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Original Article

The Role of Monoamine Oxidase and Atherogenic Index in Newly Diagnosed and Tamoxifen Treated Women with Breast Cancer Disease

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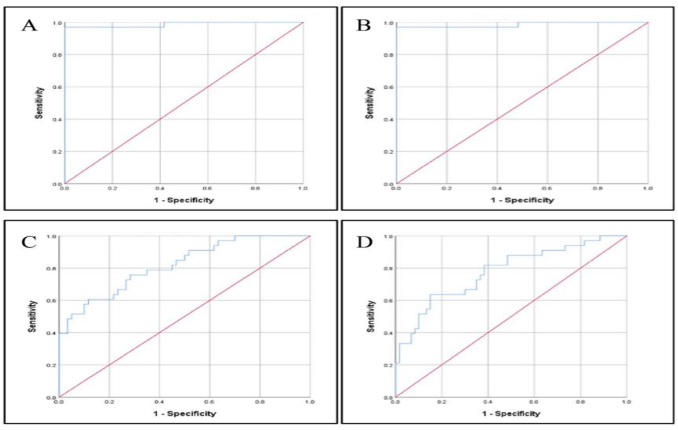
ABSTRACT

Breast cancer (BC) is the most epidemic malignancy of women worldwide that leads to cause of morbidity and mortality. Tamoxifen (TAM) is the common therapy used in the BC treatment. Monoamine oxidases are enzymes linked to the progression of many types of carcinomas through its consideration on the production of reactive oxygen species. This study aimed to clarify the correlations between MAO isoforms (MAOs), atherogenic index, TAM, and their roles in the BC progression. 60 newly diagnosed and 60 TAM treated women with BC, as well as 50 healthy volunteers were included in this study. Parameters including MAOs activities, lipid profile, malondialdehyde, and total protein were determined before and after treatment with TAM. The activities of total MAO, MAO-A, MAO-B, and semi-carbazide-sensitive amine oxidase (SSAO) were significantly (P<0.0001) decreased in newly diagnosed and TAM-treated women compared with healthy individual. However, the activities of all tested enzymes were elevated significantly (P<0.0001) in TAM-treated women compared with the newly diagnosed women. The strong positive correlations were found among MAOs in response to TAM treatment. Receiver operating characteristic showed a higher sensitivity and specificity for MAOs in discrimination between newly diagnosed and TAM-treated women. Atherogenic index was significantly increased (P<0.0001) in newly diagnosed and in TAM-treated women compared with control. The findings of this study indicated that BC patients are more vulnerable to cardiovascular diseases, independent of TAM and MAOs effect. Based on the forgoing, MAOs can be used as a diagnostic marker for BC progression.

GRAPHICAL ABSTRACT



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Introduction

Breast cancer (BC) is a form of malignant tumors found in the breast tissues of women [1, 2], and much less frequently in men [3, 4]. Breast cancer represents a significant global health challenge: it is the most frequently diagnosed cancer in the world with an estimated 2.26 million cases recorded in 2020 and it is the leading cause of cancer mortality among females [5, 6]. In Iraq, BC is the common type of malignancy in females [7]. The incidence rates of BC in Iraq region were generally stable between 2000 to 2009, but newer data from the Iraqi cancer registry showed the growing rates since 2009 with women over age 50 making the major contribution to the increase incidence of BC. In Iraq, patients fewer than 30 years old age formed about 5% of cases, whereas about 75% of the cases signed in women with age 40-60 years old and the rest 20% represented women older than 60 years old [8]. Several studies reported that the premature diagnosis of BC through detecting certain biomolecules is a key master in controlling the case and its treatment [9, 10].

Estrogen receptor (ER), progesterone receptor (PR), and Her2/neu (HER2) have been a principal determinant of adjuvant and metastatic BC therapy [11]. Estrogen has a major role in cell growth and division in BC. Antiestrogens have been effectively utilized to prevent the activation of genes by the ER. However, clinical resistance to antiestrogen treatment develops eventually [12]. Tamoxifen (TAM) is the first antiestrogenic drug that has been used in controlling BC [13]. It acts as a competitive inhibitor to impede cell growth stimulated by estrogen [14]. Due to its low cost and accessibility to underfunded medical organizations, TAM has gained more recognition as a BC miracle drug on a global scale [15].

Amine oxidases metabolize monoamines, diamines, polyamines of endogenous or xenobiotic origin, rendering ammonia, aldehydes, and hydrogen peroxide as the final products. According to their co-factor, amine oxidases are classified into two groups [16]. The FAD-dependent amine oxidases (E.C.1.4.3.4) are sensitive to acetylenic type inhibitors, which include the monoamine oxidases (MAO) and polyamine oxidases. In the second group, the Cu-dependent amine oxidases (E.C.1.4.3.6) are sensitive to carbonyl reagents such as semicarbazide, comprise the diamine oxidase, and semicarbazide-sensitive amine oxidase (SSAO), which deaminates both aromatic and aliphatic primary amines, such as methylamine and aminoacetone [17]. MAO has two isomers termed as A and B. The B-type is only found in human platelet mitochondria, while the A-type is produced in human placental mitochondria. According to the species of mammals under investigation, other tissues have varying amounts of MAO-A and MAO-B [18]. The MAO enzyme has been linked to the carcinoma progression through its consideration on the production of reactive oxygen species (ROS) via the oxidative deamination activity [19]. More recently, the accumulative evidence indicated that the expression of MAO isoforms has been mainly suppressed by estrogen [19-21].

Atherogenic index of plasma (AIP), which is considered as an indicator for cardiovascular diseases (CVD) [22], has been reported to be increased in patients with BC, and consequently those patients are more vulnerable to CVD [23]. There are no data available on the correlation between TAM and AIP in patients with BC. Thus, the effect of treatment with TAM on AIP in BC patients was a part of the main goal of this study.

To the best of our knowledge, no study has been conducted to examine the relationship among MAOs, atherogenic index, and TAM in human BC. Therefore, this study tried to explore the TAM effect on MAOs and atherogenic index and the possibility to use MAOs as an indicator for TAM action. Likewise, the sensitivity of these parameters was determined to search the possibility of using them as biomarkers for the early diagnosis of BC in women.

Materials and Methods

Subjects and specimens collection

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 (group I) in the consultancy of the Tumor

Teaching Center. Another sixty women with BC disease under TAM treatment for two years (group II) were also included in the study. This work was controlled with 33 healthy women (group III) who 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 done 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, University of Baghdad.

Evaluation of total MAO activity

The evaluation of total MAO activity was proceeded by using a modified spectrophotometric method and based on tyramine molar extinction coefficient (1200 $cm^{-1}M^{-1}$) [24]. In test tube, 1650 µL of phosphate reagent (*p*H 7.2, 100 mM) were mixed with 100 µL of the serum sample and incubated at 37 °C for 30 minutes. Then, 50 µL of the tyramine solution (4 mM) were added to the tube and incubated a second time for 1 hour. After that, 200 µL of HCl solution (2 M) were added to stop the reaction and the absorbance was read against the blank at 275 nm. The enzyme unit was defined as the amount of enzyme that catalyzes the degradation of one µmol of the substrate per minutes under well-defined conditions.

Evaluation of MAO-B plus SSAO

The evaluation of MAO-B plus SSAO activities were proceeded according to the procedure described by (Vinel P. *et al*. 2021) [25]. In test tube, 100 µL of serum were mixed with 1200 µL of phosphate buffer (*p*H 7.6, 25 mM) and incubated at 37 °C for 20 minutes. Then, 200 µL of benzylamine solution (16 mM) were added to the reaction tube and incubated at 37 °C for 20 minutes. After that, a volume of 400 µL of 2,4-dinitrophenylhydrazine (DNPH; 2 M in 1M HCl) was added to the reaction mixture and incubated at room temperature for 40 minutes. At last, 2000 µL of NaOH (1.25 M) was added to the reaction mixture and the absorbance of the solution was read against blank at 465 nm.

Evaluation of MAO-A plus MAO-B

The evaluation of MAO-A plus MAO-B has proceeded by using a modified spectrophotometric method and based on tyramine molar extinction coefficient (1200 $cm^{-1}M^{-1}$) [24]. In test tube, 100 µL of serum were mixed with an equal volume of semicarbazide (10 mM) and incubated at 37 °C for 30 minutes. Then, 50 µL of tyramine (100 µM) were added to the serum mixture with 1.55 mL of phosphate buffer (*p*H 7.2, 100 mM) and incubated a second time for 60 minutes. After that, 200 µL of 2 M HCl were added to the reaction mixture and the absorbance of the mixture was read at 275 nm.

Evaluation of malondialdehyde

Determination of malondialdehyde (MDA) levels in serum was measured by precipitation method by using thiobarbituric acid, as described previously (Stocks and Dormandy, 1971) [26]. The supernatant absorbance was measured at 532 nm and the result of MDA concentration expressed as a (nmol/mL).

Evaluation of lipid profile parameters

The levels of triglyceride (TG), total cholesterol (TC), and HDL-cholesterol (HDL-C) were determined by using commercially available assay kits (Abbott, Chicago, Ill) with an Abbott Aeroset auto-analyzer (Chicago, IL, USA), while the LDL-C level was calculated by the Friedewald formula AIP.

Evaluation of total protein

Total protein concentration (Tp) in serum was determined by using AGAPPE kit. The Tp was calorimetrically determined based on the principle of the Biuret reaction (copper salt in an alkaline medium). The absorbance of blue colored complex was measured at 550 nm.

Statistics

The data were analyzed statistically by using SPSS program version 26.0 software, for mean

comparison by 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. The sensitivity of the MAO types in BC screening was analyzed by using receiver operating characteristic (ROC) curve.

Results and Discussion

The demographic presentation of the women who enrolled in this study is summarized in Table 1. The family history of BC was positive in 28.33% of women with breast cancer.

Table 1: Demographic characteristics and some biochemical parameters of women with newly diagnosed BC, women with BC on TAM treatment, and control.

Parameter	Group III	Group I	Group II	*P*-value
n	33	60	60	-
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/m^2)	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]
TC (mg/dL)	144.06±14.72 144.00 125.0-188.0	127.02±11.99 127.35 107.20-171.30	131.71±17.03 128.85 98.80-186.60	0.0001 [a,b], 0.083 [c]
TG (mg/dL)	112.85±19.77 110.00 78.0-155.0	107.47±16.62 102.60 83.20-152.70	105.82±15.19 102.50 82.40-145.10	0.142 [a], 0.056 [b], 0.593 [c]
HDL-C (mg/dL)	51.76±7.34 50.00 40.0-72.0	40.78±7.24 39.50 24.60-56.90	39.36±6.46 38.80 24.70-56.90	0.0001 [a,b], 0.268 [c]
LDL-C (mg/dL)	69.73±14.24 65.40 39.60-106.0	64.75±13.73 64.51 35.08-106.60	71.19±17.55 68.72 35.96-115.94	0.139 [a], 0.664 [b], 0.024 [c]
VLDL-C (mg/dL)	22.57±3.95 22.00 15.60-31.0	21.49±3.32 20.52 16.64-30.54	21.16±3.04 20.50 16.48-29.02	0.142 [a], 0.056 [b], 0.593 [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]
MDA (nmol/mL)	6.51±1.27 6.78 0.67-8.17	18.88±7.36 17.32 7.51-39.04	39.99±14.53 41.76 14.00-71.61	0.0001 [a,b,c]
Atherogenic ratio-1	2.83±0.45 2.74 2.03-3.98	3.21±0.61 3.19 1.96-5.11	3.43±0.71 3.39 2.15-6.03	0.006 [a], 0.0001 [b], 0.047 [c]
Atherogenic ratio-2	1.38±0.38 1.33 0.67-2.20	1.66±0.53 1.63 0.66-3.21	1.88±0.64 1.82 0.75-4.28	0.021 [a], 0.0001 [b], 0.029 [c]
Atherogenic index	0.34±0.11 0.35 0.06-0.59	0.42±0.10 0.43 0.18-0.65	0.43±0.09 0.44 0.21-0.66	0.0001 [a,c], 0.649 [b]

The results are presented as mean±SD, median, and min-max. P-value≤0.05 is considered as significant between a (group III and group I), b (group III and group II), and c (group I and group II).

No significant differences were obtained among three groups regarding Tp. Regarding lipid profile, the TC level was significantly decreased (P<0.0001) in group I and group II compared with group III. Also, HDL-C was significantly declined (P<0.0001) in group I, and group II compared with group III. Nevertheless, TG, LDL-C, VLDL-C, and Tp were observed with no significant differences (P>0.05) among the three groups. In addition, the MDA level was increased significantly (P<0.0001) in group I and group II compared with group III.

In Table 2, the clinical outcomes of MAO parameters are demonstrated in the three groups. The activity of total MAO was reduced significantly (P<0.0001) in group I and group II compared with group III. Moreover, the total MAO was observed to be significantly lower in group I compared with group II.

The MAO-A activity was reduced significantly (P<0.0001) in group I and group II compared with group III. Moreover, group I has depicted a significant (P<0.0001) lower activity of MAO-A compared with group II. In comparison to group III, the MAO-B activity was significantly reduced (P<0.0001) in group I. However, a non-significant decreased (P>0.05) was observed in group II. Moreover, group I illustrated a significant (P<0.05) lower activity of MAO-B compared with group II. The SSAO activity was also reduced in group I, and group II, compared with group III. Furthermore, group I indicated a significant lower activity of SSAO compared with group II.

The correlations among the enzymes activities in group I showed a strong positive correlation between the total MAO and MAO-A, whereas a negative moderate correlation was found between SSAO and MAO-B (r=-0.682, P=0.0001), as listed in Table 3. In addition, AIP has correlated positively with TG (r=0.660, P=0.0001), VLDL (r=0.660, P=0.0001), atherogenic ratio-1 (r=0.663, P=0.0001), and atherogenic ratio-2 (r=0.513, P=0.0001), while SSAO has correlated negatively with TG (r=-0.336, P=0.009), and AIP has correlated negatively with HDL (r=-0.780, P=0.0001).

The correlation among the activities of enzymes in group II indicated a positive strong correlation between the total MAO and MAO-A (r=0.995, P=0.0001), and negative weak correlation between SSAO and MAO-B (r=-0.381, P=0.003), as presented in Table 4. In addition, AIP was correlated positively with the level of TG (r=0.586, P=0.0001), LDL (r=0.268, P=0.038), VLDL (r=0.586, P=0.0001), atherogenic ratio-1 (r=0.653, P=0.0001), and atherogenic ratio-2 (r=0.526, P=0.0001), while AIP was correlated negatively with HDL (r=-0.733, P=0.0001).

Table 2: The activities of MAO isoforms in control and BC women

Parameter	Group III	Group I	Group II	P-value
Total MAO (U/L)	1100.76±113.95 1093.47 735.69-1362.36	706.62±87.61 704.39 493.56-828.83	974.25±136.27 977.22 553.19-1362.08	0.0001[a,b,c]
MAO-A (U/L)	1047.22±113.32 1043.30 684.59-1309.41	677.09±86.49 669.83 471.70-804.51	927.03±138.51 930.60 498.88-1321.21	0.0001[a,b,c]
MAO-B (U/L)	29.45±11.37 30.36 8.94-50.22	15.72±8.84 15.23 1.08-34.29	26.50±13.78 27.03 0.73-64.78	0.0001[a,c], 0.240 [b]
SSAO (U/L)	24.10±10.41 25.97 5.69-44.03	13.81±7.44 11.61 2.72-33.00	20.72±10.56 19.72 3.47-57.92	0.0001[a,c], 0.100[b]

The results are presented as mean±SD, median, and min-max. P-value≤0.05 is considered as significant between a (group III and group I), b (group III and group II), and c (group I and group II).

Table 3: Correlation in newly diagnosed BC women

Variable	Total MAO		MAO-A		MAO-B		SSAO		AIP	
	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Total MAO	-	-	0.997*	0.0001	0.225	0.083	-0.085	0.520	0.131	0.318
MAO-A	0.997*	0.0001	-	-	0.185	0.158	-0.102	0.438	0.142	0.280
MAO-B	0.225	0.083	0.185	0.158	-	-	-0.682*	0.0001	0.126	0.338
SSAO	-0.085	0.520	-0.102	0.438	-0.682*	0.0001	-	-	-0.254	0.050
AIP	0.131	0.318	0.142	0.280	0.126	0.338	-0.254	0.050	-	-
MDA	-0.099	0.451	-0.104	0.430	0.065	0.621	-0.040	0.764	0.156	0.233
Age	0.020	0.882	0.021	0.875	0.023	0.860	-0.038	0.773	0.184	0.160
BMI	-0.099	0.453	-0.106	0.422	0.140	0.285	-0.102	0.438	0.264*	0.041
TP	-0.011	0.932	-0.008	0.950	-0.068	0.604	0.043	0.741	0.021	0.872
TC	0.120	0.361	0.119	0.364	0.025	0.850	-0.004	0.978	-0.121	0.356
TG	-0.021	0.876	-0.016	0.903	0.236	0.069	-0.336*	0.009	0.660*	0.0001
HDL	-0.200	0.126	-0.208	0.110	0.017	0.897	0.048	0.714	-0.780*	0.0001
LDL	0.215	0.099	0.218	0.094	-0.044	0.736	0.053	0.689	0.146	0.267
VLDL	-0.021	0.876	-0.016	0.903	0.236	0.069	-0.336*	0.009	0.660*	0.0001
Atherogenic ratio-1	0.234	0.072	0.245	0.059	-0.044	0.740	-0.050	0.707	0.663*	0.0001
Atherogenic ratio-2	0.239	0.066	0.249	0.055	-0.075	0.571	0.007	0.958	0.513*	0.0001

*The results are expressed in r and P-value, * Significant at P<0.05*

Table 5 contains the information of ROC curve analyses. The ROC curves of MAO enzymes demonstrated that total MAO can be used as excellent sensitive biomarker in the prognosis of breast cancer, in which the AUC of total MAO was 0.987 with 97% sensitivity and 100% specificity at a cut-off value of 877.8 U/L, as displayed in Figure 1**a**. MAO-A illustrated an excellent sensitivity in the prognosis of breast cancer, in which the AUC of MAO-A was 0.985 with 97% sensitivity and 100% specificity at a cut-off value of 837.6 U/L, as depicted in Figure 1**b**. MAO-B represented a good sensitivity in the prognosis of breast cancer, in which the AUC of MAO-B was 0.819 with 75.8% sensitivity and 71.7% specificity at a cut-off value of 22.1 U/L, as indicated in Figure 1**c**. Furthermore, the SSAO activity illustrated a fair sensitivity in the prognosis of breast cancer, in which the AUC of SSAO was 0.778 with 72.7% sensitivity and 65% specificity at a cut-off value of 21.39 U/L, as demonstrated in Figure 1**d**.

The main findings of this study revealed that total MAO, MAO-A, MAO-B, and SSAO were significantly decreased ($P \leq 0.0001$) in patients with BC, as compared with control group. The expression of MAO-A and SSAO was reported to be reduced in many types of BC [19, 27, 28]. Bharti *et al.* have indicated a decrease in the MAO-A activity in women with BC, and this reduction was associated with more progressive condition of the cancer and correlated inversely with the pro-inflammatory cytokine, interleukin-6 [29]. However, an *in vitro* study by William D. *et al.* indicated that MAO-A was increased in human BC cell lines [30]. In contrast to our data, decreasing the MAO-B level was reported in BC and many other cancers [19]. Nevertheless, the MAO-B expression diminished in gastrointestinal [31] and oral squamous cell carcinoma [32]. In this regard, evidence from human and animal studies indicated that the MAO expression has been regulated by estrogen. In human, estrogen exerts a negative regulatory effect on MAO expression [19-21]. Estrogen plays vital roles in

cell survival and division of normal and carcinogenesis of BC [33]. Cells are able to recognize and utilize of estrogen through ERs [34].

Table 4: Correlation in the treated women

Variable	Total MAO		MAO-A		MAO-B		SSAO		AIP	
	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Total MAO	-	-	0.995*	0.0001	-0.185	0.157	0.094	0.476	-0.029	0.824
MAO-A	0.995*	0.0001	-	-	-0.252	0.052	0.054	0.683	-0.032	0.807
MAO-B	-0.185	0.157	-0.252	0.052	-	-	-0.381*	0.003	0.091	0.488
SSAO	0.094	0.476	0.054	0.683	-0.381*	0.003	-	-	-0.077	0.560
AIP	-0.029	0.824	-0.032	0.807	0.091	0.488	-0.077	0.560	-	-
MDA	-0.132	0.314	-0.130	0.323	0.005	0.972	-0.010	0.941	0.335*	0.009
Age	0.014	0.914	0.002	0.986	0.139	0.289	-0.028	0.830	-0.163	0.214
BMI	-0.002	0.989	-0.006	0.967	-0.079	0.549	0.151	0.249	0.191	0.144
TP	0.048	0.718	0.031	0.814	0.082	0.535	0.099	0.452	0.063	0.631
TC	0.002	0.990	0.002	0.985	-0.029	0.824	0.028	0.832	0.103	0.434
TG	-0.018	0.891	-0.008	0.951	-0.109	0.409	0.014	0.918	0.586*	0.0001
HDL	0.013	0.919	0.025	0.849	-0.193	0.140	0.096	0.465	-0.733*	0.0001
LDL	0.0001	0.999	-0.005	0.967	0.061	0.642	-0.011	0.936	0.268*	0.038
VLDL	-0.018	0.891	-0.008	0.951	-0.109	0.409	0.014	0.918	0.586*	0.0001
Atherogenic ratio-1	-0.029	0.828	-0.040	0.762	0.179	0.171	-0.080	0.545	0.635*	0.0001
Atherogenic ratio-2	-0.023	0.864	-0.034	0.795	0.178	0.173	-0.074	0.575	0.526*	0.0001

*The results are expressed in r and P-value, * Significant at P<0.05*

Table 5: ROC results of parameters in the BC diagnosis in women

Parameter	AUC	*p*-value	SE	Cut-off value	Sensitivity	Specificity
Total MAO	0.987	<0.001	0.013	877.8 U/L	97%	100%
MAO-A	0.985	<0.001	0.015	837.6 U/L	97%	100%
MAO-B	0.819	<0.001	0.045	22.1 U/L	75.8%	71.7%
SSAO	0.778	<0.001	0.052	16.2 U/L	72.7%	65%

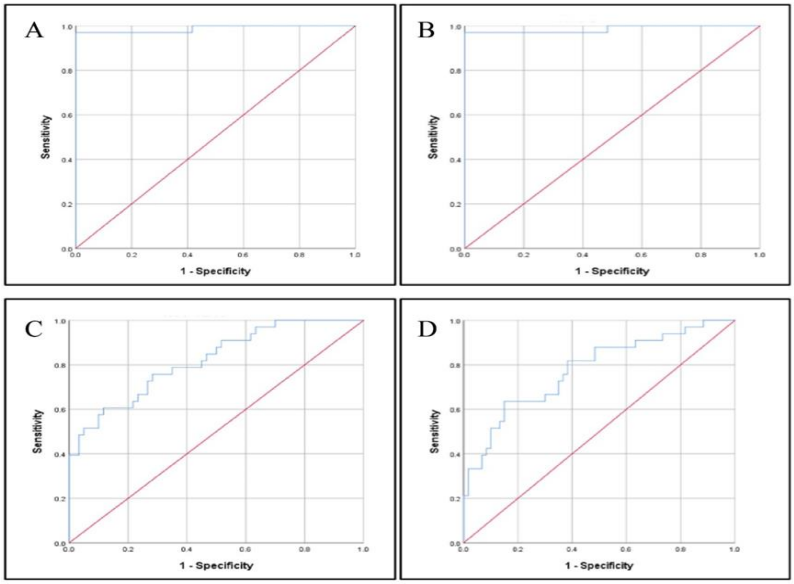

Figure 1. The ROC curves of MAO enzymes

Estrogen receptors are over-expressed in about 70–75% of all BC [21]. Therefore, this study suggested that highly intake of estrogen mediated by ERs of BC cells may contribute in the downregulation of MAO-A, MAO-B, and SSAO.

TAM has been widely used as a first‑line adjuvant treatment for pre- and postmenopausal BC patients with ER tumors [21]. Our data showed that total MAO, MAO-A, MAO-B, and SSAO activities were also dropped in BC patients who were under the TAM treatment compared with control group. However, these activities were not extensively decreased compared with patients who did not receive the TAM treatment. It is well-known that TAM competes with estrogen for a selectively binding to ERs leading to inhibit estrogen function through reducing estrogen levels in BC cells [14]. We hypothesized that the treatment with TAM might lead to decrease the estrogen intake by ERs of BC cells, and consequently diminished the MAO downregulation due to estrogen effect. It seems that all MAO isoforms displayed the same correlation with TAM. Thus, the current study suggests the ability to use MAO activities as an indication of TAM action. This study also showed that total MAO, MAO-A, MAO-B, and SSAO activities have higher sensitivity and specificity to discriminate between women with BC and healthy individuals.

It was also found that there was a decrease in the levels of all lipids (i.e. TC, TG, HDL-C, and VLDL-C) in women with BC including those who were under TAM treatment, but LDL-C level was slightly increased in patients who received TAM compared with control group. Accordingly, AIP showed a higher value in newly diagnosed and TAM-treated women compared with healthy individual. This indicated that BC patients are more vulnerable to CVD.

Moreover, the MDA level was significantly increased in patients with BC as compared with healthy women and this was found to be higher in patients under TAM treatment. Our findings are in agreement with study conducted by Sabina *et al*. who reported that MDA level increased in patients with BC [35]. MDA is one of the final products of lipid peroxidation. It is usually used as an indicator for oxidative stress in many diseases. Several studies reported that oxidative stress contributes in the antioxidant reduction and the development of many diseases [36-42]. It has been reported that TAM induces the oxidative stress generation [43]. Furthermore, MAO is considered as one of the main sources of ROS in the mitochondria that generate a significant amount of H_2O_2 through its deamination activity [19, 44]. Therefore, the increase in the MDA level might be due to the ROS increase mediated by the combined effect of TAM and MAO activities.

Conclusion

In conclusion, this study showed the positive correlations among MAO isoforms in BC patients. Furthermore, a negative correlation between MAO isoforms, TAM, and synchronous changes in the levels of MAO isoforms before and after receiving TAM was demonstrated in this study. Consequently, the TAM effect on BC progression can be monitored from the level of MAO isoforms. This study also revealed the increase in AIP and MDA levels in BC patients, especially, after receiving TAM which may indicate that those patients are more vulnerable to CVD. Based on the forgoing, MAO isoforms can be used as a diagnostic marker for the BC progression and oxidative stress assessment.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

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