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THE RELATIONSHIP BETWEEN ELEVATED SERUM GAMMA-GLUTAMYL TRANSFERASE (GGT) AND BREAST CANCER INCIDENCE

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ABSTRACT

Background: Breast cancer is the most common malignancy in females, and the second most common cause of cancer-related death in women in developed countries, but it is the first cause of cancer-related death in women in developing countries. For the early detection of breast cancer, a number of biochemical markers have been studied to evaluate the malignancy. **Aim:** The present study aimed to evaluate the gamma-glutamyl transferase (GGT) levels in the circulation of patients of breast cancer and comparing with controls. **Materials and Methods:** This was a prospective case – control study included 130 patients with stage (I-III) breast cancer and 110female controls matched for age at Tishreen University Hospital, Lattakia during the period between 30/01/ 2020 –30/01/ 2021. The serum GGT was estimated. The statistical analysis was done by using SPSS software. The results were expressed as Mean ± SD. The student's paired 't'-test and ANOVA were carried out for comparison of data & p-value <0.005 was considered statistically significant. **Results:** The mean serum GGT level in breast cancer patients was significantly (p<0.001) increased as compared to controls, and we also found that the levels was gradually increased with advancing stages and grades of breast cancer. Serum GGT level in post-menopausal breast cancer patients was significantly increased as compared to premenopausal breast cancer patients. **Conclusion**: Serum GGT levelis reliable and inexpensive promising enzyme marker with prognostic and diagnostic importance in breast cancer patients.

INTODUCTION

Breast cancer is the most common malignancy in females, and the second most common cause of cancer-related death in women after lung cancer in developed countries, but it is the first cause of cancerous death in women in developing countries.[1] Many causes are involved in the development of cancer in general and breast cancer in particular, and they can be categorized into modifiable and non-modifiable causes, modifiable causes are described as factors that can be modified or changed such as body weight, reproductive factors, the use of hormone therapy, the Diet and some environmental factors, while non-modifiable factors include gender, genetic mutations, menstrual history and family history of breast cancer.[2,3] Theories explaining the development of cancer are still under investigation and several existing theories explain the role of oxidative stress and antioxidant biomarkers in the development of cancer at the molecular level. The role of free radicals and oxidative stress in the pathogenesis of many types of cancerous and non-cancerous diseases has been extensively studied.[4]

The essential role of gamma-glutamyl transferase GGT is in the extracellular catabolism of glutathione (GSH) which is a major antioxidant in mammalian cells and is involved in several important processes including deoxidation, detoxification, modulation of cell proliferation, apoptosis and fibrinogen synthesis[5]

Since we know the important role that antioxidants play in protecting against cancer[6] we are searching in this article for a possible relationship or predictive value of gamma-glutamyl transferase with breast cancer.

MATERIALS AND METHODS

This was a prospective case – control study included 130 patients with stage (I-III) breast cancer and 110 female controls matched for age at Tishreen University Hospital, Lattakia during the period between 30/01/2020 – 30/012021.

3-5 ml of peripheral venous blood was taken under sterile conditions using disposable syringes from all patients and control womens and placed in a chemistry tube containing heparin as an anticoagulant, The centrifugation was carried out at a speed of 4000 rpm, The measurement of GGT level was done on a Mindari® device based on the kinetic chromaticity method.

All patients had a pathological study and a study of hormonal receptors (ER,PR) and HER2

The statistical analysis was done by using SPSS software. The results were expressed as Mean ± SD. The student's paired 't'-test and ANOVA were carried out for comparison of data & p-value <0.005 was considered statistically significant.

RESULTS

340 women participated in the study, 130 breast cancer patients and 110 controls, The mean age of breast cancer patients was 46.5 ± 9.17 years, with a range of 25-76 years. The mean age of women in the control group was 45.2 ± 9 years, with a range of 25-75 years.

The mean GGT of breast cancer patients was 34.1 ± 1.9 IU/L with a range of 18-60 IU/L, while the mean GGT of females in the control group was 28.9 ±2.4 IU/L in a range of 15-41 IU/L. Table (1) shows a comparison of the average of GGT tests among breast cancer patients and the control group.

Table (1): A comparison of the average of GGT tests among breast cancer patients and the control group.

test	Breast cancer (200 patient)	Control group (180 women)	t-test	P-value
GGT	34.1 ± 1.9 IU/L	28.9 ±2.4 IU/L	**23.52**	**<0.001**

Breast cancer patients had a higher mean GGT with a statistically significant difference compared to the controls.

The mean GGT of breast cancer patients≤ 50 years of age or younger was 32.2 ± 1.9 IU/L and for patients> 50 years of age 35 ± 1.9 IU/L, With a statistically significant difference.

Table (2): the relationship between the mean GGT and the age of breast cancer patients.

Age	Number of patients	GGT (UI/L)	t-test	P-value
≤50	66	32.2±1.9	8.4	<0.0001
>50	64	35±1.9		

The mean GGT of premenopausal breast cancer patients was 32.5 ± 2 IU/L and for postmenopausal patients 35.8 ± 1.9 IU/L With a statistically significant difference.

Table (3) illustrate the comparison of mean GGT by menstrual status.

Table (3): Comparison of mean GGT by menstrual status in breast cancer patients.

Menstrual status	Number of patients	GGT (UI/L)	t-test	P-value
premenopausal	59	32.5±2	9.6	0.0001
postmenopausal	71	35.8±1.9		

Regarding the histological grade of breast cancer, The statistical analysis showed a statistically significant relationship between the mean GGT and the histological grade of breast cancer, as the value of GGT increased with the increase in the histological grade of breast cancer, as shown in table(4)

Table (4): The relationship between the mean GGT and the grade of breast cancer.

Greeding	Number of patients	GGT (UI/L)	T-test	P-value
G1	21	32.8±2	6.497	0.002
G2	85	33.5±2.1		
G3	24	34.9±1.9		

When two-way comparison of breast cancer grades, there was no statistically significant difference in mean GGT between cancer G1 and cancer G2 (P = 0.17), but G3 breast cancer patients had a significantly higher mean GGT compared to G1 cancer patients (P = 0.0008), as well as G3 breast cancer patients had a statistically significant higher mean GGT compared to G2 cancer patients (P=0.004) as shown in Table (5).

Table (5): the two-way comparison of breast cancer grades.

Comparison	T-test	P-value
G1 VS G2	1.38	0.17
G1 VS G3	3.6	0.0008
G2 VS G3	2.94	0.004

By studying the relationship between mean GGT and the stage of breast cancer, The statistical analysis showed a statistically significant relationship between the mean GGT and the stage of breast cancer, as the value of GGT increased with the increase in the stage of breast cancer, as shown in table (6):

Table (6): The relationship between the mean GGT and the stage of breast cancer.

Staging	Number of patients	GGT (UI/L)	T-test	P-value
Stage I	23	33.2±1.8	3.813	0.025
Stage II	55	33.9±1.9		
Stage III	52	34.5±2		

In this study, we did not find any statistically significant association between mean GGT and body mass index (BMI), estrogen receptor status (ER), progesterone receptor status (PR), and HER new2 status.

DISCUSSION

This research was conducted to study gamma-glutamyltransferase (GGT) as a promising, inexpensive, accurate, and easy-to-detect biochemical marker that may be have a diagnostic and prognostic importance.

The primary role of GGT is the extracellular catabolism of glutathione (GSH) which is a thiol responsible for alleviating oxidative stress produced during normal metabolism, and detoxing endogenous and exogenous compounds including carcinogens.

Most large biological molecules are destroyed by free radicals, including DNA, whose destruction may directly inhibit the biosynthesis of proteins and enzymes and indirectly cause cell death or mutation, This diffuse intensity can induce changes in gene expression that may induce the cell in which the neoplastic transformation has begun. Thus, higher serum GGT levels from rapidly proliferating tumor cells may be due to an increased production of reactive oxygen species (ROS) in the blood.

The results of our study agree with most international studies such as the Swedish AMORIS study, which included 545,460 people. After a follow-up of 12.26 years, 37,809 people developed cancer. There was an increased association with the risk of developing cancer in general and breast cancer in particular with higher GGT values.[7]

In the study of (Rajput et al) in 2021 comparing GGT concentration between 60 breast cancer patients and 60 healthy controls, the serum GGT concentration of breast cancer patients was significantly higher than that of the control group.[8]

A study (Mohammed Saheb et al) in 2020 compared GGT concentration between 60 breast cancer patients and 60 healthy controls, and the serum GGT concentration of breast cancer patients was significantly higher by a statistically significant difference compared to women in the control group (57.7 ± 13.8 units/L versus 20.7 ± 3.8. unit/liter).[9]

CONCLSIONS

1. Breast cancer patients have a higher serum level of GGT with a statistically significant difference compared to healthy controls, and therefore GGT may be useful in diagnosing breast cancer.
2. The mean serum GGT of postmenopausal breast cancer patients is higher with a statistically significant difference compared to premenopausal breast cancer patients.
3. GGT may be useful in determining breast cancer prognosis and response to treatment, as we found that the concentration of GGT in the serum increases in breast cancer patients with the increase in the histological grade of the cancer and with the increase in the stage of cancer.

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