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A PROSPECTIVE STUDY: ANTIOXIDANT STATUS IN RELATION TO LIPID PEROXIDATION AND BIOCHEMICAL PARAMETER IN AFFECTED WOMEN WITH BREAST CANCER

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Abstract

Background – Breast cancer is the most common type of cancer that affects women's life. Many causes have been implicated in the development of cancer such as diet, obesity, environmental factors, family history and many more. The objectives of the study to rule out the correlation between the antioxidant status and lipid peroxidation with biochemical parameters in breast cancer patients as compare to the healthy groups.

Methods – The prospective study including 76 women who were grouped into two equal groups (38 breast cancer patients as case and 38 as a healthy control). Serum antioxidant enzymes (SOD, CAT, glutathione) and degree of lipid peroxidation (MDA) were estimated by kit method. In addition we evaluate the biochemical parameters by automated analysers. Result can be expressed as mean ± S.D with a 95% confidence interval. Statistical analysis is done by student's t-test using SPSS 20.0. Significant value were be considered as $P<0.05$.

Result – MDA level were highly significant in the breast cancer patients as compare to healthy control ($P<0.05$). Compared to healthy group, the antioxidant enzymes (Glutathione, SOD and CAT) activity were significantly decreased in breast cancer patients ($P<0.05$). On the other hand serum LDH, ALP, Uric acid, and GGT were found significantly increased in breast cancer patients as compared to healthy control ($P<0.05$).

Conclusion – Oxidative stress plays an important role in development and progression of breast cancer. We concluded that the biochemical parameters and antioxidant enzyme along with MDA as an important diagnostic tool in the disease monitoring and treatment. Further studies in future on it may more helpful for treatment and management of breast cancer.

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Keywords – Breast Cancer, Oxidative stress, Antioxidant Enzyme, Lipid peroxidation, Biochemical Parameter,

1. Introduction

Breast cancer is one of the heterogeneous cancer diseases which are caused by breast tissue malignant cells with diverse clinical symptoms and molecular profiles. This disease causes a serious decline of the quality of women life. [1] Millions of new cancer patients are diagnosed each year, and the disease accounts for many fatalities, now breast cancer becoming a major public health concern around the world. [2]

Breast cancer has a complex etiology. Age, early menarche age, late menopause age, late age of first pregnancy, obesity, oral contraception, HRT (hormone replacement therapy), diet, family history, lactation, and past history of benign breast disease are all significant breast cancer risk factors. [3]

Oxygen-free radicals (OFR) generated by a number of processes in vivo are highly reactive and toxic. [4] However, biological systems have evolved an array of enzymatic and non-enzymatic antioxidant defence mechanisms to combat the deleterious effect of OFR. Superoxide-dismutase (SOD) and Catalase (CAT) play a key role in the detoxification of superoxide anion and peroxide (H_2O_2), respectively, thereby protecting against OFR- induced damage. Reduced glutathione (GSH) in conjunction with glutathione peroxidise (GPx) and glutathione-S-transferase (GST) plays a central role in the defence against free radicals, peroxides and a wide range of xenobiotics and carcinogens. [5] [6]

Oxidative stress arises when there is an imbalance between OFR formation and scavenging by antioxidants. Excess generation of OFR can cause oxidative damage to biomolecules resulting in lipid peroxidation, mutagenesis and carcinogenesis. OFR-induced lipid peroxidation has been implicated in neoplastic transformation. [7]

Impaired lipid peroxides yields a wide range of end products including malondialdehyde (MDA). Lipid peroxidation induced by oxygen-free radicals can lead to malignant transformation. [8] [9] Several studies shown that oxidative stress increases in breast cancer diseases. [10] [11]

Biochemical profile analysis the levels of chemicals, enzymes and organic waste found in the blood and it determine the status of various organs. The abnormal levels of biochemical indicate the various infection and diseases. Only a few studies have investigated the association of biochemical parameter (LFTs and KFTs) with mortality in breast cancer. [12][13]

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2. Material and Methods

The study was conducted at Index Medical College, Hospital and Research Center, Indore (M.P). Study was approved by the ethical committee of the institute. Informed consent was obtained according to institutional guidelines.

Totally 38 patients diagnosed with breast cancer (mean age 42.62 ± 2.25 years) as case group and 38 healthy women (mean age 40.84 ± 2.04 years) as control group was enrolled during 15th January 2022 to 28th July 2023. Breast cancer patients having any other clinical conditions or any drug history were excluded from the study. Inform consent was signed by each patient from both groups before enrolment in the study.

2.1. Sample collection

Breast cancer patients suffering with any clinical disorder were excluded from the study. The breast cancer had undergoing radiation or chemotherapy treatment. 5 ml blood sample was collected from each participant in SST or EDTA tube under aseptic conditions. The tube was centrifuged at 3000 to 4000 rpm for 15-20 minutes. Serum or plasma collected carefully and stored in sterile aliquots and freeze at -20^0 C to -80^0 C until ready for assay.

2.2. Determination of Assay

Oxidative stress status was evaluated by measuring MDA as an indicator of lipid peroxidation (by thiobarbituric acid method - spectrophotometrically at 530nm) and SOD (by hydroxylamine method - spectrophotometrically at 450nm), CAT (spectrophotometrically at 520nm) and GPX (spectrophotometrically at 340nm) as the indicator of antioxidant in the patients with breast cancer. Other biochemical parameters such as Liver function test (SGOT, SGPT, ALP GGT Bilirubin and Albumin), kidney function test (Urea, Creatinine, Uric acid), Glucose and Lactate Dehydrogenase was estimated by their standard methods. These results can be useful as diagnostic and therapeutic finding for the patients in breast cancer.

3. Statistical Analysis

The data for the biochemical analyses are expressed as mean and Standard deviation (S.D). Statistical comparisons were performed by student's t-test using the SPSS 20.0 software. The P value <0.05 was considered to be statistically significant.

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4. Results

The main demographic characteristics of the two groups (cases and controls) are represented in table no.1. This result shows that the levels of lipid peroxidation, antioxidant status and biochemical parameters.

BMI was found not significant in the patients having breast cancer when compared to healthy groups with the mean ± S.D (26.9 ± 9.73 and 23.6 ± 4.56). Age was also found non-significant in the patients having breast cancer when compared to healthy groups with the mean ± S.D (53.41 ± 4.84 and 51.24 ± 5.24).

Table no.1: showing levels of antioxidant status, lipid peroxidation and biochemical parameters in blood samples of patients having breast cancer compare to healthy groups.

S. No	Parameters	Healthy patients (n=38)	Breast cancer (n=38)	P value <0.05
1.	Age (years)	51.62 ± 5.24	53.41 ± 4.84	0.12
2.	BMI (kg\m^2)	23.6 ± 4.56	26.9 ± 9.73	0.06
3.	Heart Rate (beats/min)	74 ± 11	78 ± 14	0.17
4.	Respiration Rate (breath/min)	18 ± 5	20 ± 8	0.19
5.	Glucose (mg/dl)	104.8 ± 18.1	98.7 ± 20.6	0.20
6.	LDH (IU/L)	320.8 ± 50.26	679.9 ± 44.6	**<0.0001**
7.	SGOT (U/L)	42.3 ± 10.3	38.9 ± 8.14	0.07
8.	SGPT (U/L)	25.4 ± 8.92	27.9 ± 10.2	0.26
9.	ALP (IU/L)	114.6 ± 15.8	215.5 ± 22.9	**<0.0001**
10.	γ-GT (U/L)	34.7 ± 12.6	144.6 ± 11.4	**<0.0001**
11.	Urea (mg/dl)	26.8 ± 16.2	32.58 ± 15.7	0.12
12.	Creatinine (mg/dl)	0.9 ± 0.2	1.05 ± 0.5	0.09
13.	Uric acid (mg/dl)	5.4 ± 1.5	8.6 ± 2.3	**<0.0001**
14.	SuperOxide Dismutase (U/L)	13.42 ± 2.87	10.98 ± 1.86	**<0.0001**
15.	Catalase (KU/L)	42.5 ± 10.5	28.4 ± 6.72	**<0.0001**
16.	Malondialdehyde (nmol/L)	196.8 ± 84.8	452.8 ± 2.82	**<0.0001**
17.	Glutathione peroxidase (U/L)	315.9 ± 76.4	169.2 ± 44.8	**<0.0001**

Note: the results are expressed as mean and Standard Deviation (S.D) with the range value with 95% confidence intervals.

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The levels of Blood glucose, blood urea, Creatinine, SGOT, SGPT was found significantly decrease among the both groups (breast cancer and healthy controls). On the other hand the level of LDH, ALP, γ-GT and uric acid was significantly higher in patients with breast cancer as comparison in healthy controls.

In regarding to the degree of lipid peroxidation there is significant level of MDA in breast cancer patients as compare to healthy controls (P = <0.0001). The mean levels of MDA in the breast cancer patients (452.8 ± 2.8nmol/L) and healthy control groups (196.8 ± 84.8nmol/L).

In addition to antioxidant status, the breast cancer group shows significantly lower activity of SOD, Catalase and GPx compare with the healthy control group (P = <0.0001). The mean level of SOD in the patients with breast cancer (10.98 ± 1.86 U/L) and healthy control groups (13.42 ± 2.87 U/L). The mean level of Catalase in patients with breast cancer (28.4 ± 6.72 KU/L) and healthy control groups (42.5 ± 10.5 KU/L). The mean level of GPx in patients with breast cancer (169.2 ± 44.8U/L) and healthy control groups (315.9 ± 76.4 U/L).

5. Discussion

Increase body mass index (BMI) is a risk factor for developing adult malignancy [14]. Excess body weight has been linked to an increase risk of post menopausal breast cancer and growing evidence also suggest that obesity is associated with poor prognosis in women with initial stage of breast cancer [15]. This analysis shows significant difference between breast cancer patients and healthy controls.

According to **Balch CM et al (2009),** total serum LDH level elevation is a predictive marker of tissue damage and inflammation. Its prognostic value on the follow up of patients with malignant hematologic diseases and solid tumors is known. Serum LDH levels are used as a prognostic factor in chronic lymphocytic leukemia and metastatic melanoma. [16][17] In the current study serum LDH levels are highly significant in breast cancer group as compare to healthy control group.

The progressive increase in the serum alkaline phosphatase (ALP) activity in breast cancer patients is an indication of metastasis [18, 19]. This study shows increased ALP levels in breast cancer patients as compare to healthy control group.

Veni et al. (2011) observed a significant rise in uric acid level in untreated women of breast cancer patients, which may be due to high oxidative stress. [20] In the present study, uric acid level is found to be higher in breast cancer patients when compare to normal healthy group.

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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. In a Swedish cohort study involving 545,460 persons, they found that there is an association between γ-GT and different types of cancer, and high association with breast cancer particularly. [21] Our results indicate the high significant levels of γ-GT and the level of γ-GT increased in breast cancer patients as compare to healthy patients.

Several researches were considered SOD and Catalse (CAT) enzymes act as anti carcinogens, antitoxins and inhibitors at initiation, promotion and transformation of carcinogenesis. [22][23][24] In the present study, SOD and CAT activities were significantly decreased in the breast cancer patients as compare to healthy control group.

The increased level of oxidative factors can be feature of early stages of cancer progression. Increased MDA level in breast cancer patients may be response to the aggregation of ROS, which result in extensively elevated cellular lipid peroxidation. [25][26] The current study shows increased level of MDA in breast cancer patients as compare to healthy controls.

Glutathione is found to be an important marker in patients with breast malignancy that is not dependent of hormone receptor status and clinical stage of the tumor, it may indicate disseminated disease. [27] In our study shows decreased level of glutathione in all patients with breast cancer as compare to healthy controls.

6. Conclusion

Breast cancer is relatively associated with increased lipid peroxidation in plasma with decreased antioxidant defence capacity. Increased lipid peroxidation and decrease antioxidant status are the main causes of breast cancer. In our study, decreased antioxidant enzymes (SOD, CAT and glutathione) level and increased MDA level (as an indicator of lipid peroxidation) was found in breast cancer patients as compare to healthy control. On the other hand, elevated levels of LDH, ALP, Uric acid and GGT were seen in patients with breast cancer. These serum biochemical parameters may be a helpful diagnostic tool in the monitoring of disease and different strategies of breast cancer. It is concluded that the biochemical changes of Superoxide dismutase, Catalase, Glutathione and Malondialdehyde may used as enzyme biomarker for early detection and for therapeutic follow up of patients with breast cancer.

7. Conflict of interests

The authors have no conflict of interests to declare.

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