

## TOTAL ANTIOXIDANT STATUS IN WOMEN WITH BREAST CANCER

Isam Hamo Mahmood<sup>1</sup>, Kassim Salih Abdullah<sup>2</sup>, Mohammed Salih Abdullah<sup>3</sup>

### ABSTRACT

**Objective:** To measure the concentration of total antioxidant status (TAS) in women with breast cancer.

**Methodology:** This is a case control study conducted in Al-Salam Hospital and Department of Pharmacology in Mosul Medical College. Twenty women having histologically confirmed breast cancer and twenty age-matched healthy volunteer women participated in the study. Serum total antioxidant status (TAS) was measured in both groups.

**Results:** Mean TAS of the patient group ( $0.91 \pm 0.32$  mmol/l) was significantly lower ( $P < 0.001$ ) than that of the control group ( $1.82 \pm 0.14$  mmol/l).

**Conclusion:** The present study demonstrated that women with breast cancer have a low level of TAS as compared to those of healthy women. It further emphasizes the growing concern that oxidative damage may occur in those patients that exhaust the antioxidant defense of the body leading to a low levels of TAS. Administration of antioxidant supplements such as a combination of vitamins A, C and E are necessary in women at high risk of developing breast cancer or after surgery or with anticancer drugs.

**KEY WORDS:** Oxidative stress, Antioxidants, Breast cancer.

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### INTRODUCTION

Breast cancer is one of the most common neoplasm in women and is a leading cause of cancer-related deaths worldwide.<sup>1</sup> It accounts for around 20-25% of all female cancers in both

India and the UK, but the incidence in the UK per hundred thousand women is three times higher than Mumbai.<sup>2</sup> People with the following conditions or characteristics are at a higher-than-average risk for developing breast cancer: increasing age, history of cancer in one breast, history of benign breast cancer, never giving birth or first pregnancy after thirty years family history (first degree relative) of breast cancer, early onset of menstruation and late menopause, high doses of ionizing radiation before age 35, history of cancer of the colon, thyroid, endometrium, or ovary, diet high in animal fat, excessive alcohol consumption, and possibly, obesity, possibly, long term oral contraceptive use.<sup>3</sup>

Oxidative stress is considered to be involved in the pathophysiology of all cancers<sup>4</sup> including breast cancer.<sup>5,6</sup> Oxidative stress is defined

1. Isam Hamo Mahmood, PhD,
2. Kassim Salih Abdullah, PhD,
- 1-2: Department of Pharmacology, College of Medicine, Mosul, Iraq.
3. Mohammed Salih Abdullah, Arabic Board in Surgery, Surgeon in Al-Salam Hospital, Mosul, Iraq.

#### Correspondence

Isam Hamo Mahmood,  
Assistant Professor, Dept. of Pharmacology,  
College of Medicine, Mosul, Iraq.  
Email: isam\_mahmood@yahoo.com

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as the excess formation and/ or insufficient removal of highly reactive molecules (free radicals) such as reactive oxygen species and reactive nitrogen species.<sup>7,8</sup> It usually occurs when the available supply of the body's antioxidants is insufficient to handle and neutralize free radicals of different types. The result is massive cell damage that can result in cellular mutations, tissue breakdown, and immune compromise.<sup>9</sup>

An antioxidant is a substance that when present in low concentrations relative to the oxidizable substrate significantly delays or reduces oxidation of the substrate.<sup>10</sup> They are essential ingredients in maintaining a fit and healthy body. They bind with free radicals, rendering them harmless and stop the chain reaction formation of new free radicals, protecting other chemicals of the body from damaging by oxidation reactions caused by free radicals.<sup>11</sup>

Oxygen-free radicals generated by a number of processes in vivo are highly reactive and toxic.<sup>12</sup> Excess generation of oxygen free radicals can cause oxidative damage to biomolecules resulting in lipid peroxidation, mutogenesis and carcinogenesis. Oxygen free radicals induced lipid peroxidation has been implicated in neoplastic transformation.<sup>13</sup> Reactive oxygen species are involved in initiation, promotion and progression of carcinogenesis, where inactivation or loss of certain tumor suppressor genes is occurred.<sup>14</sup>

The role of reactive oxygen species in breast carcinoma may not be limited to early mutagenic events, however, carcinoma cells are frequently under persistent oxidative stress. Human tumor cell lines in vitro produces reactive oxygen species at a far greater rate than do non transformed cell lines<sup>15</sup> and markers of constitutive oxidative stress have been detected in samples from in vivo breast carcinoma.<sup>16,17</sup>

Trials dealing with the measurement of total antioxidant status in women with breast cancer are limited. The present study was designed to measure the concentration of TAS in a number of women having breast cancer and to compare the results with those of healthy controls.

## METHODOLOGY

Twenty women having primary, histologically confirmed breast cancer were identified and participated in the study. The patients were newly diagnosed cases of breast cancer, taking no anticancer treatment; they have attended the department of surgery, hospital of Al-Salam complaining from a mass in their breasts. The women were subjected to clinical examination and ultrasound test of their breasts, followed by fine needle aspiration for cytological examination. Patients with positive results of breast cancers were included in the study. Another twenty age-matched healthy volunteer women were included in the study as the control group. Controls consisted of members of the public with no previous history of breast cancer or other cancer-related diseases. Participant's age range was 25 to 50 years. All participants completed a consent form, and the study protocol was approved by the Research Ethics Committee.

No participant had a history of hyperlipidaemia, cardiovascular diseases, kidney disease, diabetes mellitus or any other systemic disease. Further exclusion criteria were current use of trace elements or antioxidants or vitamin B complex and none of them had received medication during the study period and for two months before the study period. The total dietary intake of fruits and vegetables were good and not significantly different between the studied groups.

The study was performed during fasting time in the morning. Total antioxidant status was measured by using an antioxidant assay kit (Cayman Chemical Company/ U.S.A).

*Statistical Methods:* Paired t-test was used to compare TAS of the patients and controls individuals and ages of the two groups. All values were expressed as Mean  $\pm$  SD and a P value of  $<0.05$  was considered statistically significant.

## RESULTS

The individuals in the cancer and control groups were comparable in terms of age (Mean  $39.75 \pm 6.87$  year for the cancer group and

39.65±6.67 year for the control group,  $P > 0.5$ ). Mean TAS for the breast cancer group (0.91±0.32 mmol/l) was significantly lower ( $P < 0.001$ ) than that for the control group (1.82±0.14 mmol/l).

## DISCUSSION

This study indicates that women having breast cancer have lower values of TAS compared to normal healthy women. This may indicate that oxidative stress had occurred in such patients, which may have exhausted the antioxidant capacity of the body.

There is accumulating evidence of altered antioxidant components in women with breast cancer. In a recent study made by Sharhan et al.,<sup>6</sup> revealed that poor antioxidant status and high oxidative stress are associated with breast cancer risk as evident by a low levels of plasma vitamins E and A antioxidants as compared with the controls. Another recent study reported by Kasapovic et al.,<sup>18</sup> showed that women with breast cancer have low plasma levels of the antioxidant substances including: copper, zinc superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase enzymes, as well as the level of total glutathione and CuZnSOD protein were measured in blood cells of breast cancer patients. Yuvaraj et al.,<sup>19</sup> showed that the various circulating enzymatic and non enzymatic antioxidants were low in a group of women with breast cancer. The results of the above studies are in consistence with the results obtained from our study which indicate a low level of antioxidant status in the women with breast cancer.

Other studies concerning antioxidant status in women with breast cancer showed a higher levels of antioxidant substances. Portakal et al.,<sup>17</sup> showed that the activities of mitochondrial and total superoxide dismutase, glutathione peroxidase and catalase in tumor tissues significantly increased compared to the controls. Rajneesh et al.,<sup>1</sup> showed a significant elevation in both enzymic and non-enzymic antioxidants (superoxide dismutase, catalase, reduced glutathione, glutathione peroxidase

and glutathione S-transferase) in serum samples of 40 breast cancer patients.

In the present study total antioxidant status was measured and not the individual antioxidants. Measuring total antioxidant activity is better than measuring the individual antioxidant activity because: The measurement of all known antioxidant in biological fluid is time consuming, many antioxidants may be as yet undiscovered, the total activity may be greater than the sum of the individual antioxidants because of cooperative interaction.<sup>20</sup> Review of literature revealed one report that also measured total antioxidant status<sup>4</sup> and demonstrated a significantly lower-levels of total antioxidant capacity in patients with breast cancer in comparison with controls.

The results of the present study and those of other studies that demonstrated a low level of antioxidant capacity in women with breast cancer are in consistence with the fact that oxidative stress have occurred in those patients which exhaust the antioxidant components of the body leads to a low antioxidant status. Recent studies have demonstrated the enhanced lipid peroxidation in breast cancer tissues and support the oxidative stress hypothesis in breast carcinogenesis.<sup>1,5,6</sup>

Many clinical or epidemiological studies have examined the relationship between antioxidant supplements and risk of breast cancer recurrence or breast cancer-related mortality. Fleischauer et al.,<sup>21</sup> showed that risks of breast cancer recurrence and disease-related mortality were reduced among women using vitamin C and vitamin E supplements for more than three years. Thirty two typical patients with breast cancer were studied for 18 months. Nutritional protocol was added to the surgical and therapeutic treatment of breast cancer. The added treatment was a combination of nutritional antioxidants (Vitamin C, Vitamin E, beta carotene, selenium plus secondary vitamins and minerals, essential fatty acids and Coenzyme Q 10). The main observations obtained from the study are:

1. None of the patients died during the period.
2. None of the patients showed signs of

further distant metastases.

3. Quality of life was improved.
4. Six patients showed apparent partial remission.<sup>22</sup>Dorjqochoo et al.<sup>23</sup> suggests that vitamins E and B supplements may confer protection against breast cancer among women who have low dietary intake of those vitamins.

## CONCLUSION

The present study demonstrated that women with breast cancer have a low levels of TAS as compared to those of healthy women. It further emphasizes the growing concern that oxidative damage may occur in those patients that exhaust the antioxidant defense of the body leading to a low levels of TAS. Administration of antioxidant supplements such as a combination of vitamins A, C and E are necessary in women at high risk of developing breast cancer or after surgery or with anticancer drugs. Further studies with larger patient's size may be needed to confirm our results.

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