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Oxidant/Antioxidant Status, Lipids and Hormonal Profile in Overweight Women with Breast Cancer

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Abstract This study was carried out to determine the relationships between leptin concentrations, lipid alterations, oxidant/ antioxidant status, in vitro LDL oxidizability and LDL-fatty acid composition in overweight breast cancer patients. Glucose, insulin, leptin, lipids, LDL-cholesteryl ester fatty acids, markers of oxidant status (MDA, Hydroperoxides, carbonyl proteins, conjugated dienes) and markers of antioxidant status (vitamins A, C, E, erythrocyte activities of the enzymes superoxide dismutase, SOD, catalase, glutathione peroxidase,GPx, and glutathione reductase, GR and the serum total antioxidant status, ORAC) were investigated in breast cancer patients and in control women. Our findings showed that insulin, leptin, triglyceride, cholesterol and LDL-C concentrations were increased in patients compared to controls. ORAC and vitamin C and E values were lower while plasma hydroperoxide, carbonyl protein and conjugated diene levels, SOD and GPx activities were higher than in controls. Alterations in LDL-fatty acid composition were associated with their enhanced oxidative susceptibility. There were significant positive correlations between leptin concentrations and LDL-C, hydroperoxides, carbonyl proteins, SOD activity, baseline conjugated diene levels and oxidation rate, and significant negative correlations between leptin and ORAC, lag time and LDL-PUFA in patients. In conclusion, breast cancer is associated with lipid alterations and enhanced oxidative stress linked to high leptin levels in overweight.

Keywords Breast cancer · Fatty acids · Leptin · Lipids · Lipoproteins · Oxidative stress

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Introduction

Breast cancer is the most commonly diagnosed cancer among women and is a leading cause of cancer-related deaths worldwide [1]. Breast cancer risk factors include early age at menarche, late age of menopause and at first pregnancy, overweight, oral contraception, hormone replacement therapy, diet, family history, lactation and prior history of benign breast disease [2, 3]. There is ample evidence supporting a causative role of oxidative stress in breast cancer [4]. The

following mechanisms are thought to be involved in the increased oxidative stress in breast cancer: genetic variability in antioxidant enzymes, estrogen treatment, excess generation of reactive oxygen species as well as reduced antioxidant defence systems [5, 6].

In addition to the known risk factors, other factors, including fatty acids, are likely to play an important role in determining risk of breast cancer [7]. Several studies have demonstrated changes in serum lipids and lipoproteins in cancer patients including elevated plasma lipid level such as total lipids, triglycerides, total cholesterol, low density lipoprotein (LDL-C) and free fatty acids (FFA) with low concentrations of high density lipoprotein (HDL-C) [8, 9]. Lipid alterations and oxidizability of lipoproteins have been considered as contributory factors to oxidative stress. A relationship between the amount of polyunsaturated fatty acids (PUFA) in LDL and susceptibility of LDL to oxidation has been demonstrated [10]. However, the relationships between LDL oxidizability, fatty acid composition and oxidant/antioxidant status in breast cancer are still not clear.

In breast cancer patients, overweight is a problem that negatively affects serum lipid profiles and increases the risk of cardiovascular disease (CVD) [11]. Overweight is associated with glucose and lipid metabolism abnormalities, increased cardiovascular risk and oxidative stress [12]. Leptin is a hormone with multiple biological actions which is produced predominantly by adipose tissue. Leptin concentration is increased in overweight people [13]. Several actions of leptin, including the stimulation of normal and tumor cell growth, migration and invasion, and enhancement of angiogenesis, suggest that this hormone can promote an aggressive breast cancer phenotype which can be estrogen-independent [14]. Levels of leptin increase in the blood of breast cancer patients [15]. We hypothesized that the combination of oxidative stress, high leptin levels and altered lipid and fatty acid profile led to an increase in breast cancer risk. A relationship between this metabolic association and breast cancer has not, however, been reported.

The present work is an attempt to determine oxidative stress status, lipid and lipoprotein levels, the in vitro LDL oxidizability and its fatty acid composition in overweight breast cancer patients. The oxidative stress status was evaluated by assaying both plasma total antioxidant capacity (ORAC), markers of lipid and protein oxidation and blood antioxidant defences, namely erythrocyte superoxide dismutase, catalase, glutathione peroxidase and reductase activities, plasma vitamin A, C and E levels. This investigation was aimed at assessing whether increased oxidative stress in breast cancer is associated with increased LDL oxidizability and fatty acid alterations, and whether these relationships are related to leptin concentrations in overweight women.

Patients and Methods

Patients

The protocol was approved by the Tlemcen Hospital Committee for Research on Human Subjects. The purpose of the study was explained to all participants and investigation was carried out with their written consent. A total of 38 newly-diagnosed breast cancer women were recruited in the department of obstetrics and gynecology at Tlemcen Hospital, Tlemcen, and in the private clinic for surgery, Maghnia, Algeria. They had not undergone any previous treatment for their tumours, and were clinically categorised as stage II (18 patients) and stage III (20 patients) infiltrative ductal carcinoma of the breast, according to the Tumor-Node-Metastases (TNM) classification. The subjects were ranging in age 35–45 years. The patients were all using oral contraceptives and were all in pre-menopausal status. They had all a body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) of > 25.0 to < 30.0 kg m^{-2} and were classified as overweight. None of them had concomitant diseases such as diabetes mellitus, liver disease, thyroid disease, nephrotic syndrome, hypertension and rheumatoid arthritis and none of them was using vitamin supplements. Fifty healthy age matched (between 35 and 45 years) pre-menopausal women were selected as controls. They had all a BMI below 25 and are considered normal weight. None of the controls had a previous history of breast cancer and other cancer-related diseases. Participants were asked to complete a questionnaire with epidemiologic information on demographic and lifestyle factors, personal and medical history, and family history of breast cancer. Permission was also requested to incorporate clinical and personal data into the research database, and for collection of a blood specimen before the surgery and the initiation of therapy. The characteristics of the population studied are reported in Table 1.

Blood Samples

Fasting venous Blood samples were collected in heparinized tubes, centrifuged and plasma was separated for glucose, insulin, leptin, lipids, vitamins, total antioxidant capacity, hydroperoxides and carbonyl proteins determinations. The remaining erythrocytes were washed three times in isotonic saline, hemolysed by the addition of cold distilled water (1/4), stored in refrigerator at 4°C for 15 min and the cell debris was removed by centrifugation (2,000g ×15 min). The hemolysates were appraised for antioxidant enzyme activities.

Glucose, Insulin and Leptin Determination

Plasma glucose was determined by glucose oxidase method using a glucose analyzer (Beckman Instruments, Fullerton,

Table 1 Population characteristics

Characteristics	Group 1 (controls)	Group 2 (breast cancer)
Number	50	38
Age (years)	40±5	41±4
BMI (Kg/m^2)	23.80±1.3	27.84±1.7
Parity	3±1	2±1
Age at menarche (%)		
Before 14 years	10 (20)	18 (47.37)
Age at first live birth		
≤24 years	15 (30)	3 (7)
25–29 years	30 (60)	24 (63)
≥30 years	5 (10)	11 (30)
Duration of oral contraceptive use		
<5 years	28 (56)	14 (37)
≥5 years	22 (44)	24 (63)
Family history of breast cancer	6 (12)	15 (40)

Values are means ± SD or number (percentage)

BMI body mass index (weight/height^2)

CA, USA). Leptin and Insulin were analysed using RIA kits with antibodies to human leptin or insulin (Linco Research).

Lipoprotein and Lipid Determination

Plasma lipoprotein fractions (LDL, d<1.063; HDL, d< 1.21 g mL^{-1}) were separated by sequential ultracentrifugation in a Beckman ultracentrifuge (Model L5-65, 65 Ti rotor), using sodium bromide for density adjustment. Plasma triglyceride and total cholesterol, LDL- and HDL- cholesterol contents were determined by enzymatic methods (Sigma).

Scavenging Capacity of Plasma

The oxygen radical absorbance capacity of plasma (ORAC) employs the oxidative loss of the intrinsic fluorescence of allophycocyanin (APC) as we have previously described [10]. APC fluorescence decay shows a lag or retardation in the presence of antioxidants, related to the antioxidant capacity of the sample. Trolox was used as a reference antioxidant for calculating the ORAC values, with one ORAC unit defined as the net protection area provided by 1 mM final concentration of trolox.

Determination of Plasma Levels of Vitamins A, C and E

Plasma a-tocopherol (vitamin E) and retinol (vitamin A) were determined by reverse phase HPLC and detected by an UV detector at 292 nm for vitamin E and 325 nm for vitamin A. Vitamin C levels were determined in plasma using the method of Roe and Kuether [16].

Determinations of Erythrocyte Antioxidant Enzyme Activities

Catalase (CAT EC 1.11.1.6) activity was measured by spectrophotometric analysis of the rate of hydrogen peroxide decomposition at 240 nm [17]. Glutathione peroxidase (GSH-Px EC 1.11.1.9) was assessed by Paglia and Valentine method [18] using cumene hydroperoxide as substrate. Glutathione reductase (GSSG-Red EC 1.6.4.2) activity was determined by the measuring of the rate of NADPH oxidation in the presence of oxidized glutathione [19]. Superoxide dismutase (EC 1.15.1.1) activity was measured by the NADPH oxidation procedure [20].

Determination of Plasma Hydroperoxides

Hydroperoxides (marker of lipid peroxidation) were measured by the ferrous ion oxidation-xylenol orange assay (Fox2) in conjunction with a specific ROOH reductant, triphenylphosphine (TPP), according to the method of Nourooz-Zadeh et al. [21].

Determination of Plasma Carbonyl Proteins

Plasma carbonyl proteins (marker of protein oxidation) were assayed by 2,4-dinitrophenylhydrazine reaction [22].

LDL Susceptibility to In Vitro Oxidative Stress

LDL-protein content was determined according to Lowry et al. [23]. LDL fraction was diluted to a final concentration of 100 μg/ml protein using PBS. Oxidative modification of LDL was initiated by addition of freshly prepared 10 μM

CuSO4 solution at 37°C for 6 h, as reported by Esterbauer et al. [24]. LDL oxidation kinetics was continuously monitored by measuring the conjugated diene formation, with the increase in absorbance at 234 nm. Absorbance was analyzed at 5-minute intervals. Using experimental curves of oxidation kinetics, the following parameters were evaluated: the lag time (Tlag, min), which represents the resistance to oxidation and defined as the intercept of the straight lines derived from the lag phase and the propagation phase; maximal conjugated diene production (CDmax, μmol/L) determined from the difference between the absorbance at the maximum slope of the absorbance curve and the absorbance at time zero; the rate of conjugated diene formation (oxidation rate) expressed in μmoles of dienes formed per minute (μmol/L/min) and time to reach maximal amounts of conjugated dienes formed (Tmax, min). The concentration of conjugated dienes at baseline levels (BCD) and after in vitro oxidation (oxidation rate, CDmax) was calculated by using the molar extinction coefficient 2.95×10^4 M^{-1} cm^{-1}.

Fatty Acid Analysis

For the determination of the fatty acid content in LDL, lipids were extracted by chloroform/methanol, 2/1, *V/V*. LDL-cholesteryl esters were isolated by thin layer chromatography. After saponification with NaOH/methanol, fatty acids were transmethylated by boron trifluoride/methanol. Fatty acid methyl esters were analyzed by gas liquid chromatography as previously reported [10].

Statistical Analysis

The data were expressed as mean ± SD. Statistical analysis was carried out using Statistica (version 4.1, Statsoft, Paris, France). The significance of the differences between group 1 (controls) and group 2 (patients) was determined by Student's *t*-test. Univariate associations between variables were analyzed using Pearson's correlation coefficients. $P<0.05$ was considered as significant.

Results

Population Characteristics

As shown in Table 1, breast cancer patients were more likely, than control subjects, to be overweight, to having an earlier age at menarche, fewer childbirths, being older at first child birth, to have used oral contraceptives for a long period and to have family history of breast cancer.

Glucose, Insulin, Leptin and Lipid Levels

Breast cancer patients demonstrated significantly higher levels of triglycerides, total cholesterol and LDL cholesterol compared with the control group, whereas HDL cholesterol levels were similar among the two groups (Table 2). Fasting plasma glucose did not differ significantly between the control and breast cancer groups. Insulin and Leptin plasma levels were significantly higher in patients than in the control group (Table 2).

Oxidative Stress Markers

Plasma total antioxidant status (ORAC) was lower, whereas plasma hydroperoxide and carbonyl protein levels were higher in breast cancer patients than in control women (Table 3). While vitamin A levels did not differ between the breast cancer and control groups, vitamin C and E levels were significantly lower in patients compared to controls.

Erythrocyte SOD and glutathione peroxidase activities were significantly higher whereas erythrocyte catalase and glutathione reductase activities were unchanged in breast cancer patients when compared with controls (Fig. 1).

Table 2 Plasma glucose, insulin, leptin and lipid levels in breast cancer patients and control women

Parameters	Group 1 (controls)	Group 2 (breast cancer)
Glucose (mmol/L)	5.55±0.15	5.83±0.22
Insulin (pmol/L)	64.34±5.72	75.45±4.39 *
Leptin (ng/mL)	7.96±1.33	13.75±1.79 *
Total cholesterol (mmol/L)	4.99±0.46	6.54±0.37 *
Triglycerides (mmol/L)	1.20±0.14	1.66±0.17 *
HDL-C (mmol/L)	1.44±0.08	1.36±0.11
LDL-C (mmol/L)	3.00±0.23	4.44±0.17 *

Values are means ± SD. The significance of the differences between two groups was determined by Student's *t* test

HDL-C high density lipoprotein-cholesterol; *LDL-C* low density lipoprotein-cholesterol

*$P<0.01$, breast cancer patients versus controls

Table 3 Oxidative stress markers in breast cancer patients and control women

Parameters	Group 1 (controls)	Group 2 (breast cancer)
ORAC (Arbitrary Units)	5.30±0.41	2.06±0.25 **
Vitamin A (μmol/L)	16.70±2.45	14.58±2.37
Vitamin C (μmol/L)	38.58±6.43	15±3.15 **
Vitamin E (μmol/L)	24.55±2.13	13.73±1.38 *
Carbonyl proteins (nmol/mg protein)	1.23±0.24	2.98±0.30 *
Hydroperoxides (μmol/L)	2.90±0.34	4.52±0.27 *

Values are means ± SD. The level of ORAC was determined as described in Patients and Methods. The significance of the differences between two groups was determined by Student's *t* test

* $P<0.01$, ** $P<0.001$, breast cancer patients versus controls

In Vitro LDL Copper-induced Oxidation Parameters

Oxidizability markers of LDL isolated from breast cancer patients showed a shorter Tlag and Tmax compared to that of the controls (Table 4). In these patients, baseline conjugated diene (CD) levels and oxidation rate were increased while CDmax amounts were not significantly different from that of control subjects.

LDL—Cholesteryl Fatty Acid Composition

Significant increases in saturated fatty acid (SFA) contents with a significant decrease in polyunsaturated fatty acid (PUFA) levels were observed in LDL—cholesteryl esters of breast cancer patients compared with controls (Fig. 2).

Correlations Between Leptin and Metabolic Parameters

Pearson regression analysis did not show a significant correlation between plasma leptin levels and lipid or oxidative stress parameters in the control population. In contrast, in the breast cancer group, a significant association was found. Thus, leptin levels were statistically and positively correlated with LDL-C ($r=0.26$, $P<0.05$), hydroperoxides ($r=0.31$, $P<0.01$), carbonyl proteins ($r=0.30$, $P<0.01$), SOD ($r=0.27$, $P<0.05$), LDL-BCD ($r=0.42$, $P<0.001$), and LDL oxidation

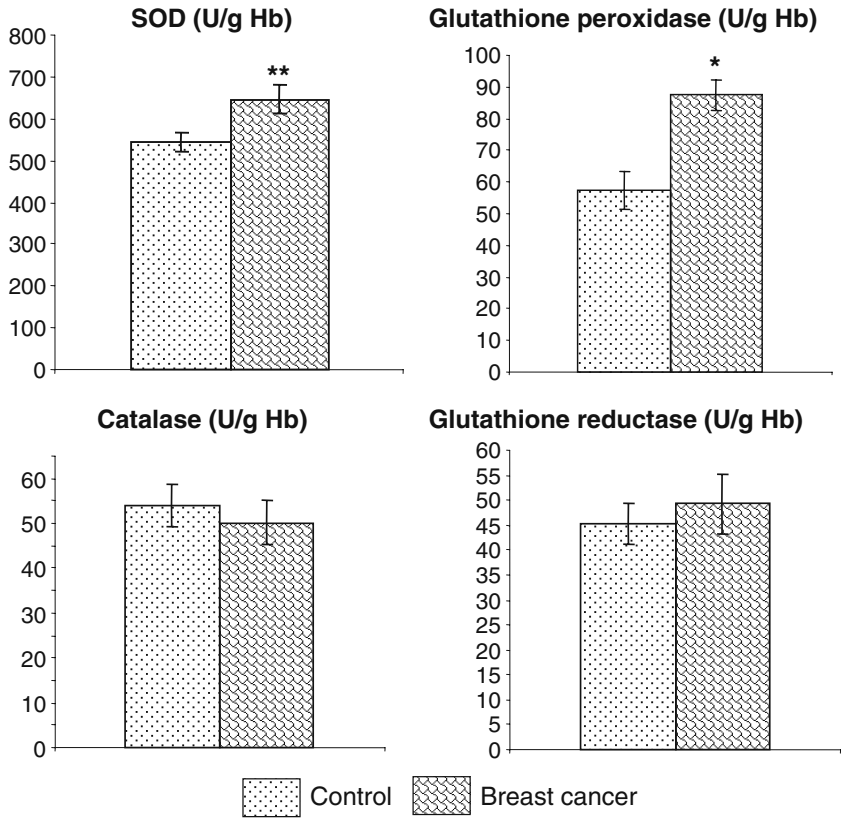

Fig. 1 Erythrocyte antioxidant enzyme activities in breast cancer patients and control women. Values are means ± SD. The significance of the differences between two groups was determined by Student's *t* test. * $P<0.01$, ** $P<0.001$, breast cancer patients versus controls

Table 4 Parameters of the copper-induced in vitro oxidation of LDL in breast cancer patients and control women

Parameters	Group 1 (controls)	Group 2 (breast cancer)
LDL-BCD (μmol/L)	43.78±4.75	52.98±3.11 *
Tlag (min)	106.73±10.22	49.27±6.94 **
Oxidation rate (μmol/L/min)	0.24±0.02	0.33±0.03 **
CDmax (μmol/L)	28.99±3.41	30.50±4.07
Tmax (min)	236.43±17.19	146.88±18.35 **

Values are means ± SD. LDL oxidisability was measured as the kinetics of the formation of conjugated dienes after incubation with CuSO4 as described in Patients and Methods

LDL-BCD baseline conjugated diene levels in LDL; *Tlag* lag time; *CDmax* maximal conjugated diene production; *Tmax* time to reach maximal amounts of conjugated dienes formed

The significance of the differences between two groups was determined by Student's *t* test

* $P<0.01$, ** $P<0.001$, breast cancer patients versus controls

rate ($r=0.47$, $P<0.001$) in breast cancer patients. In these women, leptin concentrations were also statistically and negatively correlated with ORAC ($r=-0.33$, $P<0.01$), Tlag ($r=-0.45$, $P<0.001$) and LDL-PUFA ($r=-0.24$, $P<0.05$).

Discussion

Recent evidences suggest that breast cancer patients are under oxidative stress and that etiology of cancer and complications seem to be mediated by oxidative stress [4–6]. However, the relationships between free radical production, antioxidant levels, lipoprotein oxidation, fatty acid composition, and the presence or absence of overweight are still unclear.

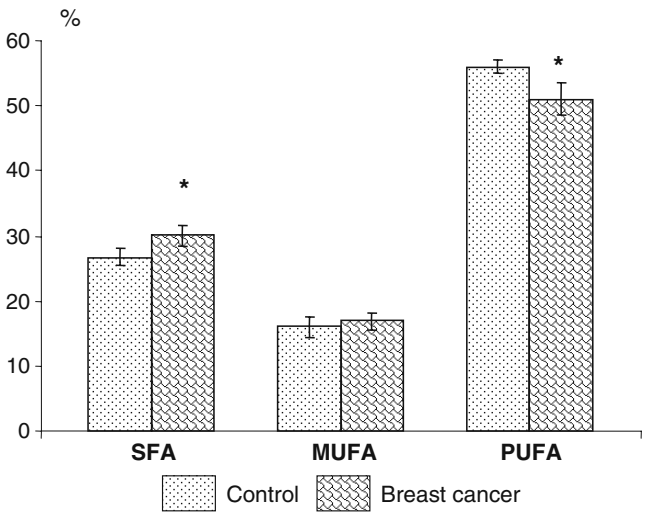

Fig. 2 Cholesteryl fatty acid composition of LDL in breast cancer patients and control women. Values are means ± SD. *SFA* saturated fatty acids; *MUFA* monounsaturated fatty acids; *PUFA* polyunsaturated fatty acids. The significance of the differences between two groups was determined by Student's *t* test. * $P<0.01$, breast cancer patients versus controls

In this study, all breast cancer patients were overweight and had normal glucose concentrations but increased plasma insulin levels compared with control values, reflecting probably an insulin resistance state. Overweight represents a risk factor for the development of insulin resistance and insulin resistance/hyperinsulinemia is believed to be an important link between overweight and the associated metabolic abnormalities and cardiovascular risk [13]. Hyperinsulinemia, a biomarker for insulin resistance, was seen most commonly in conjunction with increased adiposity and has been associated with an increase in both premenopausal and postmenopausal breast cancer risk [25]. We also observed an increase of leptin concentrations in breast cancer patients. These results are in agreement with previous studies which reported high serum insulin and leptin levels in overweight women [13, 26]. Leptin is primarily synthesized in adipocytes and its concentration has been shown to increase as a direct function of increasing fat mass [15]. In our study, leptin, in association with insulin, has an important role in the known adverse effect of overweight on breast cancer.

Several investigations focused attention on the serum lipid and lipoprotein patterns in breast cancer and the results were different [8, 9, 27, 28]. The alterations in lipid profile levels showed a significant correlation with breast cancer risk and disease status [28].

The results of the present study demonstrated an increase in plasma lipid levels of breast cancer patients compared to the control women. This is in agreement with results of other studies [8]. We observed a significant increase in total plasma cholesterol and LDL-C levels of patients, which is in agreement with other studies [29]. Our results show a significant increase in serum triglyceride levels in breast cancer patients as compared with the control women, which is consistent with results reported by other studies [30], although some researchers reported normal serum triglyceride levels in premenopausal breast cancer patients [8].

HDL-C in our patients was similar to that found in controls, in agreement with previous reports [29]. However, in some studies, HDL-C level was noted to be significantly decreased in breast cancer patients [9]. In fact, HDL-C levels were low in obese patients, particularly in postmenopausal patients [27, 29]. In our study, all patients were premenopausal and only overweight which could explain lipid profile differences with previous findings.

Our data revealed that the total antioxidant activity (ORAC) was decreased in the plasma of breast cancer patients in favour of an oxidative stress in such patients. These results are in agreement with previous studies [4, 31]. The reduction of ORAC was associated with increased oxidative stress markers such as hydroperoxide and protein carbonyl levels in patients. Elevated levels of oxidant markers in breast cancer patients could result from their hyperinsulinemic and hyperleptinemic states. Excessive lipid peroxidation occurring in patients could also be attributed to their hypercholesterolemia. Protein carbonyl contents were found to be increased in overweight breast cancer women [32] and reflect the amount of oxidative stress the person has been exposed to during a long time period. Increased protein carbonyl levels in this study indicated that free radical mediated oxidative damage occurred for a long time in these patients, in accordance with previous studies [32], probably before breast cancer development. Excess adiposity due to overweight or lower intakes of antioxidants, such as vitamins, may increase the formation of reactive oxygen species in cells [33].

As far as the vitamins are concerned, we found no alteration in the levels of vitamin A, whereas the levels of vitamin C and E were lower in breast cancer patients than control subjects. Low plasma levels of vitamin C and E could reflect their high utilisation rate, suggesting that these vitamins may be used to reduce oxidative stress in breast cancer patients. It is well reported that oxidative stress is induced by both the increases in free radicals and disturbance of the free radical scavenging system in breast cancer [4–6]. Alternatively, it is also possible that reduced vitamin C and E concentrations reflect low intake, which resulted in decreased antioxidant defence system in breast cancer patients.

The increase in plasma lipid peroxidation and protein oxidation in breast cancer seen in the present study was associated with enhanced erythrocyte antioxidant SOD and glutathione peroxidase activities. In contrast, catalase and glutathione reductase activities were unchanged in breast cancer. Our findings agree with the observations of Surapaneni et al. [34] who have reported increased erythrocyte SOD and glutathione peroxidase activities in breast cancer patients. The over expression of SOD might be an adaptive response and it results in increased dismutation of superoxide to hydrogen peroxide. The rise in the activity of GPX could be due to its induction to counter the effect of increased oxidative stress. Reactive oxygen species often stimulate the production of antioxidant molecules, and the production and the activity of antioxidant enzymes increase corresponding to the high oxidative stress.

In our study, despite high antioxidant enzyme activities, enhanced oxidative products were still present in breast cancer patients. Indeed, our results demonstrated a higher susceptibility to oxidation of LDL from these patients, in agreement with previous reports [35]. Measurement of diene conjugation has become the most popular method to monitor LDL oxidation in vitro, and the oxidation-induced increase of diene conjugation in LDL lipids is well documented. In our study, breast cancer patients presented higher basal levels of conjugated dienes in LDL suggesting the presence of circulating minimally oxidized LDL. The lag time indicating intrinsic antioxidant activity of LDL particles was shorter in patients compared to controls. In addition, the oxidation rate of these LDL was higher than in control values. These findings indicate that LDL particles in breast cancer subjects may be particularly susceptible to oxidative modification. Earlier studies have shown that there are several intrinsic properties of lipoproteins that can affect their susceptibility to oxidation. Lipid levels, lipoprotein antioxidant content, fatty acid composition and LDL size are among the factors that have been shown to have an impact on oxidation parameters. We hypothesize that hypertriglyceridemia and hypercholesterolemia with changes in LDL core surface composition and/or antioxidant depletion especially vitamin E may have contributed to alteration in LDL oxidation in breast cancer. The oxidizability of LDL is also dependent on the presence of oxidizable lipids, i.e., PUFA. Positive correlations were found between PUFA levels and the susceptibility of LDL to oxidation [10]. However, in our study, despite increased in vitro oxidation of LDL isolated from patients, LDL-PUFA contents were low while SFA levels were high compared to control values. Our results are in line with other authors who found similar results concerning red blood cells fatty acid concentrations in breast cancer [36]. The potential in vivo oxidation of polyunsaturated fatty acids might explain the low levels of LDL-PUFA observed in breast cancer. The high level of saturated fatty acids in breast cancer patients can be attributed to the high intake of fat-rich dietary products, or to an increased endogenous synthesis. Fatty acid synthase (FAS) is frequently overexpressed in breast cancer [36, 37]. On the other hand, a direct relation was previously found between overweight and markers of oxidative stress and the susceptibility of lipids to oxidative modification in humans independently of other coronary heart disease risk factors [12, 13, 35]. Overweight in breast cancer patients is probably an important factor aggravating metabolic alterations.

An interesting finding in our study was that leptin levels correlated with several lipid and oxidant/antioxidant markers only in breast cancer women. There were significant positive correlations between leptin concentrations and LDL-C, hydroperoxides, carbonyl proteins, SOD activity, baseline conjugated diene levels and oxidation rate, and significant negative correlations between leptin and ORAC, lag time and LDL-PUFA in patients. These results suggested that leptin may have contributed to alterations in lipid profile and to oxidant/antioxidant imbalance during breast cancer in overweight women. These metabolic abnormalities related to leptin may also be linked to the development of breast cancer in these women. However, there were some limitations to the small sample size used in this study. Metabolic alterations in overweight breast cancer women might be confirming by collecting data with a larger number of patients.

In conclusion, our data supported an imbalance of the oxidant/ antioxidant systems in favor of an oxidative stress in breast cancer patients. This oxidative stress was associated to hyperinsulinemia, hyperleptinemia and lipid and fatty acid alterations. Overweight, via high leptin concentrations, was an important factor responsible and/or aggravating metabolic abnormalities in breast cancer.

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Competing interests The author(s) declare that they have no competing interests.

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