

Estimation of Trace Elements (Selenium, Iron) and Their Biological Effect in Serum Levels of Breast Cancer Patients

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Abstract

Background: Breast cancer (BC) is the most commonly occurring cancer that records a significant percentage of all cancers among women. The most common type of BC is ductal carcinoma. The trace elements, selenium (Se) and iron (Fe), have an important role in the metabolism of human body in which they have very vital biological effect on the enzymes involved in antioxidants and immune system. **Materials and Methods:** Venous blood samples were collected into plain vials from 50 patients and 50 controls, which were transported to the laboratory on ice and centrifuged at 3000 rpm for 15 min, and the serum was stored at -4°C until the day of mineral estimation, using SHIMADZU Atomic Absorption Spectroscopy AA7000 using Graphite Furnace Technique. **Results:** There was a significant ($P < 0.05$) decrease in the concentration of Se in serum samples of BC patients as on comparison with the healthy individuals. Level of difference of Fe remains insignificant ($P > 0.05$) in the serum of BC patients as compared with normal healthy controls. **Conclusion:** We found a significant association between trace elements (serum Se and Fe) with BC.

Keywords: Atomic absorption spectrophotometer, breast cancer, iron, selenium

INTRODUCTION

Cancer nowadays is the problem of the world. Breast cancer (BC) is the most commonly occurring cancer among women, and its incidence is increasing worldwide.^[1] BC records a significant percentage of all cancer incidence among women, making it the most common type of nonskin cancer in women and the fifth most common cause of death due to cancer.^[2] However, BC is responsible for the death of millions of women worldwide every year. Malignancy of the breast is one of the most common causes of death in women aged between 40 and 45 years.^[3]

The incidence of BC increases proportionally with age in many countries including developing nations and has become a main public health problem, with one woman in ten, developing it in her lifetime throughout the world. BC is uncommon below the age of 32 years; however, its behavior varies from slow to rapid progressive disease despite available treatment depending on many factors, such as genetics, age, lifestyle, and healthy nutrition.^[4]

BC is a major clinical challenge due to poor diagnosis or delay due to the lack of tests to detect the disease in its early

stages as well as the relative resistance of chemotherapy and radiotherapy. Minerals have been given much attention because differences in the concentration of the metal in the serum are associated with increased risk of various cancers in humans. Selenium (Se) plays a vital role in cancer prevention and appears to play important structural and enzymatic roles such as antioxidant activity and immune system.^[5-7]

Antioxidant system and immune system can be disturbed and changed in women with BC which causes significantly increased oxidative stress and decreased total antioxidant capacity. Free radicals are neutralized by some antioxidant enzymes such as glutathione peroxidase, catalase, and superoxide dismutase. The process of oxidative stress mostly occurs in an imbalance of the concentration of trace elements, which is used in the structure of antioxidant enzymes.^[8]

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Submission: 28-11-2019 **Accepted:** 03-12-2019 **Published Online:** 17-03-2020

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How to cite this article: Jasim SN, Ahmed AM, Saleh SS. Estimation of trace elements (selenium, iron) and their biological effect in serum levels of breast cancer patients. *Med J Babylon* 2020;17:89-92.

Generally, oxidative damages are often associated for reducing function of enzymatic antioxidant, and changes of some trace elements can affect the activity of antioxidant enzymes.^[9,10] Oxidative stress plays an important role in the carcinogenic process, as reactive oxygen species (ROS) which induce oxidative damage, DNA damage, and protein damage. Fe can produce ROS in which it can attack DNA causes DNA mutation and can act as an element in the pathological process of cancer as Fe may be a limiting nutrient to the growth and replication of cancer cells in the humans.^[10]

Estimation of serum levels of metal ions (Fe) and some other element such as Se may have a potential role in monitoring of patients with BC. Due to ambiguities in this regard, the present study investigated some trace elements in the serum of women with BC.^[11]

MATERIALS AND METHODS

The experimental work of the present study was carried out in Specialized Center for Oncology and Hematology/Azazdi Hospital in Kirkuk City. Analytical analysis was carried out in laboratories of Ministry of Science and Technology/Directorate of Environment and Water-Food Pollution Research Center.

A total of 50 women were diagnosed with BC by an oncologist were considered and entered into the present study. Venous blood samples in a fasting state were collected into plain vials from patients group A whose age groups have ranged from 48 to 77 years and control group B (50 healthy women) with traits compatible with those of the experimental group and were transported to the laboratory in ice and centrifuged at 3000 rpm for 5 min, and the serum was stored at -4°C until the estimation time of trace elements using SHIMADZU Atomic Absorption Spectroscopy AA7000.

The collected data were calculated and analyzed using the Statistical Package for Social Sciences (SPSS) 20th version for Windows (SPSS, IBM Company, Chicago, USA). Data were expressed as mean $\pm$ standard deviation (SD) and statistically analyzed to verify the accuracy and sensitivity of the measurements. Independent samples *t*-test, correlation, and linear regression analysis were used for the evaluation of data. A $P < 0.05$ was considered statistically significant.

Preparation of standard solutions

Original standard solutions were 1000 $\mu\text{g/ml}$ in 2% HNO_3 for interested elements. Four standard solutions were prepared by dilution from original standard stock solution using general dilution law ($N_1 V_1 = N_2 V_2$). It must prepare a series of concentrations from the highest one reaching the values required for calibration curve performs. Series of concentrations which prepared were as follows: 1000 $\mu\text{g/ml} \rightarrow 100 \mu\text{g/ml} \rightarrow 10 \mu\text{g/ml} \rightarrow 1 \mu\text{g/ml}$. The value 1 $\mu\text{g/ml}$ is equal to 1000 ng/ml , so complete preparation from this solution reaches the required concentration of the standard calibration curve as follow: 1000 $\text{ng/ml} \rightarrow 100 \text{ng/ml} \rightarrow 5 \text{ng/ml}$, 10 ng/ml , 20 ng/ml , 30 ng/ml .^[12,13]

Sample preparation

Samples were digested by transferring 20 μL of serum into Eppendorf tube; then, 40 μL of 10% nitric acid was added and mixed well for 10 min and finally the dilution volume was completed to 100 μL with deionized water. Solution was filtered and then appropriate solution volume of 20 μL was injected into the graphite tube for reading.^[14]

Determination of serum iron

Four standard solutions of iron (Fe) were prepared as previously mentioned and described. The four standards were 5, 10, 20, and 30 ng/ml for calibration curve. The concentrations of Fe in samples were measured directly and continuously beyond measuring of standard solutions depending on the calibration curve.^[12,13] Ideal conditions for Fe determination are shown in Table 1.

Determination of serum selenium

Four standard solutions of Se were prepared as previously mentioned and described. The four standards were 5, 10, 20, and 40 ng/ml for calibration curve. The concentrations of Se in samples were measured directly and continuously beyond measuring of standard solutions depending on the calibration curve.^[12,13] Ideal conditions for Se determination are shown in Table 2.

RESULTS

The mean $\pm$ SD of serum Fe concentration is summarized in Table 3 and Figure 1. The determination of serum Fe concentration in subject groups showed a statistically highly significant increase in group B when compared with the control group A ($P < 0.001$), as shown in Table 3 and Figure 1.

Table 4 and Figure 2 show that there was significant decrease of serum Se concentration in group B than in control group A, with $P < 0.001$. It is shown that, in this study, the patients with BC had significantly lower serum levels of Se than those found in healthy women.

Table 1: Ideal conditions for iron determination

Variable	Ideal condition
Lamp current (mA)	10
Wavelength (nm)	248.3
Slit width (nm)	0.5
Lighting mode	BGC -D2
Sample size (μl)	20
Replicates	3

Table 2: Ideal conditions for selenium determination

Variable	Ideal condition
Lamp current (mA)	23
Wavelength (nm)	196.0
Slit width (nm)	0.5
Lighting mode	BGC-D2
Sample size (μl)	20
Replicates	3

Table 3: Mean $\pm$ standard deviation of serum iron concentration in groups

Groups	n	Mean $\pm$ SD (ppb)	95% CI for mean		Minimum	Maximum	P
			Lower bound	Upper bound			
A Control	50	158.208 $\pm$ 5.031	155.422	160.995	150.97	170.21	<0.001*
B Patients	50	575.988 $\pm$ 5.407	572.993	578.982	568.42	589.48	
Total	100						

*The mean difference is significant <0.05 level. SD: Standard deviation, CI: Confidence interval

Table 4: Mean $\pm$ standard deviation of serum selenium concentration in groups

Groups	n	Mean $\pm$ SD (ppb)	95% CI for mean		Minimum	Maximum	P
			Lower bound	Upper bound			
A Control	50	126.924 $\pm$ 7.825	122.5908	131.2585	117.34	140.10	<0.001*
B Patients	50	69.066 $\pm$ 7.701	64.8012	73.3308	59.74	81.60	
Total	100						

*The mean difference is significant <0.05 level. SD: Standard deviation, CI: Confidence interval

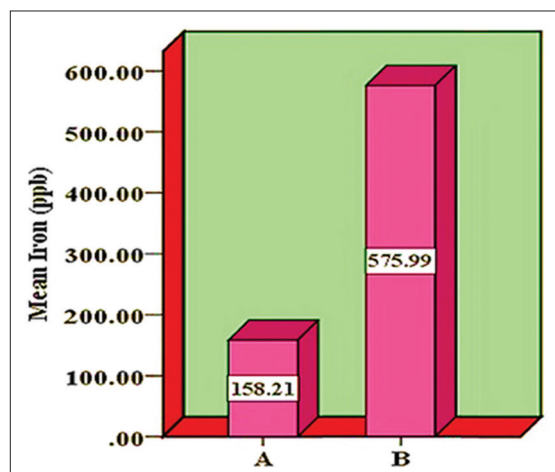


Figure 1: Mean $\pm$ standard deviation comparison of serum iron concentration in subject groups

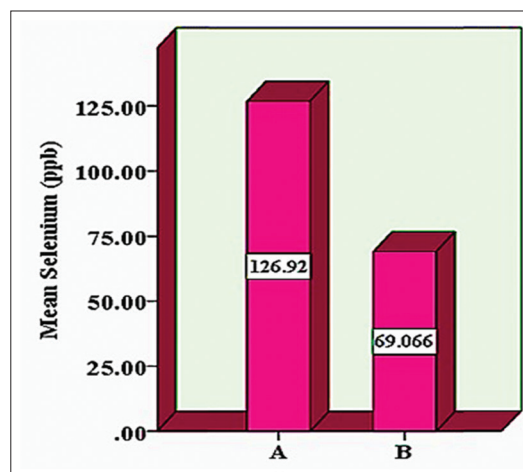


Figure 2: Mean $\pm$ standard deviation comparison of serum selenium concentration in subject groups

DISCUSSION

The reasons of differences in levels are typically found high level of Fe in patients with different types of BC. Increased serum-free Fe may be due to decrease in hemoglobin synthesis during progression of the disease which leads to anemia. Fe can thus induce free radicals which cause DNA double-strand breaks and oncogene activation. This was suggested by many epidemiological studies, showing a higher cancer risk in patients with larger Fe stores than in those with small Fe stores. In addition to its effect on carcinogenesis, Fe also maintains the growth of malignant cells as well as growth of pathogens.^[15]

These alterations in levels of Se concentrations may reflect part of the defense mechanisms against the carcinogenesis process. It was observed that alterations in serum concentrations of Se

in women with BC appear to be consequence, rather than a cause of cancer.^[16]

In accordance with the hypothesis, the findings suggested that very low Se status could be due to the nature of cancer. The antioxidant functions of Se have now been shown to reduce the risk of many cancers including BC.^[17,18] The healthy control women in this study had higher serum Se levels and lower serum Fe levels than did the patients with BC. Our data confirm previous reports of elevated serum Fe level and lowered serum Se level in BC patients.^[19]

As minerals appear to have important structural and enzymatic roles in the body, such some minerals have a role in antioxidant activities such as Se or some others have a role in stabilization of DNA, RNA, ribosome, and protein structures such as Fe, copper, and Zn. The increase or decrease of essential elements

concentration in the serum of BC patients may be one of the factors, which can lead to other biological processes to cause BC.^[20]

The detection and estimation of biomarkers in the study of malignancies were clearly interested. Alterations in the homeostatic concentrations of trace elements demonstrated to be very useful adjuncts in the estimation of extent disease and prognosis in patients with different types of cancers.^[21]

CONCLUSION

The present study findings demonstrate a significant decrease of essential trace element Se in the serum and significant increase of essential trace element Fe in BC patients compared with control group. Essential trace element helps in building the immune system including cancer prevention. These levels are important indication that there is a strong association of the population of Kirkuk with BC disease.

Acknowledgments

We would like to express the grateful and sincere thanks with all respect to all the patients who participated in this study. Special thank for Dean of Collage of Science/University of Kirkuk, supervisor, and other researchers at Chemistry Department for their help and continued support.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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