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Superoxide dismutase activity in breast cancer patients treated with anastrozole

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Abstract:
Anastrozole is an endocrine therapy which has been used for treatment of breast cancer patients. This study aimed to investigate the effect of anastrozole on superoxide dismutase (SOD) isoforms, include Cu/Zn-SOD and Mn-SOD, in postmenopausal women with breast cancer. This study included 70 postmenopausal women with breast cancer, including 40 untreated women with new diagnosed breast cancer (BC group) as well as 30 additional breast cancer women who received anastrozole therapy for three years (anastrozole group). Thirty postmenopausal women were categorized as healthy (control group). Our results showed a significant increase in SOD concentration of anastrozole group compared to BC and control groups. SODs activities (Cu/Zn-SOD and Mn-SOD) were decreased in anastrozole group compared to BC and control groups. SOD specific activities were increased under anastrozole treatment compared to BC group. We can conclude that the expression of SOD might be increased in BC patients as a response of free radical accumulation, However, not all of the SODs are expressed in active form. Furthermore, our data suggested that the treatment with anastrozole might be contributed in the improvement of the expression of activated SODs.

Key words: Breast cancer, Cu/Zn-SOD, Mn-SOD, reactive oxygen species, anastrozole.

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INTRODUCTION

Breast cancer is the most common occurring cancer in women globally and the second most frequent type after lung cancer [1, 2]. According to the Iraqi Cancer Registry, breast cancer is the most common type of female cancer accounting for almost one-third of all recorded female cancers [3, 4]. It is a complicated disease, and every woman is at risk of breast cancer injury. Several risk factors have been identified to play a possible role in developing of breast cancer, including age, previous breast cancer, genetic factors, early periods, late menopause [5, 6].

Estrogen receptors α (ERα) are expressed in approximately 70% of primary breast cancer. The endocrine therapy is a basis in treatment of hormone dependent breast cancer [7]. The mechanisms of this type of therapy depend on the interrupt the ER-signaling pathway, either through prevent interaction between estrogen and its receptor, or by reducing estrogen production through ablation of ovarian or inhibition of aromatase [8]. Aromatase inhibitor (AI), the adjuvant endocrine treatment, is a standard therapy for those cases, hormone dependent breast cancer, regardless of nodal status and tumor size [9]. Anastrozole is third-generation selective AIs that binds the aromatase enzyme reversibly and prevents androgens from being converted into estrogens. After surgery, anastrozole has been suggested as a portion of the endocrine therapy protocol for postmenopausal women with initial-stage breast cancer with hormone receptor-positive and lymph node-positive [10].

ROS has been documented to serve a pro-oncogenic role in the initial phases of cancer. The function of ROS in the progression of cancer appears to be stage-dependent [11]. Elevated ROS level often has been connected to DNA damage, infection or tissue injury, ionizing radiation, aging, cellular proliferation and mitochondrial DNA mutations [12]. However, growing evidence from recent studies reported a role of ROS in survival and other phenotypic behavior of tumor cells, signaling of proliferation, variation of DNA methylation in cancer suppressor genes and responsiveness to therapeutic interventions [13, 14]. Superoxide radicals are the main early form of ROS, which are very reactive and have an unpaired electron in an atomic or molecular space, are produced under normal conditions during aerobic metabolism and can injury almost every molecule in living

cells. Because the harmful effects of free radicals, they are normally destroyed or scavenged by antioxidants before they can cause damage to lipids, proteins, or nucleic acids [15]. The antioxidant enzymes Super Oxide Dismutase (SOD), Glutathione Peroxidase (GPx), and Catalase (CAT) are part of the complicated antioxidant defense system of human body. These enzymes prevent the start of free radical chain reactions and the negative effects of Reactive Oxygen Metabolites (ROMs) [16-18].

Super Oxide Dismutase (SOD), one of the most important antioxidant enzymes, stimulates the dismutation of extremely reactive $O_2\bullet$- to O_2 and H_2O_2, a less reactive ROS [19]. In human cells, there are two types of SOD: Mn-containing SOD (Mn-SOD), which is mostly found in mitochondria, and Cu/Zn-containing SOD (Cu/Zn-SOD), which is found mainly in the cytoplasm [20]. SOD may play an essential role in the maintenance of mammary tumors in addition to its potential effects on tumorigenesis [21, 22]. In comparison to normal mammary cells, an increase in the capacity of breast cancer cells to resist oxidative stress has been attributed in part to increase SOD activity in breast cancer cells [22, 23]. An increase in SOD expression of breast cancer cells that stimulated by ROS, in addition to interaction with circulating estradiol, may protect these cells from the harmful effects of oxidative stress [24]. Although being an antioxidant enzyme, an elevation of SOD activity may occasionally enhance oxidative stress as a result of peroxide accumulation. This oxidative stress occurs when the increase of SOD activity is not associated with increased activity of enzymes that removing of hydrogen peroxide [25].
The current study aimed to explore the effects of treatment with anastrozole on SOD levels in postmenopausal women with breast cancer compared to healthy individuals as well as the possibility of utilizing of SODs as a diagnostic marker for breast cancer progression under the effect of anastrozole therapy.

MATERIALS AND METHODS

The present research included 70 postmenopausal women with breast cancer who enrolled at Al-Amal National Cancer Hospital in Baghdad, Iraq, including 40 untreated women with new breast cancer (BC group) diagnoses by a physician consultant, as well as 30 additional breast cancer women who received anastrozole therapy for three years (Anastrozole group). Thirty postmenopausal women were categorized as healthy based on their history and had never previously had breast cancer served as the (control group), they were age and body mass index (BMI) matched to breast cancer patients. All of participants were informed about the details of the research, and their agreement was recorded. The collection of samples was done during the period from September 2022 to January 2023.

Determination of total proteins, albumin and globulins

The Total Protein (TP) level in serum was determined based on the Biuret method, using (Bio Systems kit, Spain), and the color intensity was detecting by spectrophotometer (APEL PD-303 analyzer, Japan). Albumin concentration (Alb) was determined using bromocresol green reagent (BioSystems kit, Spain). Globulins concentration (Glob) was calculated by subtracting the Alb concentration from the TP concentration.

Determination of zinc, copper and manganese elements

The zinc (Zn) and copper (Cu) concentrations in serum were measured spectrophotometrically using CENTRONIC GmbH kit (Germany). While the concentration of Manganese (Mn) in serum was measured using atomic absorption spectrometry after a 1+1 dilution with distilled water [26].

Determination of biochemical parameters

The concentrations of urea, creatinine, Glutamic Pyruvic Transaminase (GPT), glutamic oxaloacetic transaminase (GOT), and alkaline phosphatase (ALP) in serum were measured using conventional procedures and kits on a Cobas c311 auto-analyzer (Germany).

Determination of Hematology parameters.

The different parts of Complete Blood Counts (CBC) were determined using a CBC auto-analyzer (horiba, France).

Determination of carbonyls in oxidized proteins

The carbonyls in oxidized proteins have been identified using the dinitrophenyl hydrazine (DNPH) alkaline procedure [27]. The procedure involves adding 200 µL of

DNPH (10 mM in 0.5 M of H3PO4) to 200 µL of serum. After 10 minutes of incubation, 100 µL of NaOH (6M) was added. The absorbance of the sample at 450 nm was measured after 10 minutes of incubation at room temperature against a blank in which the protein solution was substituted with the same quantity of buffer solution. The concentration of carbonyl groups in serum was determined using the molar absorptivity of carbonyl group hydrazone derivatives (22308*10-6 M^{-1} cm^{-1}).

Determination of SOD Activity

The carbonyls in oxidized proteins have been identified using the dinitrophenyl hydrazine (DNPH) alkaline procedure [27]. The procedure involves adding 200 µL of DNPH (10 mM in 0.5 M of H3PO4) to 200 µL of serum. After 10 minutes of incubation, 100 µL of NaOH (6 M) was added. The absorbance of the sample at 450 nm was measured after 10 minutes of incubation at room temperature against a blank in which the protein solution was substituted with the same quantity of buffer solution. The concentration of carbonyl groups in serum was determined using the molar absorptivity of carbonyl group hydrazone derivatives (22308*10-6 M-1 cm-1).

SOD detection using native gel electrophoresis

A 1.5 mm mini-slab gel of 10% polyacrylamide in typical tris-glycine buffer (pH 8.3) was used for native polyacrylamide gel electrophoresis (PAGE). SOD protein (70 mg/mL) was mixed with loading buffer (0.05 M Tris-HCl buffer pH 6.8; 50% glycerol and 0.05% bromophenol blue) and loaded into each well to make samples (1:1). The electrophoresis ran for 15 minutes at 80V through the stacked gel and 60 minutes at 120V through the separation gel. Following native electrophoresis, the gel was stained with Coomassie Brilliant Blue R-250 (0.025% Coomassie Brilliant Blue, 10% acetic acid and 50% ethanol) for protein determination and destained in a 7.5% acetic acid, 30% ethanol solution.

SOD staining activity assay

The gel was stained for SOD activity with a modified riboflavin/NBT method [30]. SOD activity was measured using a photochemical method after electrophoresis [31]. In brief, the gel was pre-soaked for 15 minutes in a solution containing 1.225 mM Nitro Blue Tetrazolium, quickly washed, and then pre-soaked for 15 minutes in a solution included 100 mM potassium phosphate buffer, pH 7.0, containing 28 mM riboflavin and 28 mM TEMED. It was then illuminated for 15 minutes on a light box with four 18-W fluorescent lights to initiate the photochemical reaction.

Statistics

The SPSS program, version 22.0 was used for statistical assessments of the data. The data presented as median and standard deviation (SD), and for the average comparison between each of the groups, a one-way examination of variance (ANOVA) was used after the post-hoc least significant differences (LSD) test. Using Pearson's correlation, the relationship between parameters in newly diagnosed breast cancer and anastrozole -receiving women was examined. The sensitivity of the SOD for breast cancer screening has been evaluated using the receiver operating characteristic (ROC) curve.

RESULTS

Table 1 shows the demographic details of the women who participated in the study.

Tab. 1. Demographics of women with a new diagnosis (BC group) of breast cancer, women with breast cancer under anastrozole treatment (Anastrozole group), and control group

Parameter	Control	BC	Anastrozole	*p*-value
Age (year)	57.45±5.88	57.35±6.27	57.63±5.75	0.833a, 0.915b, 0.861c
BMI (kg/m^2)	25.65±3.99	27.62±4.47	26.55±3.32	0.112a, 0.421b, 0.344c
TP (g/dl)	6.74±0.64	6.97±0.55	7.11±0.58	0.226a, 0.338b, 0.437c
Alb (g/dl)	3.41±0.33	3.45±0.48	3.43±0.42	0.760a, 0.823b, 0.911c
Glob (g/dl)	3.33±0.55	3.52±0.49	3.64±0.67	0.317a, 0.074b, 0.482c
ALT (U/L)	21.05±6.01	22.15±6.80	30.57± 9.43	0.660a, 0.0001b, c
AST (U/L)	19.50±5.33	19.90±5.75	29.10±10.79	0.878a, 0.0001b, c
ALP (K.A.U)	93.55±20.99	87.15±20.93	87.50±20.60	0.334a, 0.318b, 0.954c

Urea(mg/dl)	33.85±8.61	27.15±7.27	35.20±4.95	0.003a, 0.480b,0.0001c
Creatinine(mg/dl)	0.87±0.16	0.75±0.16	0.86±0.63	0.022a, 0.873b, 0.019c
WBC (10^3/UL)	8.55±1.30	6.87±1.05	8.19±1.27	0.091a, 0.310b, 0.123c
LYM (10^3/UL)	32.70±5.82	30.20±4.32	33.70±4.82	0.162a, 0.538b, 0.054c
RBC (10^6/UL)	4.80±0.38	4.62±0.36	4.72±0.34	0.120a, 0.484 b, 0.310c
HGB(g/dl)	13.70± 0.86	13.61±0.94	13.53±0.89	0.541a, 0.985b, 0.516c
HCT (%)	41.10±2.60	40.84±2.82	40.61±2.86	0.767a, 0.533b, 0.765c
PLT (10^3/UL)	258.3±44.36	285.1±46.65	269.7±45.9	0.068a, 0.388b, 0.249c
Estrogen (pg/mL)	24.385±6.21	23.95±5.26	10.897±3.8588	0.429a 0.0001b,c

The results are presented as mean ±SD. P-value≤0.05 is considered as significant between a (control and BC groups), b (control and Anastrozole groups), and c (BC and Anastrozole groups).

No significant differences (P>0.05) were observed among three groups regarding age, BMI, TP, Alb, Glob, and ALP. Also, CBC data include WBC, RBC, HGB, HCT, and PLT did not show significant differences (P>0.05) among the studied groups. The level of ALT, AST was increased significantly (P<0.05) in Anastrozole group, compared to control and BC groups. However, a non-significant difference (P>0.05) in ALT, AST were observed between control and BC groups. The level of urea and creatinine was declined significantly (P<0.05) in BC group compared to control and Anastrozole groups. However, a non-significant difference (P>0.05) in urea and creatinine were noticed between control and Anastrozole groups. The level of estrogen hormone was non-significantly (P>0.05) changes between control and BC groups. On the other hand, estrogen level was significantly (P<0.0001) decreased in Anastrozole group compared to control and BC groups, Table 1. The statistics of SOD concentration and activities, oxidized proteins, Cu, Zn and Mn are presented in Table 2.

Tab. 2. Characteristics of SOD, oxidized proteins and trace elements of women with newly diagnosed BC (BC group), women with breast cancer under anastrozole treatment (Anastrozole group), and control group

Parameter	Control	BC	Anastrozole	*P*-value
SOD Conc. (ng/ml)	14.11±0. 95	27.61±4.67	18.47±1.66	0.0001a b,c
T-SOD activity (U/mL)	49.55±3.37	33.56±4.3	30.86±4.13	0.0001a,b, 0.022c
Cu/Zn-SOD activity(U/mL)	24.25±5.01	17.35±3.98	15.66±3.21	0.0001a,b, 0.148c
Mn-SOD activity (U/mL)	25.30±5.74	16.20±4.43	15.20±3.94	0.0001a,b, 0.457c
T-SOD specific activity(U/mg)	35.28±3.40	12.47±2.66	16.81±2.49	0.0001a,b,c
Cu/Zn-SOD specific activity(U/mg)	18.03±4.35	6.01±1.87	8.33±2.40	0.0001a,b, 0.009c
Mn-SOD specific activity(U/mg)	17.25±3.59	6.46±1.94	8.47±1.49	0.0001a, b, 0.005c
Oxidized proteins (μM)	8.26±0.79	9.98±0.31	10.87±0.71	0.0001a, b,c
Cu (mg/dl)	113.4±20.39	109.4±23.46	120.1±23.16	0.576a, 0.308b, 0.105c
Zn (μg/dl)	104.35±26.46	99.45±22.65	105.9±23.14	0.521a, 0.824b, 0.355c
Mn (ng/dl)	13.07±3.09	12.18±3.06	12.34±3.62	0.399a, 0.448b, 0.868c

The results are presented as mean ±SD. P-value≤0.05 is considered as significant between a (control and BC groups), b (control and Anastrozole groups), and c (BC and Anastrozole groups).

The clinical results also showed that SOD concentration was significantly increased (P<0.0001) in BC and Anastrozole groups compared to control group. However, a significant decrease in SOD concentration of Anastrozole group compared to BC group was observed. In comparison to control group, T-SOD, Cu/Zn-SOD and Mn-SOD activities were significantly declined (P<0.0001) in BC and Anastrozole groups. The specific activity of T-SOD, Cu/Zn-SOD and Mn-SOD was reduced significantly (P<0.0001) in BC group and

Anastrozole group compared to control group. Moreover, the T-SOD specific activity was observed to be significantly lower (P<0.0001) in BC group compared to Anastrozole group, Table 2.

The oxidized protein level was increased significantly (P<0.0001) in BC and Anastrozole groups compared to control group. Furthermore, a significant increase (P<0.0001) was observed in Anastrozole group compared to BC group. The level of C7u, Zn, and Mn was non-significantly (P>0.05) changed among the studied group, Table 2.

Based on the evaluation of all the samples, a noticeable decrease in the band intensity of BC and Anastrozole groups was appeared on PAGE gel compared to the band of control group when the same SOD amount was applied for all the examined samples, Figure 1.

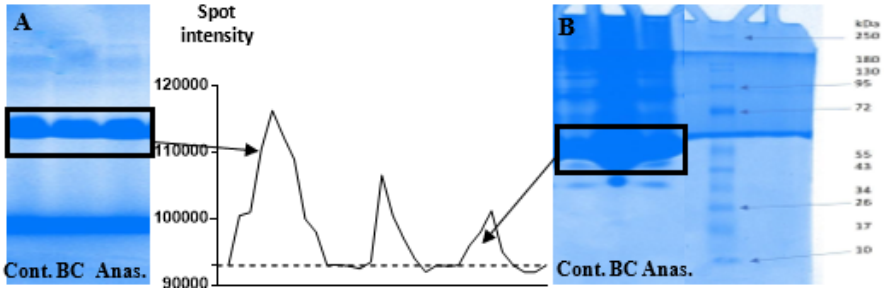

Fig 1. Comparison of SOD level in control, BC and anastrozole groups using native PAGE staining A) for SOD activity B) for protein and the histogram, the digitalized images of gel was converted into electropherograms.

The Pearson's correlations among the studied parameters of BC group showed a strong positive correlation between the T-SOD activity and Mn-SOD activity (r=0.584, P=0.007), whereas a negative moderate correlation was found between Mn-SOD activity and Cu/Zn-SOD activity (r=-0.481, P=0.032). In addition, Alb (r=-0.460, P=0.041) and Mn (r=-0.455, P=0.044) were negatively correlated with oxidized proteins (Figure 2).

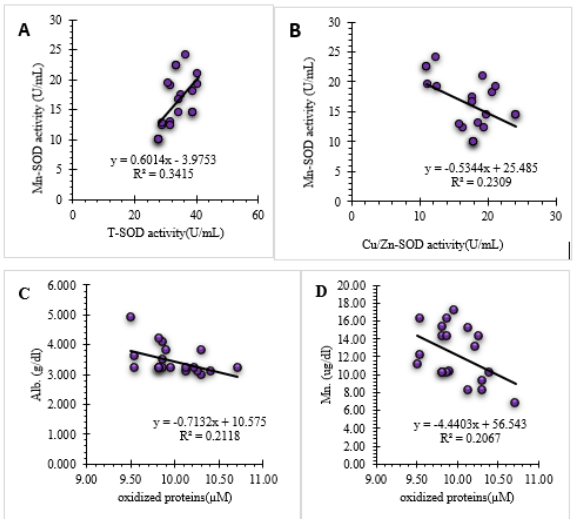

Fig 2. Pearson's correlation of A) T-SOD activity with Mn-SOD activity, B) Cu/Zn-SOD activity with Mn-SOD activity, C) Alb with Oxidized protein, and D) Mn with oxidized protein.

The Pearson's correlation among the studied parameters of Anastrozole group showed a positive correlation between the Cu/Zn-SOD activity and each of SOD concentration (r=0.451, P=0.012) and T-SOD activity (r=0.447, P=0.013). Also, a strong positive correlation was found between Mn-SOD activity and T-SOD activity (r=0.686, P=0.0001). However, T-SOD activity (r=-0.439, P=0.015) and Mn-SOD activity (r=-0.474, P=0.008) have negative correlations with oxidized proteins (Figure 3).

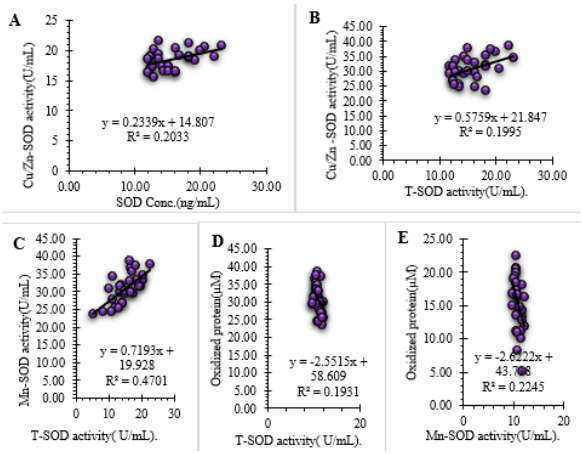

Fig 3. Pearson's correlation of A) Cu/Zn-SOD activity with SOD concentration, B) T-SOD activity with Cu/Zn-SOD activity, C) Mn-SOD activity with T-SOD activity, D) T-SOD activity with Oxidized protein, and E) Mn-SOD activity with Oxidized protein.

The ROC curves of SOD enzymes demonstrated that T-SOD specific activity can be used as an excellent sensitive biomarker in the prognosis of breast cancer under anastrozole treatment, in which the AUC of total SOD specific activity was 0.878 with 77% sensitivity and 98% specificity at a cut-off value of 12.98 U/mg. Mn-SOD specific activity showed an excellent specificity in the prognosis of breast cancer under anastrozole treatment, in which the AUC of Mn-SOD specific activity was 0.780 with 65% sensitivity and 90% specificity at a cut-off value of 6.87 U/mg. Cu/Zn-SOD specific activity represented a good specificity in the prognosis of breast cancer under anastrozole treatment, in which the AUC of Cu/Zn-SOD specific activity was 0.812 with 69% sensitivity and 93% specificity at a cut-off value of 6.62 U/mg (Table 3).

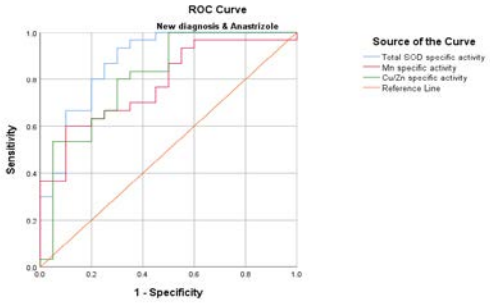

Fig 4. The ROC curve of T-SOD, Cu/Zn-SOD, and Mn-SOD specific activities in differentiation between newly diagnosed BC and Anastrozole-treated patients.

Tab 3. ROC results of SOD isoforms in the differentiation between newly diagnosed BC and Anastrozole -treated patients.

Parameter	AUC	*p*-value	Cut-off	Sensitivity	Specificity
T-SOD specific activity	0.878	0	12.98	77%	98%
Mn-SOD specific activity	0.78	0.001	6.87	65%	90%
Cu/Zn-SOD specific activity	0.812	0	6.62	69%	93%

DISCUSSION

The first aim of this study was to assess the effect of anastrozole on some biochemical parameters that are linked to renal function, liver function and CBC in postmenopausal women with breast cancer. It was noticed that there were no significant differences in TP, Alb, Glob, ALP, WBC, RBC, LYM, HGB, HCT and PLT in

postmenopausal women with breast cancer compared to control. These results are consistent with results reported by Goss,P.E. *et al* [32]. However, urea and creatinine were significantly decreased in those patients compared to control. It has been reported that protein catabolism leads to release of nitrogen molecules, a highly toxic metabolite, in the form of ammonia [33]. The organisms are usually stimulating specific pathways, the urea cycle, to dispose the excess of ammonia by converted it to urea and excreted through urine. Recent studies propose a potential relationship between dysregulation of the urea cycle and cancer pathogenesis [34]. In cancer cells, dysregulation of urea cycle stimulates cell proliferation through redirecting of nitrogen molecules from converting to urea to biosynthesis of molecules, thus enabling cancer growth [35]. *In vitro* experiments on ovarian cancer, melanoma and hepatocellular carcinoma cell lines confirmed that perturbations of urea cycle enzymes stimulate the proliferation of malignant cells, through a redirecting of the nitrogen substrate to the biosynthesis of pyrimidine[36] . In breast cancer and lung cancer cell lines, increase ammonia was not converted to urea but was involved into amino acids and other macromolecules biosynthesis, such as nucleotides and lipids, providing energy to the metabolically depleted cells [37]. Creatinine, the end product of glycine and arginine catabolism, has also been studied in several types of cancer, and used as prognostic marker in different types of epithelial cancers [38]. The association between low creatinine and breast cancer may be attributed to low production creatinine volume, which are resulted from low muscle mass and reduced food intake, and/or a high filtration rate of renal [39]

Under effect of Anastrozole treatment, parameters include TP, Alb, Glob, ALP, WBC, RBC, LYM, HGB, HCT and PLT did not appear a noticeable change compared to control and BC patients. Regarding to urea and creatinine, it was observed an improvement in these parameters after treatment with anastrozole to be comparable with control group. Nevertheless, ALT and AST were significantly increased under effect of anastrozole compared to BC and control groups. This result is consistent with the results from Li Y.C. *et al.* which reported that anastrozole can significantly increase the level of ALT and AST in patients with breast cancer [40]. It was reported that this mild elevation in ALT and AST levels has been rare instances of clinically apparent liver injury linked with anastrozole therapy. This result was agreement with Nakayama T. *et al.* study [41].

Estrogen level was markedly decreased in patients under treatment of anastrozole[42, 43]. Estrogen has been demonstrated to support neoplastic and cancer development via relationships with ER alpha and beta (ER)[44]. It has a major role in cell growth and division in breast cancer. Anti-estrogen therapies have been effectively utilized to prevent the activation of genes by the ER. Our data indicated that in breast cancer patients, the estrogen level was remarkably reduced in patients under anastrozole compared to untreated patients and healthy women. Anastrozole are effective estrogen therapy for ER+ breast cancer in postmenopausal women because they can deactivate aromatase, prevent aromatase action, decrease estrogen synthesis, and lower blood estrogen concentrations[32, 45]. It might decrease estrogen-dependent breast cancer growth through changing androgen activity via the androgen receptor (AR) [46].

The second and main aim of this study deals with the effect of anastrozole on the level of SOD isoenzymes. Several studies have revealed that mechanisms of antioxidant resistance are significantly compromised in patients with malignant breast tumors. Reduced SOD levels make cells produce free radicals. The imbalance between the free radical generation and mechanisms of defense that scavenge these free radicals are considered a substantial factor leading to tumor development [47, 48]. There has been a contradiction about the SOD level in breast cancer patients. The overexpression of SOD might be serving as compensatory mechanism to protect cells from oxidative stress. However, results of decrease SOD activity propose a higher consumption of antioxidant enzymes due to oxidative stress [11]. To the best of our knowledge, there has been no study investigated the level of SOD in breast cancer patients who are under anastrozole treatment. Our results indicated that SOD was overexpressed in postmenopausal women with BC compared to healthy women. This result is agreement with Rajneesh C. *et al.*[49]. Also, a study by Portakal *et al.*, which carried out on 21 breast cancer patients, found a significant increase in the expression of SOD, CAT, and GPx in breast cancer tissue in comparison to cancer-free tissue samples [50]. Under effect of anastrozole treatment, SOD concentration was decreased significantly compared to untreated women, however, it was remained at high level compared to control group. On the other hand, the

T-SOD, Cu/Zn-SOD and Mn-SOD activities were decreased dramatically in postmenopausal women with breast cancer and this declined was continued after treatment with anastrozole compared to control. Several studies are consistent with our results and reported a remarkable decrease in SOD activity of breast cancer patients compared to healthy individuals [51-52]. A study by Unfer T. *et al*. reported that estrogen enhances the Cu/Zn-SOD activity [25]. Anastrozole acts to prevent the synthesis of estrogen and consequently decreases Cu/Zn-SOD activity.

According to our results, we suggested that the expression of SOD might be increased in BC patients as a response to free radical accumulation that associated with breast cancer incidence. However, not all of SODs are expressed in active form and this can be observed clearly from the data of SOD specific activities (Table 2). Furthermore, the expression of activated SODs was improved in breast cancer patients under treatment of anastrozole to reach its corresponding level in the healthy individuals. Thus, this result might be reflected the positive effect of anastrozole treatment against the breast cancer progression.

A strong negative correlation between SODs and oxidized proteins introduces clear evidence on the protective role of SODs against free radicals. The oxidized protein was also negatively correlated with Alb and Mn which might be indicated to possible antioxidant role of Alb and Mn. Analysis data of ROC curves indicated that SOD specific activity can be used for monitoring of breast cancer progression under anastrozole treatment and introduce a potential biomarker for breast cancer progression under anastrozole treatment.

CONCLUSION

Depending on our findings, breast cancer stimulates the generation of SODs, either with or without activity. Anastrozole treatment improves the expression of activated SODs in breast cancer patients to reach its corresponding level in the healthy individuals. Furthermore, the ROC results suggest that SOD specific activities could be used as a diagnostic indicator for evaluating anastrozole effect on breast cancer progression.

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CONFLICT OF INTEREST

The authors of this paper declare that they have no conflicting goals.

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