.55) U/ml in the second group (6–10), and (43.6528.75) U/ml in the third group (> 10 doses).

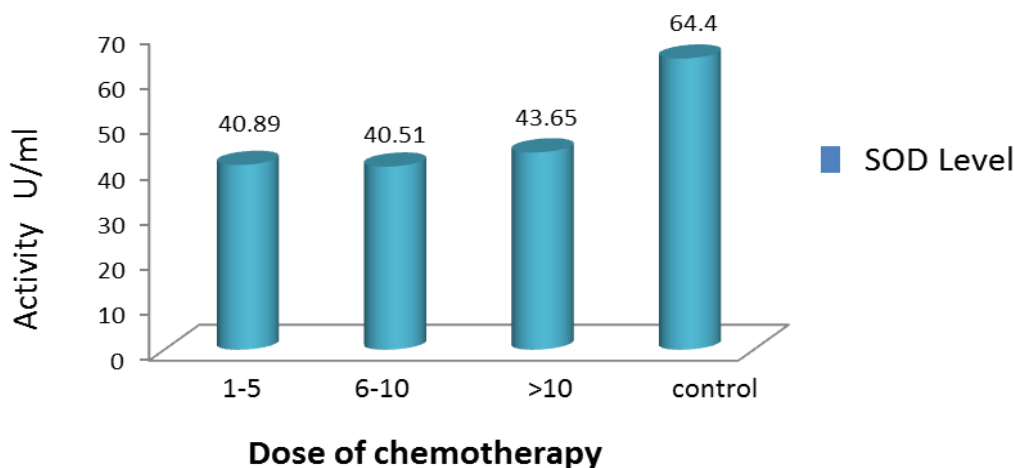


Figure 1. superoxide dismutase (SOD) activity in serum of control and breast cancer patients.

And the catalase (CAT) activity in control were  $(16.08 \pm 8.38)$  U/ml while its activity in the case were significantly decreased to reach in the first group (1-5 doses)  $(9.51 \pm 6.59)$  U/ml and in the second group (6-10 doses) reach to  $(9.90 \pm 4.66)$  U/ml and in third group (>10 doses) reach to  $(9.25 \pm 4.62)$  U/ml.

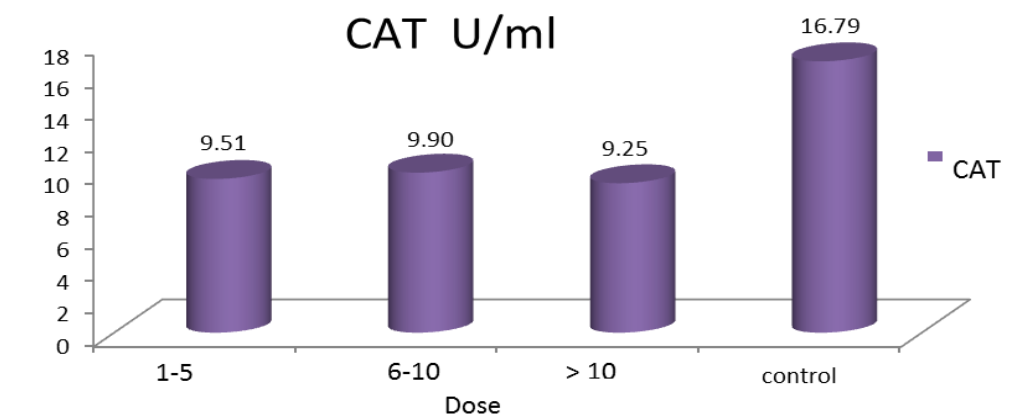


Figure 2. Catalase (CAT) activity in serum of control and breast cancer patients.

and GSH concentration in control were  $(17.57 \pm 9.09)$   $\mu$ mole/ml while its activity in the case was significantly decreased to reach in the first group (1-5 doses)  $(11.01 \pm 5.55)$   $\mu$ mole/ml and in the second group (6-10 doses) reach  $(13.03 \pm 8.29)$   $\mu$ mole/ml and in the third group (>10 doses) reach  $(11.07 \pm 5.55)$   $\mu$ mole/ml.

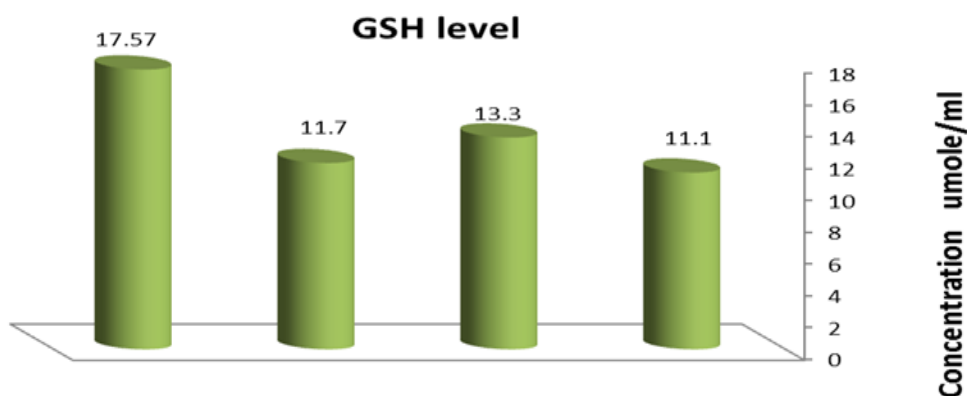


Figure (3): Glutathione concentration (GSH) in serum of control and breast cancer patients.

In our study, a decrease in the activity of the antioxidant enzymes SOD and CAT was observed, and this may be due to mutations in the gene that patients carry, or it may be due to their taking chemotherapy, as it may also cause mutations in the gene, or this decrease in SOD activity may be due to the body not responding to chemotherapy. This promotes an increase in the oxidative potential and thus

an increase in free radicals that may attack the DNA, where we showed in the third group (more than 10 doses) of patients a significant decrease in the level of SOD enzyme activity, which may be due to a decrease in the patient's immune system [22].

This study showed that after multiple courses of chemotherapy (Taxotere and Giemsa), serum antioxidant enzymes were significantly reduced in patients. Therefore, the present findings support our previous research. A limitation of this study is the limited number of breast cancer patients who received chemotherapy. The advantage of this study is that all major antioxidant enzymes, including SOD and CAT, were investigated simultaneously. Furthermore, we measured and compared these metrics in the early and late stages of breast cancer.

Superoxide dismutase and catalase are antioxidant enzymes that form the backbone of the cellular antioxidant defence system [23], and their low activity could suggest that the antioxidant defence system is depleted. The hydrogen peroxide detoxifying enzyme catalase activity was significantly lowered in more metastatic cell lines [24]. Several investigations [25, 26], [27], and [28] have suggested that SOD and CAT enzymes serve as anticancer agents, antitoxins, and inhibitors in the beginning, promotion, and transformation of carcinogenesis. Due to the accumulation of ROM from increased free radical production, the activity of superoxide dismutase and catalase in the serum and/or plasma of breast cancer patients was considerably lower than those of healthy controls in another study [25].

If there is a Various human morbidity or mortality molecules (Adriamycin and cyclophosphamide chemotherapy (doxorubicin (also known as doxorubicin) and cyclophosphamide) have been shown in other studies. Other research has found that AC chemotherapy (doxorubicin (also known as Adriamycin) and cyclophosphamide) increased oxidative stress in breast cancer patients. And the present study showed that there is a decrease in the level of antioxidant GSH enzyme activity and this is evidence of disease progression, especially in the third group of patients. It is well known that GSH depletion may be detrimental to cancer cells and may enhance the effectiveness of chemotherapy and/or ionizing radiation [29], [30], [31]. It is associated with higher levels of ROS production in cells and with the fact that some canonical tumor promoters also activate GSH synthesis and turnover mechanisms (e.g., NRF2) [32].

Lipid peroxidation marker such as the malondialdehyde (MDA) concentration in control were  $(2.06 \pm 1.39)$   $\mu\text{mol/ml}$  while its activity in the case was significantly decreased to reach in the first group (1-5 doses)  $(2.07 \pm 0.88)$   $\mu\text{mol/ml}$  and in the second group (6-10 doses) reach to  $(2.34 \pm 1.65)$   $\mu\text{mol/ml}$  and in the third group (>10 doses) reach to  $(1.28 \pm 0.18)$   $\mu\text{mol/ml}$ . figure (4).

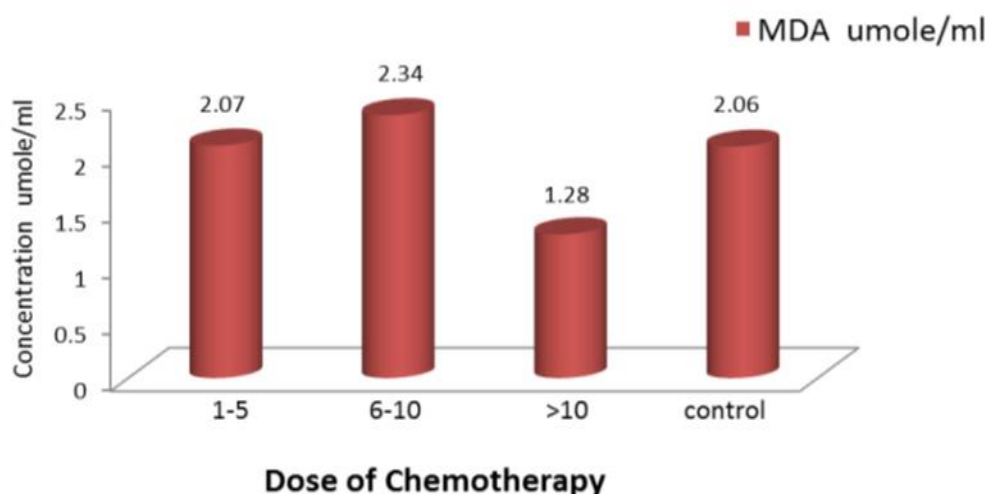


Figure (4): Malondialdehyde (MDA) concentration in serum of control and breast cancer patients.

Malondialdehyde is a low molecular weight aldehyde produced when free radicals attack polyunsaturated fatty acids. Lipid peroxidation is one of the oxidative conversion processes of polyunsaturated fatty acids to malondialdehyde, and it is one of the most sensitive characteristics of lipid peroxidation. In breast cancer patients, MDA levels in the blood were shown to be greater [33]. Several studies have identified reactive oxygen species (ROS) as markers of oxidative stress in the etiology and evolution of breast cancer, such as DNA adducts and lipid peroxidation products like malondialdehyde [34].

The findings show that MDA levels are higher in breast cancer than in controls, but lower in the third group, which could be due to the immune system of the patient after 10 doses of chemotherapy, and that a higher stage of breast cancer was associated with a significant increase in malondialdehyde, a lipid peroxidation marker [35]. Another study [36] found an increase in MDA levels in breast cancer patients with an average of  $5.8 \pm 3.2$  nmol/ml compared to a control group of  $1.9 \pm 0.28$  nmol/ml, with a p-value of 0.01 ( $p < 0.05$ ), indicating statistically significant differences between the breast cancer and control groups. MDA is a byproduct of lipid peroxidation, which is caused by an increase in reactive oxygen species (ROS) in the body, which can lead to the development of breast cancer cells [36].

Other studies measured MDA, SOD, and CAT of blood before and after chemotherapy in 24 patients with malignant head and neck tumors compared to 17 healthy people as a control group. Results obtained 24 patients with higher MDA levels than the control group, while SOD and CAT levels were lower. indicating that MDA levels were higher in patients compared with the control group. After chemotherapy, MDA levels were higher, while SOD levels gradually increased [37].

Figure 1. Types Distribution of food samples from meat and meat products  
Discussion.

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