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Assessment of systemic oxidative stress and antioxidants in Iraqi women with newly diagnosed and tamoxifen-treated breast cancer

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Breast cancer (BC) is one of the most frequently observed malignancy in females worldwide. Today, tamoxifen (TAM) is considered as the highly effective therapy for treatment of breast tumors. Oxidative stress has implicated strongly in the pathophysiology of malignancies. This study aimed to investigate the changes in the levels of oxidants and antioxidants in patients with newly diagnosed and TAM-treated BC. Sixty newly diagnosed and 60 TAM-treated women with BC and 50 healthy volunteers were included in this study. Parameters including total oxidant capacity (TOC), total antioxidant capacity (TAC), and catalase (CAT) activity were determined before and after treatment with TAM. The serum levels of TOC and oxidative stress index (OSI) were elevated significantly (P<0.001) in newly diagnosed BC patients compared with control, while the level of TAC and CAT activity were observed to be statistically declined (P<0.001). Furthermore, the BC patients on TAM treatment have shown highly significant levels of serum TOC (P<0.05) and TAC (P<0.001) with a significant reduction (P<0.001) in CAT activity compared with control. In TAM-treated patients compared with newly diagnosed BC patients, the TOC level was decreased, the TAC level was increased, the OSI level was decreased and the CAT activity was decreased. The results indicate a strong and aggressive association between oxidative stress and the first onset of BC, as well as the tendency of TAM drug to improve the levels of TOC, TAC, and OSI in BC patients, but it had a reduction influence on CAT activity.

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KEYWORDS

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Introduction

Breast cancer (BC) is one of the most frequently observed malignancies in females worldwide [1-3]. Metastasis is one of the characteristics associating with the BC progression leading to organs damage and mortality in females [4]. Although breast tumors are found in males, but it is much less than females [5]. Tamoxifen (TAM) is considered the highly effective therapy for tumors treatment, especially breast tumors [6]. Tamoxifen has an agonist effect on the skeletal, hepatic, and vascular system, and lowering total cholesterol and LDL cholesterol [7]. It also has an antagonistic impact in the uterine and mammary cells, or a dual impact based on the species, target gene, and tissue [8]. Tamoxifen has been used to treat BC depending on its regulatory effect on

the estrogen receptor [7,8]. The association of oxidative stress with BC has been reported extensively in patients and suggested to play an important part in the development, physiology, and treatment resistance in BC patients [9,10].

The oxidative stress has implicated strongly in the malignancies pathophysiology [11]. It can be defined by using two parameters; the first came from the first part of the term, oxidative, which implies the oxidants presence. The oxidants in biological systems are materials have more electrons than their stabilization required which called free radicals [12]. Nevertheless, it is not necessary for the biological oxidant material to be free radicals; it can comprise the other materials with short half-life that upon composition yield free radicals. The most common oxidant materials in the biological system are termed reactive oxygen species (ROS) [13,14]. This term involves any oxygen-contained materials in the biological system with short-life, high reactivity, and low-stability which may be a free radical such as hydroxyl radical, and superoxide anion, or non-radical materials such as hydrogen peroxides and lipid peroxides [15]. The other parameter on which oxidative stress definition depends is the antioxidants. These materials are specialized in neutralizing the oxidant materials through several mechanisms [16]. Antioxidants are commonly categorized into enzymatic and non-enzymatic classes [17,18]. Eventually, oxidative stress can result from either high content of oxidants or low capacity of antioxidants, or both [19]. The oxidative stress is also known as the damage occurring to the macromolecules of the cells as a consequence of overproduction in the ROS or a reduction in the antioxidants [20-25]. The ROS generation and susceptibility to ROS-induced cytotoxicity are two traits linked with the mitochondrial dysfunction. Higher ROS quantities have been identified in several varieties of cancer and it was proposed that the elevated ROS amounts in non-transformed cells or tumor cells may have pro-tumorigenic consequences by destroying nucleic acids and causing genomic instability [26]. Among the most abundant antioxidant enzymes is catalase (CAT; EC 1.11.1.6) [27]. The major biological activity of CAT is to dismutase hydrogen peroxide into molecular oxygen and water. As a result of its capacity to adjust H_2O_2 levels, CAT is engaged in several H_2O_2-regulated activities. Hydrogen peroxide is generated via complicated lipid metabolic processes in peroxisomes, the mitochondrial electron transport chain, and the other metabolic activities [28]. It has the ability to generate other forms of ROS via Fenton reaction. Catalase is critical in preserving cells from the cellular damaging impacts of ROS [29]. Catalase and the other antioxidant enzymes are frequently changed in tumor cells and it is well-recognized that CAT and other antioxidant enzymes play a key contradictory effect in malignancy [30]. The link between CAT and tumor cells was documented in the literature as a mechanism in which tumor cells develop resistance to the endogenous ROS by overexpressing CAT to detoxify hydrogen peroxide and protect the tumor cell from eventual apoptosis [31]. In contrast, the recent investigations have revealed that CAT expression is downregulated in certain malignancies [32]. Catalase expression, on the other hand, is strongly expressed in certain cancer cells, notably in acute myeloid leukemia. It is also worth noting that cells from patients who remain in complete remission for a longer period have greater CAT levels than patients who develop treatment resistance, implying that medication resistance is connected with the increased ROS levels [33].

This work aimed to investigate the redox imbalance in newly diagnosed BC patients to evaluate the influence of oxidative stress on the BC development. Moreover, the oxidative stress was examined in BC patients under the treatment with TAM to explore the effect of

TAM on the redox balance in these patients. Total oxidant capacity (TOC) has been used as an oxidants indicator, while total antioxidant capacity (TAC), and the activity and specific activity of CAT have been used as indicators of antioxidants.

Materials and methods

Study design

The women with BC disease were registered at Tumor Teaching Center at the Medical City of Baghdad, Iraq. The current study was included sixty untreated women with new diagnosis of BC (BC group) in the consultancy of Tumor Teaching Center. Another sixty women with BC disease under TAM treatment for two years (TAM group) were also included in the study. This work was controlled with 33 women (control group) who were considered healthy according to their history, without prior BC, and were matched the age and body mass index (BMI) of BC women. All of the included women were informed about the criteria of this study and their agreement was registered. The sample collection was preceded during the period from November 2021 to June 2022. Furthermore, the study was approved by the consultancy of the scientific board at the Department of Chemistry, College of Science, Baghdad University. Patients who take of alcohol, smoking, and TAM therapy before admission and/or medication were excluded from the study. Patients with a history of chronic diseases before admission were further excluded from this study.

Evaluation of total oxidant capacity

The TOC level in sera samples was evaluated according to the method of Erel O. [34]. Briefly, 675 µL Reagent A (xylenol orange 150 µM, NaCl 140 mM, and glycerol 1.35M in 25 mM H_2SO_4 solution, pH 1.75) was mixed with 105 µL of serum and the first absorbance of samples was read spectrophotometrically at 560 nm as a sample blank. Then, 33 µL Reagent B (5 mM of $Fe(NH_4)_2(SO_4)_2.6H_2O$ and 10 mM of O-dianisidine in 25 mM H_2SO_4 solution) was added to the mixture and mixed for 4 minutes, and then the second absorbance was read at 560 nm. TOC was calculated based on the absorbance differences at 560 nm before and after adding the Reagent B. The assay was calibrated with H_2O_2 and the results were expressed in terms of µM H_2O_2 equivalent per liter (µmol H_2O_2 Equiv/L).

Evaluation of total antioxidant capacity

The TAC level was evaluated according to the method of Erel O. [35]. For the TAC measurement in sera samples, 1 mL Reagent A (10 mM of O-dianisidine and 45 µM of $Fe(NH_4)_2(SO_4)_2.6H_2O$ in 75 mM KCl solution, pH 1.8) was mixed with 25 µL of serum and the first absorbance of samples was read spectrophotometrically at 444 nm as a sample blank. Then, 50 µL Reagent B (H_2O_2, 7.5 mM in 75 mM KCl solution, pH 1.8) was added to the mixture and mixed for 4 minutes and the second absorbance was read at 444 nm. The total antioxidant capacity was calculated based on the absorbance differences at 444 nm before and after adding the Reagent B. The assay was calibrated with uric acid and the results were expressed in terms of millimolar uric acid equivalent per liter (mmol uric acid Eq./L).

Calculation of oxidative stress index

The oxidative stress index (OSI) was calculated after converting of TAC unit into (µmol uric acid Eq./L) according to the following equation:

$$OSI\ (arbitrary\ unit) = \frac{TOC\ (\mu mol\ H_2O_2 Eq./L)}{TAC\ (\mu mol\ uric\ acid\ Eq./L)} \times 100$$

Evaluation of catalase activity

The CAT activity was determined in serum using spectrophotometric method described by Goth L. [36]. For the measurement of CAT activity in sera samples, 250 µL Reagent A (H_2O_2, 65 µmol/mL) was mixed with 50 µL of serum. The assay was corrected using blank 1 containing 250 µL Reagent A and 50 µL Reagent B (Sodium-Potassium buffer, 6 mM, pH 7.4) and blank 2 containing 300 µL Reagent B. All tubes were incubated at 37 ºC for 60 seconds. Finally, 250 µL ammonium molybdate 32.4 mM was added to the mixture and the absorbance was read at 405 nm.

Evaluation of serum proteins

The level of total protein (TP) in the serum was determined using cobas kit. This kit depends on a colorimetric assay in which divalent copper reacts in alkaline solution with protein peptide bonds to form the characteristic purple-colored biuret complex. The color intensity which is directly proportional to the protein concentration was determined photometrically in cobas c311 autoanalyzer, and the TP concentration was obtained in g/dL unit.

Evaluation of serum albumin and globulins

The level of albumin (Alb) in the serum was determined using cobas kit. This kit depends on a colorimetric assay in which acidic buffer with *p*H 4.1 used to force albumin to have negative net charge that enables it to bind with bromcresol green, an anionic dye, to form a blue-green complex. The color intensity is directly proportional to the Alb concentration which was determined photometrically in cobas c311 autoanalyzer, and the Alb concentration was obtained in g/dL unit. Globulins (Glb) level was calculated by Alb subtraction from TP concentrations.

Statistics

The data were analyzed statistically using SPSS program version 26.0 software for mean comparison using one-way analysis of variances (ANOVA), and followed by the post-Hoc least significant differences (LSD) test for the mean comparison between each two groups. Pearson's correlation was used to analyze the association among the parameters in the early diagnosed BC and TAM-treated women. In addition, the sensitivity of using TOC, TAC, OSI, and CAT in the BC prognosis was analyzed using receiver operating characteristic (ROS) test through measuring the area under the curve (AUC).

Results

The statistically processed data are expressed in the form of mean, standard deviation (SD), median, and mix-max. The demographic characteristics with the oxidative stress parameters and serum proteins are listed in Table 1. The TOC and OSI levels were extremely elevated (P<0.001) in BC patients, while TAC and CAT were extremely declined (P<0.001). It was also observed that the TOC and TAC levels were significantly higher (P<0.01) in TAM-treated patients compared with control, while the CAT activity was statistically decreased (P<0.001), as compared with control. Although a dramatic surge (P<0.0001) can be clearly observed in BC patients, the OSI values were not shown a significant increase (P>0.05) in TAM-treated patients compared with control. In TAM-treated patients compared with newly diagnosed BC patients, the TOC level was decreased, the TAC level was increased, the OSI level was decreased, and the CAT activity was decreased. Furthermore, no significant change was observed in the levels of serum proteins among the studied groups.

TABLE 1 Demographical and biochemical data of control, BC, and TAM-treated females

Parameter n	Control 33	BC 60	TAM 60	*P*-value -
Age (year)	44.97±6.76 45 35-56	43.03±4.50 43 32-51	44.15±5.05 44.50 34-55	0.092 [a], 0.474 [b], 0.247 [c]
BMI (kg/m²)	23.41±2.15 23.78 18.91-28.19	22.49±2.81 23.003 15.09-27.78	22.06±2.66 22.19 16.45-31.77	0.107 [a], 0.019 [b], 0.375 [c]
TP (g/dL)	7.00±0.62 6.90 5.40-8.20	7.02±0.67 7.10 6.0-8.30	7.01±0.71 6.95 6.0-8.50	0.909 [a], 0.936 [b], 0.968 [c]
Alb (g/dL)	4.21±0.49 4.10 3.40-5.30	4.13±0.58 4.05 3.10-5.30	4.14±0.61 4.00 3.10-5.30	0.535 [a], 0.598 [b], 0.912 [c]
Glb (g/dL)	2.79±0.37 2.80 2.0-3.50	2.89±0.44 2.90 1.40-3.80	2.87±0.34 2.90 2.20-3.50	0.269 [a], 0.363 [b], 0.816 [c]
TOC (µmol H_2O_2 Eq./L)	17.88±12.19 27.50 5.0-60.0	29.38±12.11 27.50 10.0-78.0	24.95±11.84 25.00 9.0-60.0	0.0001 [a], 0.007 [b], 0.045 [c]
TAC (mmol uric acid Eq./L)	4.95±0.68 4.81 4.08-6.61	1.32±0.64 1.28 0.12-3.48	6.09±0.45 6.12 5.01-6.78	0.0001 [a,b,c]
OSI	371.25±258.5 312.38 87.78-1143.71	2948.81±2482.9 2512.27 786.85-16934.73	408.18±185.4 374.06 155.29-920.31	0.0001 [a,c], 0.914 [b]
CAT (kU/L)	276.91±65.18 288.73 23.14-358.15	222.46±40.84 222.70 150.12-288.51	122.32±90.36 89.38 4.84-307.54	0.0001 [a,b,c]
CAT (kU/g)	4.0±1.07 4.185 0.34-5.59	3.22±0.75 3.162 1.86-4.69	1.73±1.28 1.206 0.06-5.04	0.001 [a], 0.0001 [b,c]

The results are presented as mean±SD, median, and min-max, *P*-value≤0.05 is considered as significant between a (control and BC), b (control and TAM), and c (BC and TAM).

The correlation between variables in newly diagnosed BC patients is presented in Table 2. TAC has illustrated the significant negative moderate correlation with OSI, and the positive weak correlation with CAT. Moreover, OSI has shown the significant negative weak correlation with CAT. Moreover, CAT has demonstrated the significant negative weak correlations with TP, Alb, and BMI.

TABLE 2 Pearson correlation in newly diagnosed BC women

Variables	TOC		TAC		OSI		CAT activity		CAT specific activity	
	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Age	0.042	0.748	0.127	0.334	-0.236	0.070	0.018	0.892	0.055	0.676
BMI	-0.094	0.473	-0.045	0.733	-0.001	0.996	-0.268*	0.038	-0.267*	0.039
TP	0.052	0.964	-0.125	0.341	0.080	0.542	-0.351*	0.006	-0.669*	0.0001
Alb	0.080	0.545	-0.064	0.627	0.132	0.315	-0.346*	0.007	-0.575*	0.0001
Glb	-0.026	0.842	-0.104	0.429	-0.052	0.695	-0.075	0.571	-0.252	0.052
TOC	-	-	0.124	0.346	0.249	0.055	0.134	0.307	0.095	0.472
TAC	0.124	0.346	-	-	-0.608*	0.0001	0.306*	0.017	0.288*	0.026
OSI	0.249	0.055	-0.608*	0.0001	-	-	-0.300*	0.020	-0.271*	0.036
CAT(kU/L)	0.134	0.307	0.306*	0.017	-0.300*	0.020	-	-	0.926*	0.0001
CAT(kU/g)	0.095	0.472	0.288*	0.026	-0.271*	0.036	0.926*	0.0001	-	-

The correlation between variables in TAM-treated patients is listed in Table 3. TOC has shown the significant positive strong correlation with OSI. Moreover, TAC has shown the significant positive weak correlation with TP and Alb.

TABLE 3 Pearson correlation in TAM-treated women

Variables	TOC		TAC		OSI		CAT activity		CAT specific activity	
	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Age	-0.002	0.987	0.057	0.665	-0.009	0.947	-0.164	0.212	-0.130	0.324
BMI	-0.069	0.599	-0.104	0.430	-0.049	0.708	0.052	0.693	0.047	0.723
TP	0.084	0.521	0.260*	0.045	0.054	0.683	0.235	0.071	0.086	0.513
Alb	-0.034	0.798	0.254*	0.050	-0.068	0.605	0.188	0.150	0.062	0.636
Glb	0.235	0.071	0.081	0.536	0.233	0.073	0.149	0.257	0.066	0.614
TOC	-	-	0.252	0.052	0.985*	0.0001	0.041	0.757	0.032	0.811
TAC	0.252	0.052	-	-	0.094	0.477	-0.008	0.952	-0.070	0.597
OSI	0.985*	0.0001	0.094	0.477	-	-	0.043	0.745	0.042	0.751
CAT(kU/L)	0.041	0.757	-0.008	0.952	0.043	0.745	-	-	0.984*	0.0001
CAT(kU/g)	0.032	0.811	-0.070	0.597	0.042	0.751	0.984*	0.0001	-	-

The ROC curve of TOC has shown a fair usefulness (AUC 0.785) in the BC prognosis with cut-off value of 22.50 µmol H_2O_2 Eq./L in 65% sensitivity and 75.8% specificity, as displayed in Figure 1A. TAC has shown the high sensitivity (AUC 1.000) in the prognosis of BC with cut-off value of 3.78 mmol uric acid Eq./L, in 100% sensitivity and 100% specificity, as depicted in Figure 1B. OSI has shown the excellent sensitivity (AUC 0.994) in the BC prognosis with cut-off value of 967.20 in 95% sensitivity and 97% specificity, as indicated in Figure 1C. Moreover, CAT activity has shown good sensitivity (AUC 0.883) in the prognosis of BC with cut-off value of 267.71 kU/L in 81.8% sensitivity and 81.7% specificity, as exhibited in Figure 1D. The specific activity of CAT has shown fair sensitivity (AUC 0.767) in the BC prognosis with cut-off value of 3.71 kU/g in 75.8% sensitivity and 75% specificity, as demonstrated in Figure 1E.

TABLE 4 ROC of TOC, TAC, OSI, and CAT in the BC prognosis

Variables	AUC	SE	*P*-value	Cut-off	Sensitivity	Specificity
TOC	0.785	0.054	0.0001	22.50	65%	75.8%
TAC	1.000	0.0001	0.0001	3.78	100%	100%
OSI	0.994	0.005	0.0001	967.20	95%	97%
CAT(kU/L)	0.883	0.054	0.0001	267.71	81.8%	81.7%
CAT(kU/g)	0.767	0.057	0.0001	3.71	75.8%	75%

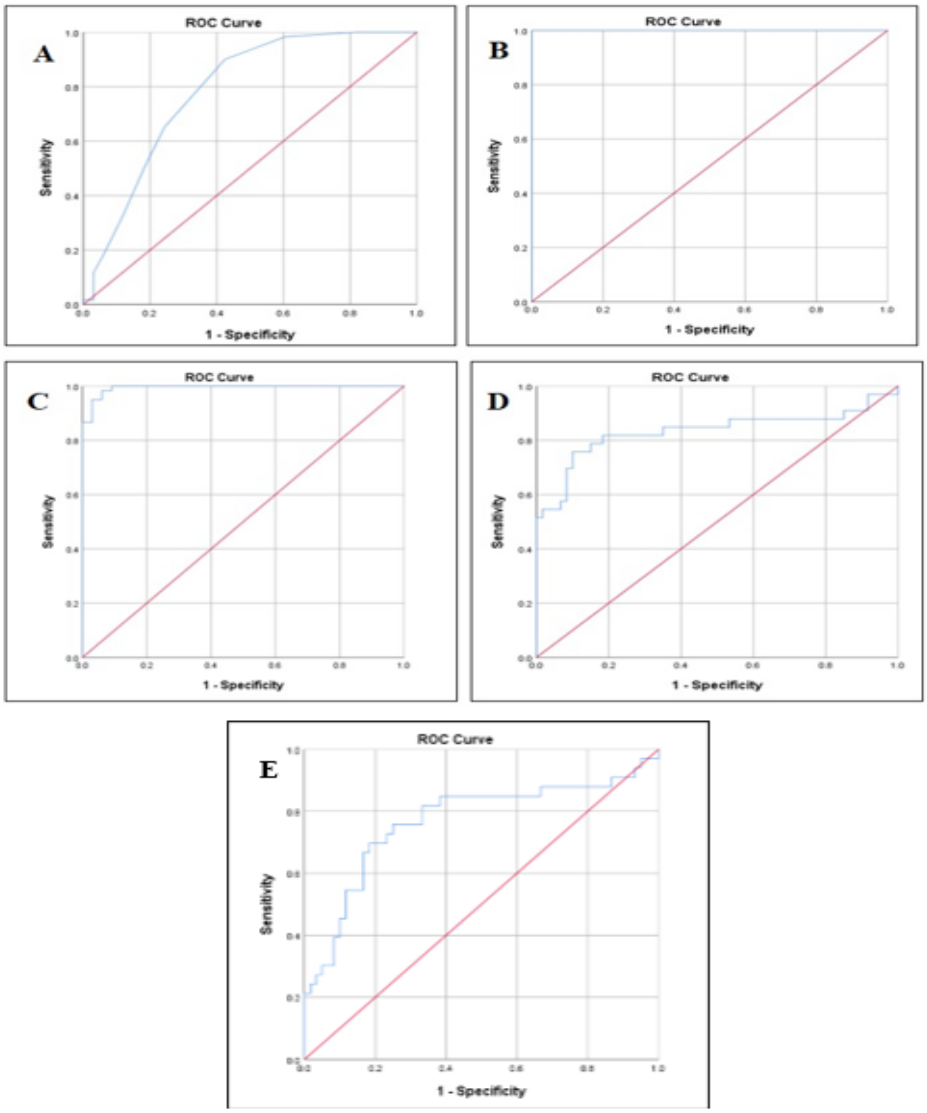

FIGURE 1 The ROC of TOC (A), TAC (B), OSI (C), CAT (D), and CAT specific activity (E) in the BC prognosis

ROC analysis was also used to differentiate newly diagnosed BC from TAM-treated BC patients (Table 5). The ROC curve of TOC has shown a poor usefulness (AUC 0.614) in the differentiation between newly diagnosed BC and TAM-treated patients with cut-off value of 27.50 μmol H_2O_2 Eq./L in 50% sensitivity and 61.7% specificity, as illustrated in Figure 2A. TAC has shown very excellent sensitivity (AUC 1.000) in the differentiation between newly diagnosed BC and TAM-treated patients with cut-off value of 4.25 mmol uric acid Eq./L, in 100% sensitivity and 100% specificity, as represented in Figure 2B. OSI has shown the excellent sensitivity (AUC 0.998) in the differentiation between newly diagnosed BC and TAM-treated patients with cut-off value of 720.64 in 100% sensitivity and 95% specificity, as provided in Figure 2C. Moreover, CAT activity has shown good sensitivity (AUC 0.807) in the differentiation between newly diagnosed BC and TAM-treated patients with cut-off value of 182.29 kU/L in 80% sensitivity and 70% specificity, as revealed in Figure 2D. The specific activity of CAT has shown fair sensitivity (AUC 0.818) in the differentiation between newly diagnosed BC and TAM-treated patients with cut-off value of 2.56 kU/g in 80% sensitivity and 71.7% specificity, as displayed in Figure 2E.

TABLE 5 ROC of TOC, TAC, OSI, and CAT in the in the differentiation between newly diagnosed BC and TAM-treated patients

Variables	AUC	SE	*P*-value	Cut-off	Sensitivity	Specificity
TOC	0.614	0.051	0.031	27.50	50%	61.7%
TAC	1.000	0.0001	0.0001	4.25	100%	100%
OSI	0.998	0.002	0.0001	720.64	100%	95%
CAT(kU/L)	0.807	0.042	0.0001	182.29	80%	70%
CAT(kU/g)	0.818	0.040	0.0001	2.56	80%	71.7%

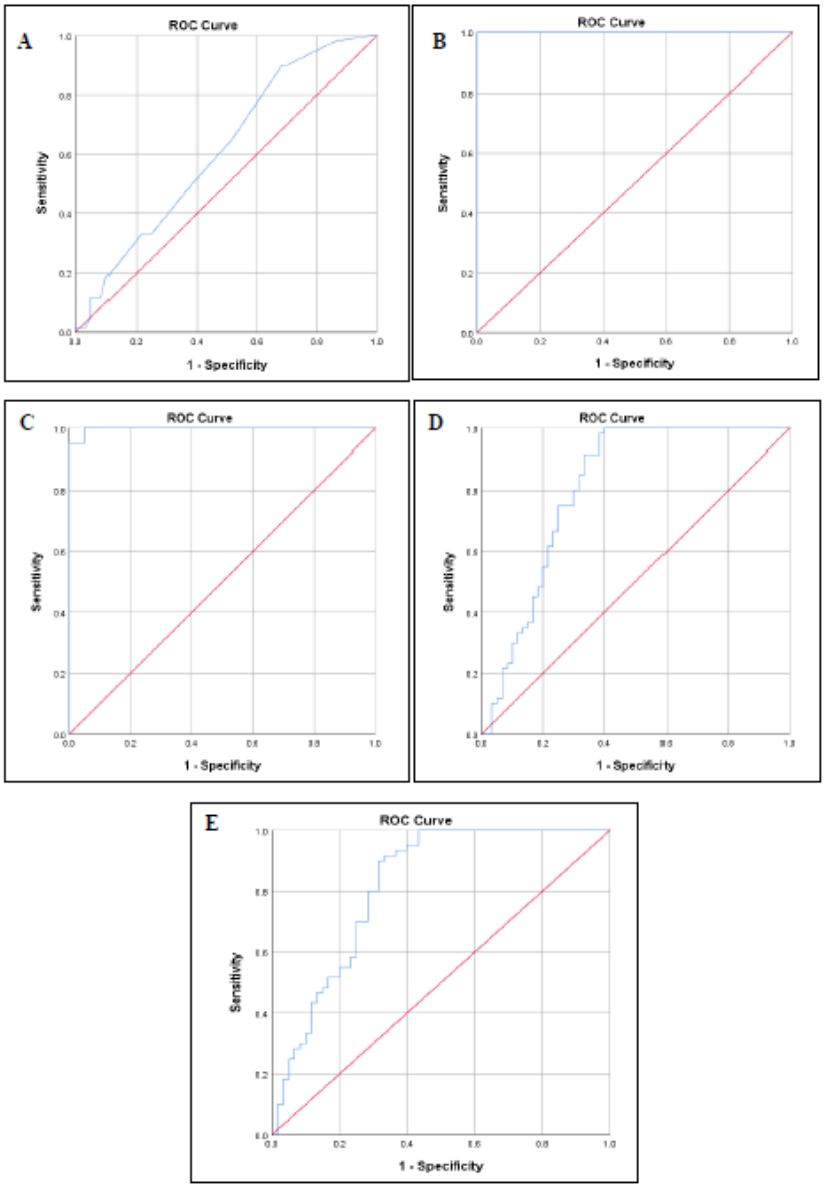

FIGURE 2 The ROC of TOC (A), TAC (B), OSI (C), CAT (D), and CAT specific activity (E) in differentiation between newly diagnosed BC and TAM-treated patients

Discussion

This study was conducted on females with breast tumors to investigate the alterations of oxidative stress associating with the first onset of BC, and also to investigate the effect of TAM drug on the oxidative stress in

females with BC. In this study, TOC and OSI levels were increased significantly in BC patients and reduced in TAM-treated patients. Total antioxidant capacity level, the activity, and specific activity of CAT were reduced significantly in BC patients, yet only the TAC level was re-elevated in TAM-treated patients, while the activity and specific activity of CAT were further decreased in TAM-treated patients. An agreement was found with Mehdi *et al.* who have reported significant increase in the TOC and OSI levels with a significant decrease at the TAC level in women with BC compared with the healthy women. The authors have declared this imbalance of redox substances to the ROS high levels, which are mainly produced due to macrophages and tumor factors during BC. When ROS is elevated, the oxidants are increased, and then the antioxidants would deplete to control these ROS, leading to increase TOC and OSI and decrease TAC [37]. In the study of Gönenç *et al.* the authors have reported significant elevated levels of oxidant markers in the plasma of pre- and post-menopausal women with BC compared with the corresponding healthy women. They have indicated a link between BC and lipid peroxidation which arise from the increase of free radicals in the patients [38].

Concerning TAM, several animal trials have been conducted to investigate the TAM effect on the oxidative stress. Karimi *et al.* conducted a study on TAM in tumorized mice to investigate the TAM effect on oxidative stress. They have found that high doses of TAM can reduce the severity of oxidative stress in mice by reducing TOC and raising TAC [39]. Nevertheless, TAM is known to induce oxidative stress, which is a key responsible for relapses in patients [40]. Tamoxifen induces the oxidative stress through hepatotoxicity in xenobiotic detoxification mechanism [41]. However, such extensive studies have not been performed on clinical trials. The current study investigated the oxidative stress status in TAM-treated BC patients compared with newly diagnosed BC patients and healthy individuals. The results of the present study showed that despite the TOC level has been increased in TAM-treated BC patients compared with control; this level has appeared to be significantly lower compared with newly diagnosed BC patients. This was also observed when compared the OSI values between these two groups of patients. Interestingly, it was noticed that the TAC level has been dramatically increased after treating with TAM. Based on the results, it is supposed that TAM might be played a different role in non-tumorigenic cells of BC patients through the improvement the TAC level in BC patients and consequently depleting of TOC levels. This suggestion needs to prove by conducting more clinical studies about the TAM actions.

Because the CAT role in the converting the highly reactive oxidant H_2O_2 into H_2O, it was investigated in this study as one of the most important antioxidant enzymes. The results of this study showed that CAT activity was significantly dropped in BC patients compared with control and this activity was noticed to be more decreased in those patients under the TAM treatment. This result is in agreement with Sahu *et al.* who have reported a significant decrease of the CAT activity in women with BC compared with control of their study. They have suggested that elevated ROS in BC can lead to a downregulation of CAT expression in patients, which therefore weakening the antioxidant system and increases the risks of the disease [42]. It has been further reported that estrogen plays as a positive mRNA signal for the expression of antioxidant enzymes such as CAT, GPx, and SOD. TAM competes with estrogen for binding with estrogen receptors and leads to decrease of estrogen intake by cells. Estrogen deficiency decreases the antioxidant enzymes and increases the oxidant levels. It was also reported that the

hydrogen peroxide level has potentially suppressed by TAM which compensates the decrease in the CAT activity [43].

The levels of serum proteins were not significantly changed among BC, TAM, and control groups. The similar results regarding albumin were reported by Gönenç *et al.* who find that albumin level was non-significantly changed in women with BC compared with the control of their study [38]. Chauhan et al. have also reported that the levels of total protein and albumin were conserved within the normal ranges in women with BC even during the courses of chemotherapy despite the changes of their values [44].

The ROC curve of TOC, TAC, and OSI levels, as well as the activity and specific activity of CAT showed that all exhibited high sensitivity and specificity to discriminate between women with BC and the normal women. Moreover, TAC and OSI exhibited excellent sensitivity in the differentiation between newly diagnosed BC and TAM-treated BC patients, while the TOC sensitivity was low. The activity and specific activity of CAT exhibited the good sensitivity in the differentiation between newly diagnosed BC and TAM-treated BC patients. Accordingly, we suggest the use of TOC, TAC, OSI, and the activity and specific activity of CAT in the routine diagnosis of BC patients. Likewise, these parameters (except TOC) are good indicator for the TAM action.

Conclusion

According to the findings of the present study, redox imbalance (i.e. TOC and OSI increase as well as TAC and CAT decrease) was observed in newly diagnosed BC patients and TAM-treated BC patients. However, TAM has shown significantly influence on the improvement of redox balance in BC patients as seen in the results of TOC, TAC, and OSI. Nevertheless, the activity and specific activity of CAT have been affected negatively by TAM drug; this may result from the TAM ability to reduce the substrate of this enzyme in tumor cells. Therefore, it is suggested that these parameters are potential biomarkers which might be used in the prognosis of BC and determined the health condition of BC patients when administrated with TAM drug to avoid serious consequences. This suggestion was supported by ROC data which indicated that these parameters are highly sensitive and specific for the BC progression and TAM activity. Yet, further information is required on the relationship between TAM and oxidative stress in the BC patients.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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