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RESEARCH PAPER

Effect of oxidative stress on tumor suppressor protein p53 and some biochemical markers in breast cancer patients in Erbil governorate

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A B S T R A C T:
The present study was conducted to observe the effect and association of oxidative stress on breast cancer, as well as evaluate the alteration of the serum lipid profile, hepatic and kidney biomarkers and serum tumor suppressor protein p53 in breast cancer patients in female as an important objective and determine the relationship between serum p53 with nitric oxide NO, malondialdehyde MDA, superoxide dismutase SOD, lipid profile, liver and kidney functions. In this study 80 subjects were conducted 50 women who had breast cancer as a patient group, and 30 healthy women were conducted as a control group. Blood samples were taken from both patients and control group, who were aged between (18-75) years old. The results of this study revealed that the median levels of serum NO, creatinine and the mean level of serum HDL are significantly lower in patients group with breast cancer than those in control group. Whereas, the median levels of serum MDA, TG, LDL, ALT, AST, and the mean level of serum CH are significantly higher in patients group with breast cancer rather than in control group. While, there are negative weak significant correlations between p53 with MDA, CH, TG and ALT. ROC curve analysis exhibit that serum NO, MDA, TG, HDL, ALT and AST are excellent biomarkers for the diagnostic accuracy of breast cancer in female as a result of the high level of AUC. Whereas, this study demonstrates that serum p53 is not a good biomarker for female breast cancer with AUC value 0.5636. Although, it is known that serum p53 is a tumor suppressor protein that plays a crucial role in the inhibition of cancer development.
In conclusion, the results revealed that patients with breast cancer have a systemic oxidative stress rising due to human tumor cells produce large quantity of ROS, which plays a crucial role in liver diseases, abnormality of renal function and hyperlipidemia. Most possibly due to the endothelial dysfunction which consequently is risk factor for patient's health.

KEY WORDS: Oxidative stress; breast cancer; tumor suppressor protein p53; Liver function.
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1. INTRODUCTION:

Oxidative stress (OS) is a biochemical state that is considered as the inequality between the existence of relatively high levels of toxic reactive species, mainly involving of reactive oxygen species (ROS), reactive nitrogen species (RNS), and mechanisms of the antioxidative defense (Thannickal and Fanburg, 2000).

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Oxidative stress cause an extreme formation of ROS that overcomes the system of antioxidant defense or while there is a substantial decrease or absence of antioxidant agents (Kang, 2002). There are Higher ROS formations in a number of pathological states such as myeloid leukemias, diabetes, rheumatoid arthritis and atherosclerosis have been related with defective functions of neutrophil (Karaa et al., 2005).

Breast cancer could be defined as the most prevalent cancers of women worldwide (Organization, 1998). In the Middle East, the most ubiquitous malignancy in women was breast cancer (Kahan et al., 1997). The precise reason of

breast cancer is not exactly recognized but at present it characterizes a complex interaction of environmental and genetic factors (Wesseling et al., 1999). Substantial breast cancer risk factors consist of: age, early age monarchal, late age menopausal, first pregnancy at late age, obesity, intense breast tissue, using oral contraception, hormone surrogate treatment, alcohol, diet, tobacco smoke, lactation, family history and previous history of benign breast illness (Gönenç et al., 2006). Several genes, such as BRCA1 and BRCA2, HER2/neu, and p53, have been related to breast cancer receptivity and improvement (Yeh et al., 2005).

The p53 protein is produced by a tumor suppressor gene situated on the human seventeenth chromosome that encodes a 53-kilodalton nuclear protein (P53) establish in scant magnitudes in normal tissue. Thru the production of this protein, the gene applies an inhibitory influence on proliferation of cell and transformation (Ostrowski et al., 1991). Since tumor suppressor protein p53 works as a transcription factor which able to induce G1 cell cycle stay or apoptosis in reply to DNA damage (Clarke et al., 1993), also adjust normal cells proliferation through controlling initiation and/or adjusting of DNA replicating and programming of cell death (Montenarh, 1992).

H_2O_2 is recognized to breaks DNA in unbroken cells and purified DNA. The damage of DNA as a result of ROS has been revealed in the base damage form (Baker and He, 1991). malondialdehyde (MDA) is an aldehyde which the lipid peroxidation (LPO) final product arising from polyunsaturated fatty acids degradation via free radical, and lead to cross-linking in lipids, nucleic acids and proteins (Flohe et al., 1985). Superoxide anion radical (O_2^{-}•) is not highly toxic prime free radical produced in the cell via the molecular oxygen reduction, as seen in (Figure 1). Superoxide anion radical (O_2^{-}•) dismutation catalyzed by the spontaneous or mitochondrial superoxide dismutase (SOD) and produces hydrogen peroxide (H_2O_2), that produces a highly toxic free radical as hydroxyl radical (•OH) which is in the existence of reduced iron or copper through the reactions of Fenton or Haber–Weiss (Freeman and Crapo, 1982).

Definitely, hypercholesterolemia motivates the production of superoxide anion radical (O_2^{-}•) of vascular smooth muscle cells, that could do further oxidation of LDL (O'Hara et al., 1993). Moreover, superoxide anion radical may result in endothelial dysfunction through scavenging of endothelial-derived nitric oxide NO cause limitations of bioavailability of NO and results in nitrate tolerance, hypertension and vasoconstriction (Münzel et al., 1995). Superoxide speed up the NO destruction because NO binds superoxide radical (O_2^{-}•) to produce the effective oxidant peroxynitrite anion ($ONOO^{-}$) and also its conjugate acid peroxynitrous acid (Saran et al., 1990). Actually, the reaction rate for the peroxynitrite production is nearly six times quicker than the Superoxide anion radical (O_2^{-}•) scavenging via SOD, indicating that peroxynitrite production can take place in vivo (Beckman and Koppenol, 1996). Reactive species can react with cellular macromolecules, such as lipids, DNA and proteins to which cause irreversible damaging by oxidative and interpose to indispensable cellular functions. DNA can be attacked directly by ROS and RNS and lead to mutagenic lesions (Aydin et al., 2006).

Liver is a main organ hit by ROS (Apel and Hirt, 2004). Parenchymal cells are essential cells exposed to oxidative stress resulted damage in the liver. As well as, in hepatic stellate cells proliferation and collagen synthesis is induced via lipid peroxidation made by oxidative stress (Weiss, 1992). Also, oxidative stress is considered as one of the pathological mechanisms that causes instigation and progress of different liver diseases, for instance alcoholic liver diseases, chronic viral hepatitis and steatohepatitis (Singal et al., 2011). The oxidative stress not only causes hepatic injury via inducing irreversible variation of lipids, DNA and proteins and more significantly modifying pathways which regulate normal biological functions. Furthermore, systemic oxidative stress rising in liver disease can also result in damage to other organs, for example kidney failure and brain impairment (Palma et al., 2014). As regards kidney failure, systemic oxidative stress is deliberated to play a serious role in the various kidney diseases pathophysiology (Valente et al., 2012).

There is quite of indication for rising levels of oxidative stress markers with declining

renal function, launch from early stages of chronic kidney disease CKD (Tbahriti et al., 2013). While, systemic oxidative stress could considerably participate to endothelial dysfunction (Annuk et al., 2005) with overstatement of atherosclerosis (Esper et al., 2006) and also progress of CVD (Paoletti et al., 2005). while extreme ROS are genotoxic (Stopper et al., 2004), oxidative stress might be a cause participate to higher rates of malignancy in patients with end-stage renal disease ESRD (Shang et al., 2016).

The present study was conducted to observe the effect and association of oxidative stress on breast cancer, as well as evaluate the alteration of the serum lipid profile, hepatic and kidney biomarkers and serum total tumor suppressor protein p53 in breast cancer patients in female as an important objective. In addition to, evaluate the relation between all of them with serum p53 (tumor suppressor p53).

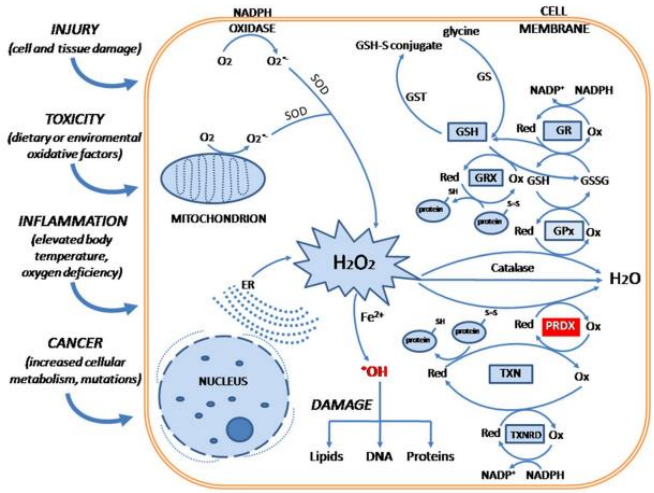

Figure 1: Cellular mechanisms related to oxidative stress.

2. MATERIALS AND METHODS

2.1 Study population

This study was conducted at Nanakali Hospital in Erbil Governorate during the period from March to June in 2019. Blood samples included 80 individuals; they were drawn in 50 women who had breast cancer as a patient group. The other samples were taken from 30 subjects (women) as a control group who had no breast cancer. Both patient and control groups were aged between (18-75) years old. The file of patients was used to get information about the stages of breast cancer of patients.

2.2 Procedures and measurements

In this study, nearly 5 ml of blood sample was taken from each individual and put into the collection tube containing gel and clot activator but no anticoagulant. Also, blood samples were left for around 20 minutes and allowed to clot at room temperature. Furthermore, serum samples were prepared through centrifugation of blood samples for about ten minutes at 4000 rpm and kept frozen at (-86 C˚) until further analysis. The biochemical test parameters of serum p53 was assessed with human total p53 (Tumor Protein p53) ELISA Kit (mybiosource) via fully automated enzyme-Linked Immunosorbent Assay (ELISA) of USA origin. Moreover, nitric oxide (NO), malodialdehyde (MDA) and superoxide dismutase (SOD) were assessed with NO, MDA and SOD ELISA Kit (ZellBio GmbH assay kit) respectively via fully automated enzyme-Linked Immunosorbent Assay (ELISA) of Germany origin. As well as, serum total cholesterol (CH), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), ALP, ALT, AST, uric acid, creatinine and blood urea measured by using fully automated chemical analyzer of Cobas c 111 with diagnostic kits (Roche/Hitachi Cobas), of Germany origin.

2.3 Statistical analysis

The whole statistical analyses are implemented by applying computer program as Graph pad-prism version. The data consequences existing as either mean ± standard error of mean (Mean ± SEM) or median with interquartile ranges. In the comparison of nonparametric (not normally distributed data) and parametric values (normally distributed data) between two groups used Mann-Whitney U test and independent student's t-test (unpaired t-test) correspondingly. P-values which ($P < 0.05$) have been considered as significant and P-values that ($P > 0.05$) regarded as no significant (NS). ROC curve (Receiveroperating characteristic) analysis was implemented to determine the area under the curve (AUC) for the diagnostic accuracy in patients with breast cancer in women. The Pearson and Spearman correlation analysis for normally distributed and not normally distributed data were done respectively to indicate the relationship between two groups, when serum p53 represented as dependent variables, while other parameters presented as independent variables.

3. RESULTS AND DISCUSSION

These data demonstrate that median serum levels of MDA, TG, LDL, ALT, AST, and the mean serum level of CH are significantly increased in patients group with breast cancer rather than in control group. The median level of serum SOD, ALP, uric acid and the mean levels of blood urea in patients group with breast cancer for female are insignificantly increased when compared with control group. While the median levels of serum NO, creatinine and the mean level of serum HDL are significantly decreased in patients group with breast cancer than those in control group. It is also observed that the median level of serum p53 in patients group with breast cancer for female are insignificantly decreased when compared with control group, as seen in (Table 1) and (Figure 2).

Our study demonstrates that serum levels of MDA exhibit significant increasing in patients group with breast cancer. This is in agreement with previous studies that exhibited the prevalence of ROS in patients group with breast cancer disease is much higher than those in control group because human tumor cells produce large quantity of H_2O_2 (Cheeseman and Slater, 1993). The results of the present study demonstrate that the oxidative stress biomarker of serum NO and MDA are indeed potential oxidative stress biomarkers for breast cancer, due to the high levels of AUC (table 3). Since, the oxidative stress rising in breast cancer disease due to human tumor cells produce large quantity of RONS. Similar observations have been shown in the recent studies. Additionally, our study reveals that serum levels of p53 display insignificant dropping in patients group with breast cancer than those in control group. This is in agreement with earlier Experimental study exposes that ROS are contributed in cancer beginning and progression wherever certain tumor suppressor genes inactivation or loss is happened (Harris, 1989). Because DNA can be attacked directly by ROS and RNS and lead to mutagenic lesions (Aydin et al., 2006).

As well as, These antineoplastic agents that used to treating most of the breast cancer patients result in a decrease in the levels of antioxidant due to their toxicity raises the peroxidation reaction of the unsaturated fatty acids in the membrane phospholipids (Conklin, 2004), which in the case of dyslipidemia, inflammation, human tumor cells and other pathological, high quantities of H_2O_2 are produced via stimulated polymorphonuclear leukocytes and monocytes in respiratory burst pattern (Cheeseman and Slater, 1993). Our data display that serum TG, LDL and CH significantly increased and also serum HDL are significantly decreased. This is in agreement with Diniz et al., 2004, Furberg et al., 2005 and O'Hara et al., 1993. Hypercholesterolemia is illustrated as a rise in cholesterol level with rising in plasma levels of LDL and VLDL. The hypercholesterolemia enhances oxidative stress via rising lipid peroxidation and reducing antioxidant enzymes (O'Hara et al., 1993). Additionally, hypercholesterolemia is related to enhanced superoxide anion radical ($O2^{-}\bullet$) production and NO deactivation (Diniz et al., 2004, O'Hara et al., 1993). Moreover, Superoxide anion radical ($O_2^{-}\bullet$) may result in endothelial dysfunction through scavenging of endothelial-derived nitric oxide cause limitations of NO bioavailability, as shown in (Figure 3).

Our study demonstrates that serum levels of NO exhibit significant dropping in patients group with breast cancer. This is in agreement with Gryglewski et al., 1986 and Hamadamin et al., 2016. Thus, increased production of ROS decreases NO bioavailability, leading to advancement of vasoconstriction, platelet aggregation inhibition reducing, and neutrophil adhesion to endothelium initiating. These variations result in endothelial dysfunction and might contribute to modification of intracellular signaling passageway and transcription factors intermediated gene expression in endothelial cells (Münzel et al., 1995). Convincing evidence identifies that while cellular levels of Superoxide anion radical ($O_2^{-}\bullet$) or NO are raised, the effective oxidant, peroxynitrite is rapidly produced that speed up Nitric oxide (NO) destruction (Gryglewski et al., 1986, Hamadamin et al., 2016). Actually, the reaction rate for the peroxynitrite production is nearly six times quicker than the Superoxide anion radical ($O_2^{-}\bullet$) scavenging via SOD, indicating that peroxynitrite production can take place in vivo (Beckman and Koppenol, 1996).

Table (1) Comparison the serum levels of p53, nitric oxide NO, malondialdehyde MDA, superoxide dismutase SOD, lipid profile and liver function renal function parameters in patients group with breast cancer and control group.

Parameters	Patient group(n=50)	Control group(n=30)	P value
p53 (pg/ml)	0.426 (0.31, 0.5545)	0.4955 (0.35 ,0.536)	0.3582
NO (nmol/ml)	9 (6.95, 12.55)	23.9 (20.05, 27.65)	< 0.0001
MDA (nmol/ml)	1.765 (1.42, 2.173)	1.45 (1.245, 1.7)	0.0013
SOD (IU/mg)	5.1 (4.8, 5.35)	4.95 (4.525, 5.25)	0.1327
CH (mg/dl)	172.0 ± 5.694	147.9 ± 4.407	0.0048
HDL (mg/dl)	40.16 ± 1.160	54.00 ± 2.421	< 0.0001
TG (mg/dl)	194.7 (146.2, 297)	102.1 (72.28, 156.7)	< 0.0001
LDL (mg/dl)	87 (74, 108)	74 (58.5, 92.5)	0.0041
ALP(U/L)	83.45 (67.7-102.6)	76.6 (63.8-88.2)	0.0565
ALT(U/L)	16 (9.5-25.5)	8 (6-10.5)	< 0.0001
AST(U/L)	20 (16-25.25)	15 (12-17)	< 0.0001
Creatinine (mg/dl)	0.6 (0.5, 0.65)	0.6 (0.6, 0.75)	0.0054
Uric acid (mg/dl)	4 (3.5, 4.6)	3.6 (3.2, 4.55)	0.2204
Urea (mg/dl)	26.67 ± 1.055	25.45 ± 1.069	0.4462
Age (year)	50.54 ± 1.662	52.66 ± 2.341	0.4550

The values expressed as (Mean ± SEM) for urea, HDL, cholesterol but all others expressed as mean with interquartile range.

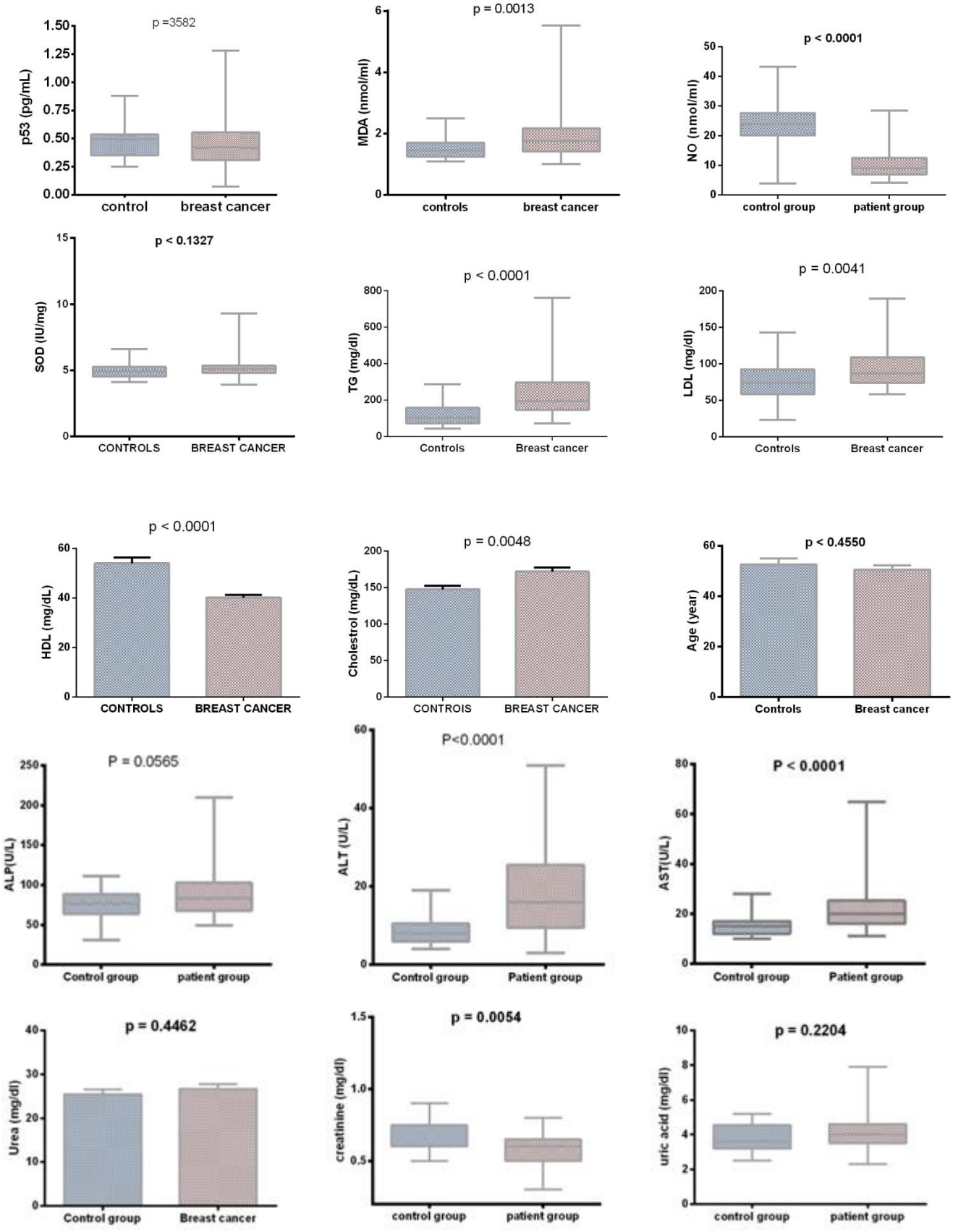

Figure 2: Serum levels of p53, MDA, NO, SOD, TG, LDL, HDL, CH, Age, ALP, ALT, AST, urea, creatinine and uric acid parameters in patients group with breast cancer and control group in women.

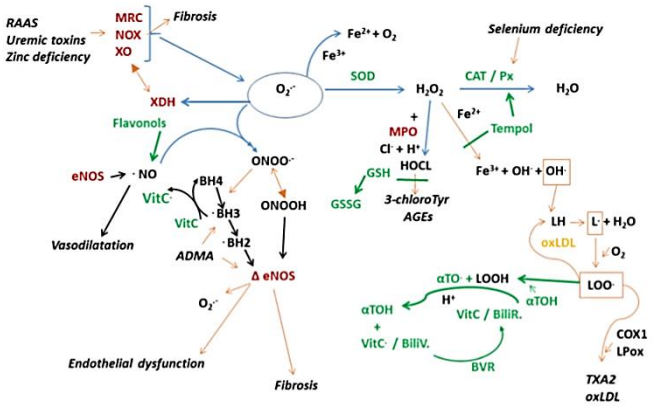

Figure 3: Mechanisms of oxidative stress damage to cellular targets and the defense of antioxidant. Where antioxidative reactions were indicated by Green arrow; inhibition of the oxidating reaction by antioxidative mechanism were written by green line; pro-oxidative reactions by red arrow. Abbreviations: ADMA is asymmetric dimethylarginine; αTOH is alpha tocopherol; AGEs is advancedglycationendproducts; BiliR is bilirubin; BVR is biliverdin reductase; biliV is biliverdin; BH4 is (6R)-5,6,7,8-tetrahydro-l-biopterin; CAT is catalase; eNOS is endothelial NO synthase; COX is cyclooxygenase; Δ eNOS is eNOS uncoupling; Fe2+ is iron; H2O2 is hydrogen peroxide; GSH/GSSH is glutathione; LOOH is fatty acid chain; HOCL is hypochlorous acid; LOO− is lipid peroxyl radical; MRC is mitochondrial respiratory complex; MPO is myeloperoxidase; NOX is NADPH oxidase; ONOO is peroxynitrite; NO is nitric oxide; O2•−, superoxide anion radical; O2, oxygen; PX is peroxidase; TXA is thromboxane; SOD is superoxide dismutase; VitC is vitamin C; XO is xanthine oxidase; XDH is xanthine dehydrogenase.

Several researches have explored whether the lipid metabolism is related to risk of evolving breast cancer, specified their relationship to obesity and overweight (Kulie et al., 2011). In the case of breast cancer alterations in the normal lipid metabolism specifically of serum triglycerides have been detected. Previous studies demonstrated the evidence for a positive relation between triglycerides and evolving these cancers riskiness (Das et al., 1987, Capasso et al., 2010). And also It has been proposed for both ovarian cancer and breast cancer that low levels of HDL (a communal obesity comorbid) can be reflective of a critical profile of hormone that, in sequence, would rise the risk (Furberg et al., 2005).

The results of the present study exhibit that the liver function parameters ALT and AST are elevated in patients with breast cancer disease in comparison with healthy group. This is in agreement with Li et al., 2014. Also, this study demonstrates that there is no significant elevation of ALP in patients with breast cancer disease compared to healthy group. This is also in agreement with Keshaviah et al., 2007 that revealed that ALP is not a potential biomarker for breast cancer disease prediction. While, CA15-3 has been better capable of expect recurrence of breast cancer than ALP, however utilize both of them with each other provided a better previous indicator of recurrence (Keshaviah et al., 2007). While the ROS is extreme, the homeostasis will be troubled, causing oxidative stress that plays a crucial role in liver sicknesses and other prolonged and degenerative diseases (Li et al., 2014).

Our study demonstrates that serum levels of urea and uric acid exhibit insignificant increasing in patients group with breast cancer although serum creatinine is significantly decreased in patients group with breast cancer than those in control group. This is in agreement with previous studies of both Himmelfarb, 2005 and Tbahriti et al., 2013. ROS play a significant role in the regulating kidney function which subsequently makes the kidney specifically susceptible to redox inequalities and oxidative stress. The influence of oxidative stress to the progress of kidney disease and consequent renal function forfeiture has been comprehensively studied (Himmelfarb, 2005, Abdoulrahman, 2017). Additionally, There is quite of indication for rising levels of oxidative stress markers with declining renal function, launch from early stages of chronic kidney disease CKD (Tbahriti et al., 2013). Abnormality of renal function is associated with endothelial dysfunction, which leads to progression of atherosclerosis in patients with CKD.

Moreover, NO and MDA are represented as specific and sensitive oxidative stress biomarkers of breast cancer. The most vital problem factors of breast cancer are the risk of systemic oxidative stress rising in the existence of tumor cells that produce large quantity of H_2O_2 (Cheeseman and Slater, 1993), which can also result in damage to other organs, for example liver disease, kidney failure and brain impairment (Palma et al., 2014). As well as, nitrate tolerance, hypertension, vasoconstriction (Münzel et al., 1995). and dyslipidemia (Diniz et al., 2004). Most possibly due to the endothelial dysfunction. The parameters of oxidative stress in this study such as decreased NO, increased MDA and insignificantly increased SOD values revealed that there was

Table (2) Correlation analysis between total serum p53 with NO, MDA, SOD, CH, TG, HDL, LDL, ALP, ALT, AST, age, creatinine, uric acid and urea in patients group with breast cancer.

Parameters	Correlation coefficient (r) (spearman correlation)	P value
serum p53 and MDA	-0.2656	0.0213
serum p53 and CH	-0.2715 (Pearson correlation)	0.0177
serum p53 and TG	-0.3349	0.0031
serum p53 and ALT	-0.2495	0.0297
serum p53 and SOD	-0.1076	N.S
serum p53 and LDL	-0.1454	N.S
serum p53 and ALP	-0.02882	N.S
serum p53 and AST	-0.05836	N.S
serum p53 and uric acid	-0.0344	N.S
serum p53 and age	-0.08389 (Pearson correlation)	N.S
serum p53 and NO	0.01766	N.S
serum p53 and HDL	0.1148 (Pearson correlation)	N.S
serum p53 and urea	0.0091 (Pearson correlation)	N.S
serum p53 and creatinine	0.0772	N.S

more production of free radicals when compared with their scavenging activity resulting in more oxidative stress in breast cancer. The present study shows that serum levels of creatinine are elevated in breast cancer patients compared to healthy subjects. This is agreement with studies. Whereas, there is no significant elevation of serum urea and uric acid levels in breast cancer patients.

In a correlation analysis, the results of this research illustrate that there are negative with significant weak correlations between serum p53 with MDA, CH, TG and ALT which the correlation (r) values for MDA (r = -0.2656), CH (r = -0.2715), TG (r = -0.3349) and ALT (r = -0.2495). Also, there are negative non-significant correlations between serum p53 with SOD, LDL, ALP, AST, uric acid and age. While, there are positive non-significant correlations among serum p53 with NO, HDL, urea, creatinine. The p values for SOD, LDL, ALP, AST, uric acid, age, NO, HDL, urea and creatinine are (P = 0.0213, 0.0031, 0.0297, 0.6214, 0.7709, 0.4712, 0.8796, 0.3234, 0.9385 and 0.5101), respectively, as seen in (Table 2).

The ROC curve analysis was proposed for determination the diagnostic accuracy of NO, MDA, CH, TG, HDL, LDL, ALT, AST and p53. The consequences of current study exhibit that the value of AUC for serum nitric oxide NO is 0.8846, the value of S.E is 0.05062 and the 95% CI value is 0.7853 to 0.9838, (< 0.0001). And also, the value of AUC for serum MDA is 0.7145, the value of S.E is 0.05757 and the 95% CI value is 0.6016 to 0.8273, (p = 0.001570). Also, The AUC value for serum TG is 0.8317 which has a high range that showed the high sensitivity than specificity. The S.E value is 0.04544 and the 95% CI value is 0.7426 to 0.9208, (P < 0.0001), and also, the AUC value for serum HDL is 0.8176, also S.E and 95% CI values are (0.04951 and 0.7205 to 0.9147) respectively, (P < 0.0001). As well as, The AUC value in serum LDL is 0.6928, S.E has been recognized with a value of 0.06167 and the 95% CI value is 0.5719 to 0.8137, also The AUC value in serum CH is 0.6721, S.E has been recognized with a value of 0.06003 and the 95% CI value is 0.5545 to 0.7898. As well as The AUC value in serum ALT is 0.7988 which has a high range that showed the high sensitivity than specificity. The S.E value is 0.05054 and the 95% CI value is 0.6998 to 0.8979, (P < 0.0001). Also, the AUC value for serum AST is 0.7803, as well S.E and 95% CI values are (0.05312 and 0.6762 to 0.8845) respectively, (P < 0.0001). And also, The AUC value in serum p53 is 0.5636, S.E has been recognized with a value of 0.06583 and the 95% CI value is 0.4345 to 0.6926, (P < 0.3539). ROC curve analysis exhibit that serum NO, MDA, TG, HDL, ALT and AST are excellent biomarkers for the diagnostic accuracy of breast cancer in female as a result of the high level of AUC. Although, LDL and CH are good but not potential biomarker for the breast cancer diagnostic accuracy. Whereas, this study demonstrates that serum p53 is not a good biomarker for female breast cancer with AUC value 0.5636. Although, it is known that serum p53 is a tumor suppressor protein that plays a crucial role in the inhibition of cancer development. The data are shown in Table 3.

Table (3): ROC curve analysis for determination the diagnostic accuracy of NO, MDA, CH, TG, HDL, LDL, ALT and AST in patients group with breast cancer.

Parameters	AUC	S.E	95% CI	P value
NO (nmol/ml)	0.8846	0.05062	0.7853 to 0.9838	< 0.0001
MDA(nmol/ml)	0.7145	0.05757	0.6016 to 0.8273	0.001570
TG (mg/dl)	0.8317	0.04544	0.7426 to 0.9208	< 0.0001
HDL (mg/dl)	0.8176	0.04951	0.7205 to 0.9147	< 0.0001
LDL (mg/dl)	0.6928	0.06167	0.5719 to 0.8137	0.0045
CH (mg/dl)	0.6721	0.06003	0.5545 to 0.7898	0.01209
ALT(U/L)	0.7988	0.05054	0.6998 to 0.8979	< 0.0001
AST(U/L)	0.7803	0.05312	0.6762 to 0.8845	< 0.0001
p53 (pg/ml)	0.5636	0.06583	0.4345 to 0.6926	0.3539

4. CONCLUSIONS

This work focused on the impacts of oxidative stress in patients with breast cancer as the oxidative stress rising in breast cancer disease due to human tumor cells produce large quantity of ROS. The results of this study reveal that the pervasiveness of the oxidative stress is a risk factor in patients group with breast cancer and it's much higher than in control group. The potential risk factors of liver diseases, abnormality of renal function and hyperlipidemia in patients with breast cancer exhibit the high levels. While, the results from the existent study show that systemic oxidative stress is raised to a greater degree in breast cancer disease and this oxidative stress causes damage to most of the cellular targets and has the highest side effect of lipid profile, hepatic and renal damage thus plays a crucial role in liver diseases, abnormality of renal function and endothelial dysfunction which consequently is risk factor for patients health. hyperlipidemia most possibly due to the This study demonstrates that serum p53 is not a good biomarker for female breast cancer. Although, it is recognized that p53 is a tumor suppressor protein that plays a crucial role in the inhibition of cancer development.

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