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Relationship of oxidative enzymes with biochemical parameters in breast cancer patients

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Abstract
Background - *Breast cancer has a complex aetiology. Significant breast cancer risk factors include age, food, obesity, inactivity, hormone replacement therapy, family history, and others. Our current study's objective was to evaluate the electrolyte and biochemical parameter values in both breast cancer patients and healthy individuals. We have also investigated the link between the antioxidant enzymes and levels of electrolytes.*
Methods- *The data came from 292 individuals who took part in closely supervised clinical research on the correlation between oxidative enzymes and biochemical indicators in breast cancer patients. Finding the connection between biochemical markers and oxidative enzymes in breast cancer patients was the goal of this open, non-randomized study.*
Results- *Aside from albumin, which has significantly increased in the healthy control patients (P = 0.04), no alterations in liver indicators like amylase and glucose were found. The most notable increases in K^+, Ca^{2+}, and PO_4^3 were seen in patients with low baseline levels (P = 0.05). In the group of patients with breast cancer, it was also discovered that Na+ and PO_4^3 increased significantly (P = 0.05).*
Conclusion*- Patients with breast cancer had elevated levels of YGT, LDH, ALP, urea, and phosphate, which might be employed as serum indicators for early identification of breast cancer. Antioxidant enzyme levels, on the other hand, were considerably lower in breast cancer patients.*

Keywords *– Breast Cancer, Antioxidant Enzymes, Biochemical Parameters, Liver-function enzymes*

1. Introduction

Millions of new cancer patients are diagnosed each year, and the disease accounts for many fatalities. As a result, cancer is a major public health concern around the world[1]. With 1.38 million cases worldwide, breast cancer is the second most common cancer to be diagnosed. Breast cancer has a complex aetiology. Age, diet, obesity, inactivity, hormone replacement treatment, family history, and others are significant breast cancer risk factors[2]. According to epidemiological research, having a body mass index (BMI) that is overweight or obese is a risk factor for developing postmenopausal breast cancer[3]. Obesity has a complex function in breast cancer and is linked to increased inflammation and changes in the serum levels of substances that may control growth, like adiponectin. Obese participants in cross-sectional studies reported greater levels of oxidative stress biomarkers than their slimmer counterparts. Additionally, these indicators are substantially more concentrated in people who are overweight[4]. In related to obesity, oxidative stress can come from a variety of sources. According to studies, there is an increase in adipose tissue, especially visceral adiposity, which is highly linked with systemic levels of oxidative stress biomarkers[5]. Reactive oxygen species (ROS) and antioxidant reaction capability are out of balance under conditions of oxidative stress, which promotes the growth of diseases such breast cancer.

The liver has a key role in the metabolism of many commonly used anticancer agents. Thus liver function assessment is a fundamental part of initial and ongoing management of patients with cancer[6]. Chemotherapy in the setting of liver dysfunction can be associated with reduced effectiveness. Furthermore, several chemotherapy agents induce liver injury or dysfunction, which can manifest as abnormal serum liver biochemistry[7]. Conventional serum liver biochemical testing does not always predict these potential complications. In the present study, we focused on current standard serum liver biochemical testing that will measurements of liver physiology and pathophysiology in the patients suffering with breast cancer. This study highlighted the comparison between the levels of biochemical parameters of healthy individuals and patients of breast cancer in correlation with the antioxidant enzymes, which is helpful of the researcher to focus on the biochemical parameters levels in patients with stage IV metastatic breast cancer (MBC).
Increasing evidence links electrolyte disorders with greater morbidity and mortality, in critically ill patients[8]. There are very few guidelines on the treatment of electrolyte disorders in critically ill patients, and most focus on individual electrolytes without taking the interrelation between specific deficits into account. Hyperkalemia, hypercalcemia, and

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hyponatremia can be chemotherapy-induced via various factors, for example, tumor lysis syndrome can cause hyperkalemia[9]. Hypercalcemia and hyponatremia are often observed in patients with breast cancer, prostate cancer, and paraneoplastic syndrome. In some cases, hypomagnesemia results from drugs targeting epidermal growth factor receptors, such as cetuximab and panitumumab[10]. Thus, careful monitoring of the serum electrolyte concentration plays an important part in the biochemical monitoring of breast cancer patients and ensures effective and safe chemotherapy dosing in cancer, which is currently poorly defined. The purpose of our present investigation was to assess the levels of electrolytes and biochemical parameters in healthy as well as breast cancer patients. We have also assessed the relationship between the antioxidant enzymes and levels of electrolytes.

2. Methods

This is a prospective study which included 292 individual women who were divided into two groups. The first group consist of 254 healthy individual women who are apparently normal with no know clinical problem and no history of chronic drugs intake whereas second group included the 38 breast cancer patients. The analysis was carried out in the Department of Biochemistry, Rajshree Medical Research Institute, Bareilly (U.P.)

2.1 Study design and participants

Prospectively collected laboratory results were obtained from 38 patients suffering from stage IV breast cancer. Study was performed as a non randomized, double-blind, and placebo-controlled, multicentre study, with a stratified semi-crossover design. All the included breast cancer patients had previously undergone at least third-line chemotherapy and several other available types of cancer treatments[11]

Venous blood samples were drawn 1 hour before breast surgery and, the serum was separated by centrifugation at 3500 rpm for 5 minutes, and then it was stored at –20°C until ready for the assay of biochemical parameters. Similarly, blood samples were drawn from healthy controls and processed.

2.2 Procedures

Blood samples were taken at baseline and was drawn via a cubital vein and separated into serum by centrifugation. Standard procedures for measurement of the different parameters were used according to the standard methodology of the participating hospitals. Approval of the ethical committees were received, along with written consent from all patients[12].

The levels of antioxidant enzymes were estimated by using manual methods. Serum glutathione was determined by a modified procedure utilizing Ellman reagent. The levels of other biochemical enzymes of oxidative stress were analysed using the commercially available kits (Roche Diagnostics, Mannheim, Germany); and the analyses were carried out according to the manufacturer's instructions using COBAS 311 Autoanalyzer and Fortress Diagnostic respective.

Table 1- Levels of antioxidant enzymes and biochemical parameters in patients having breast cancer as compare to healthy patients

	Characteristics & parameters	Healthy patients (n=254)	Breast cancer patients(n=38)	*P* value
1	**Age (years)**	54.2 (29.8- 71.2)	58.8(37.4-67.2)	
2	**BMI (kg/m^2)**	25.6 (19.2- 31.1)	29.8(19.5-36.6)	
3	**Disease duration (year)**	----------	1.8-18.0	
4	**Systolic BP (mmHg)**	112(14.6)	134(21)	
5	**Diastolic BP (mmHg)**	77 (11.7)	84(11)	**<0.05**
6	**Heart rate (beat/min)**	74 (12.8)	81(14)	**<0.05**
7	**Respiratory rate (breath/min)**	19 (4.3)	22(5.1)	**<0.05**
8	**ɤ-GT (IU/L)**	5.43(3.13-7.32)	189.3(27.8-290.7)	**0.018**
9	**LDH (mg/dL)**	280.4(117.4-343.9)	670.6(343.4-907.5)	**0.08**
10	**ALP (mg/dL)**	142.4(118.2-237.7)	401.9(107.7-647.4)	**0.0014**
11	**ALT (U/dL)**	21.20(17.27-24.31)	39.75(24.35-58.54)	**0.08**
12	**Amylase (somoggi/L)**	75.8(51.7-91.7)	71.4(53.4-96.4)	**-0.01**
13	**Glucose (mg/dL)**	5.84(5.73-6.24)	5.73(5.11-6.15)	**0.09**
14	**Creatinine (mg/dL)**	1.07(0.68- 0.78)	2.05(0.67-0.79)	**0.03**
15	**Albumin (g/dL)**	4.51(4.3-6.5)	7.4(4.3-8.6)	**0.03**
16	**Bilirubin (mg/dL)**	0.10(0.08-0.15)	0.13(0.05-0.21)	**0.05**
17	**Urea (mg/dL)**	27.42(16.29-38.55)	69.42(57.59-111.34)	**0.03**
18	**Potassium (mEq /L)**	4.05(3.83-4.28)	4.41(4.19-4.44)	**0.04**
19	**Sodium (mEq /L)**	144.7(137.4-146.0)	155.3(131.8-157.7)	**0.01**
20	**Calcium (mg/dL)**	10.33(8.25-12.40)	12.08(7.33-10.43)	**0.01**
21	**Magnesium (mg/dL)**	1.15(0.98-1.34)	1.17(0.98-1.27)	**0.02**
22	**Phosphate (mg/dL)**	1.92(1.53-2.32)	2.16(1.72-2.61)	**<0.01**
23	**AST (mg/dL)**	43.78(13.00-54.55)	43.3(12.75-53.85)	**NS**
24	**Superoxide dismutase**	0.24±0.5	0.51±0.13	**0.01**
25	**Gluthathione peroxidase**	1.2±0.6	1.7±0.6	**<0.001**
26	**Gluthathione transferase**	0.7±0.4	0.9±0.3	**<0.001**
27	**Catalase**	132.25±21.4	43.5± 11.3	**0.001**

Note: The results are expressed as mean and median with range values with 95% confidence intervals.

Abbreviations: ALP- alkaline phosphatase; ALT-alanine transaminase; ;LDH- lactate dehydrogenase; ɤ-GT- Y-glutamyl transferase

2.3 Statistical analysis

The results were expressed as mean value (standard deviation [SD]) and 95% confidence interval (CI) of the mean. For each of the observed variables, the quartiles were calculated. Changes from parameters was calculated with paired Student's t-test.

3. Results

3.1 Serum chemistry

The study comprised a total of 254 healthy controls and 38 women with histologically confirmed instances of breast cancer. In our study, 36% of patients lived in cities and 64% in rural areas. The mean ages of the controls and cases, which ranged from 37 to 69 years old, were 54.2 and 58.8 years, respectively. Between cases and controls, the age distribution was nearly comparable (Table 1). Patients with breast cancer had their levels of biochemical parameters and the activity of antioxidant enzymes tested.

When compared to the normal, healthy control group, the catalase activity was lower in the cancer patients, although glutathione peroxidase and superoxide dismutase activity were somewhat elevated. Gamma-glutamyl transferase (ɤ-GT), lactate dehydrogenase (LDH), and alkaline phosphatase (ALP) increased slightly in the overall data. In the overall data, alanine aminotransferase (ALT) increased in from healthy subjects to breast cancer patients very significantly (P=0.08). The increase in ALT was most pronounced and significant (P=0.08) among the breast cancer patients. A nonsignificant reduction was detected in groups, and a significant positive correlation (P<0.01) was not detected between the groups in the levels of SGPT (Table 1).

In the overall data, no change in amylase and glucose was detected among the groups (Table 1). Significant negative correlations (P<0.01) were detected in amylase and which was found to be high in the healthy patients as compare to breast cancer patients (Table 1). No significant changes in creatinine, albumin, or bilirubin were detected among the healthy subjects. For albumin, group belongs to breast cancer patients showed a significant increase (P=0.03) (Table 1). The analysis also detected a borderline significant increase in bilirubin (P=0.06), but no change in creatinine. No significant changes were detected for direct bilirubin among the groups.

K^+ and PO_4^{3-} increased significantly (P <0.04 & 0.01 respectively) in the overall data. The increases in K^+ and PO_4^{3-} were most pronounced among the breast cancer patients (P <0.01) as compare to Ca^{2+} (Table 1). In the breast cancer patient group, PO_4^{3-} increased significantly (P=0.04), but no changes were detected for K^+ and Ca^{2+} (Table 1). No significant change in Mg^{2+} was detected in the overall data. In healthy controls, there was a significant correlation between catalase activity and the levels of biochemical parameters (r=0.88, P = 0.03), and there was also a positive correlation between glutathione transferase and glutathione peroxidase activity in cancerous patients (r = 0.43, P = 0.04) and healthy controls (r = 0.51, P = 0.05).

4. Discussion

Glutathione is found to be an important marker in patients with breast malignancy that is not dependent of hormone receptor status and the clinical stage of the tumor, it may indicate disseminated disease[13]. In our study serum ɤ-GT was normal in all patients with breast cancer and was elevated in 83.3% of the control group. This finding is the contrary to most of the published papers which show the reverse, this may be attributed to the small sample size. Long term follows up and estimation of the glutathione may be done to predict the prognosis, the recurrence, and the responsiveness to chemotherapy, although this is still under investigation.

GGT levels are elevated in the majority of malignant and non-malignant liver disorders, however it is level have been linked to other types of cancers such as breast cancer[14]. In a Swedish cohort study involving 545,460 persons, they found that there is an association between GGT and different types of cancer, and high association with breast cancer particularly[15,16,17]. Our results suggested a significant correlation between breast cancer and ɤ-GT, its level was normal in 100% of the control group and 5.7% of the breast cancer group and the P value for this correlation was 0.018.

We looked in PubMed for articles that discussed the use of non-chemotherapy treatments to treat side effects as well as chemotherapy treatments to prevent hematological and biochemical problems[18,19]. We evaluated the value and applicability of all pertinent papers. It is well knowledge that chemotherapy medications and several biological treatments significantly lower patients' levels of amylase, glucose, bilirubin, magnesium, and SGPT[20,21].

Tumor lysis syndrome, which develops after chemotherapy and occurs when the body degrades cancer cells that have been killed, can result in hyperkalemia, hyperphosphatemia, and hypocalcemia[22,23]. Recent studies have emphasized the significance of meticulously monitoring blood Mg2+ and PO43-ions in patients receiving small-molecule targeted medications, a topic that has received little attention to far. To prevent arrhythmia and renal failure, K^+, Na^+, and PO_4^{3-} levels must be kept within a very small range[24,25]. Additionally, the majority of chemotherapy-treated cancer patients get anemia as a side effect of the medication. According to the ECAS study, which was carried out in European countries, 83% of chemotherapy patients had anemia. Fatigue, weakness, and dyspnea are frequently worsened by anemia. Cancer patients' prognosis may be impacted by anemia, increasing mortality.

5. Conclusion

Elevated levels of ɤ-GT, LDH, ALP, Urea and phosphate were seen in patients with breast cancer patients and which may be used as serum markers for the early detection of breast cancer. On the other side the levels of anti-oxidant enzymes were reduced significantly in breast cancer patients.
There is no conflict of interest in the present study.

6. References

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