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Research Article

Comparison of Preoperative and Postoperative Serum Galectin-3 Levels in Patients Newly Diagnosed with Non-Metastatic Breast Cancer

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Abstract

Objectives: Galectin-3 (Gal-3) a 31-kDa dimeric galactose-binding protein – is a member of the lectin family, and can be found in intracellular and extracellular locations where it interacts with glycoproteins, cell surface molecules and extracellular matrix proteins.The present study compares the preoperative and postoperative serum Gal-3 levels of patients with newly diagnosed non-metastatic breast cancer with the serum Gal-3 levels of healthy controls.

Methods: Peripheral blood samples were collected from the patients at two time points: one preoperatively and the other 1 month after surgery during an outpatient control visit.The study data were analyzed statistically using SPSS for Windows, Version 20.0. A $p<0.05$ was considered to indicate statistical significance.

Results: In a comparison of preoperative and postoperative serum Galectin-3 levels of the patients with newly diagnosed non-metastatic breast cancer, the mean preoperative serum Gal-3 level was 21.76 and the mean postoperative serum Gal-3 level was 21.20. There was no statistically significant difference between the groups ($p=0.690$). The mean serum Gal-3 level was 19.88 in the healthy control group, and a comparison of this with the preoperative serum Gal-3 levels of the newly diagnosed non-metastatic breast cancer patients revealed no statistically significant difference, with a $p=0.477$.

Conclusion: The study found no correlation between serum Galectin-3 levels and the presence of a mass lesion, indicating that Galectin-3 is expressed independently of the presence of a tumor in breast cancer. In conclusion, current evidence fails to allow a comprehensive understanding of the role of Galectin-3 in the pathogenesis of breast cancer, highlighting the need for further research in this area.

Keywords: Breast Cancer, Cancer, Galectin-3

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Breast cancer is the most prevalent form of cancer among women around the globe, accounting for approximately one-third of all cancers affecting the female population. Each year, around 1 million new cases of breast cancer are reported globally, as well as approximately 400,000 deaths attributable to the disease. Scientific studies and statistical analyses reveal that 17,183 women were diagnosed with breast cancer in Turkey in 2011.[1]

Numerous factors have been implicated in the etiology of breast cancer. In addition to genetic and environmental factors, family history, hormones, metabolism, early menarche, obesity, nutrition, alcohol consumption, smoking, lactation and exposure to radiation may also be involved in its pathogenesis, although its precise cause and the mechanisms behind the disease are yet to be fully understood.[2]

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Breast cancer is a hormone-dependent disease with an increased risk of development associated with estrogen exposure.[3] Changes in diet and body mass index can impact the risk of developing breast cancer.[4] While there is an increased risk of breast cancer in obese postmenopausal women, the effect of obesity on the prognosis of breast cancer remains unclear.[5]

Age is another factor influencing the likelihood of breast cancer. The 10-year risk of a woman aged in her 20s developing the disease is 0.6%, but the likelihood increases with age, reaching as high as 3.7% in women in their 70s.[6]

Although many prognostic factors for breast cancer have been identified, cancer stage remains the fundamental determinant of prognosis, and while estrogen receptor (ER) and progesterone receptor (PR) status have been identified as independent prognostic factors, patients with ER- or PR-positive tumors generally have a better prognosis.[7–9] At a molecular level, HER-2, p53 and Ki-67 also hold prognostic and predictive value.[10]

Familial factors also play a crucial role in the development of breast cancer, as in other cancer types, and studies have shown that women with a family history of breast cancer in their mother or sister are twice as likely to develop the disease.[11] The BRCA1 and BRCA2 genes are associated with both breast cancer and endometrial cancer, and as these genes can be inherited and passed on to the next generations, family history should be considered a significant finding. Obesity and accumulations of adipose tissue are risk factors for various types of cancer, including breast cancer.[12–14] At a molecular level, adipocytes – as the most important component of the stromal environment in breast tumors – are known to exert tumorigenic effects on breast cancer cells.

Galectin-3 (Gal-3) a 31-kDa dimeric galactose-binding protein, is a member of the lectin family, and can be found in intracellular and extracellular locations where it interacts with glycoproteins, cell surface molecules and extracellular matrix proteins. It is typically expressed by epithelial cells and immune cells, and studies have suggested that it plays an important role in various processes, such as cell proliferation, apoptosis, cell invasion and migration, carcinogenesis and angiogenesis, while also regulating the interaction between tumor cells and the tumor microenvironment.[15] A study by Song et al.[16] reported Gal-3 to be expressed by various tumor cells, and to be closely related to the transformation, migration, and invasion of tumor cells. Matarresse et al.[17] on the other hand, compared cells with Gal-3 overexpression with cells with Gal-3 underexpression, and found a significant increase in adhesion, both directly and through the increased expression of specific integrins in response to laminin, fibronectin, and vitronectin. The authors also observed a remodeling of microfilaments, suggesting cellular invasion, as well as increased cellular survival after exposure to various apoptotic stimuli such as cytokines and radiation.[17] Other studies have also demonstrated a relationship between Gal-3 expression and tumor progression in colorectal cancers, breast cancer and papillary thyroid cancer.[18–22]

On the basis of these molecular characteristics, the present study compares the preoperative and postoperative serum Gal-3 levels of patients with newly diagnosed non-metastatic breast cancer with the serum Gal-3 levels of healthy controls.

Methods

Included in the study were healthy subjects and patients newly diagnosed with non-metastatic breast cancer who presented to the Medical Oncology Outpatient Clinics of the İzmir Katip Çelebi University Atatürk Education and Research Hospital. Prior approval for the study was granted by the interventional clinical studies ethics committee upon the submission of our application, and all the participants provided informed consent before the commencement of the study. The study inclusion criteria were as follows: recently diagnosed with breast cancer (confirmed by biopsy), presentation to the medical oncology outpatient clinics of our hospital, no presence of synchronous malignancy other than breast cancer (no suggestion of second malignancy based on physical examination and medical history, PET-CT and/or other imaging studies including MRI/CT not suggestive of metastatic lymph node or other organ involvement), non-pregnant and non-breastfeeding women aged between 18 and 80 years, patients scheduled for breast cancer surgery, completion of preoperative workup, body mass index (BMI) between 18 and 40, no recent history of infection or trauma, no prior chemotherapy or radiotherapy, and voluntary consent granted for participation in the study.

The inclusion criteria for the healthy controls were as follows: presentation to the medical oncology and internal medicine outpatient clinics of our hospital, body mass index (BMI) between 18 and 40, aged between 18 and 80 years, absence of a history of chronic disease or malignancy, and voluntary consent granted for participation in the study.

The study exclusion criteria were as follows: male gender, age less than 18 or more than 80 years, pregnancy, breastfeeding women, diagnosis of metastatic breast cancer, presence of synchronous malignancy other than breast cancer, and patients or individuals who declined to participate in the study.

Peripheral blood samples (one tube for hemogram, one tube for biochemistry) were collected from the patients at two time points: one preoperatively, and the other 1 month after surgery during an outpatient control visit. Peripheral blood samples were collected only once from those in the healthy control group.

Anthropometric Measurements

Body weight (BW) was measured with the participant in light clothing, and height was measured without shoes. The following formula was used to calculate body mass index (BMI): BW (kg)/Height (m^2).

Sample Collection and Storage

Peripheral blood samples were collected from the patients at two time points: one preoperatively and the other 1 month after surgery during an outpatient control visit. Peripheral blood samples were collected only once from those in the healthy control group. Sera were recovered from the blood samples and stored at -80°C until the time of analysis of the serum Gal-3 levels. Gal-3 levels were measured using ELISA kits in accordance with the manufacturer's instructions.

Biochemical Parameters

The serum Galectin-3 levels of the patients and controls were measured using enzyme-linked immunosorbent assay (ELISA) kits designed specifically for scientific purposes. Upon thawing the sera at room temperature, the samples were vortexed to ensure the thorough mixing of the precipitating molecules and to obtain a homogeneous sample. The sera of the patients and controls were processed according to the instructions provided in the package insert of the ELISA test kits. After completing the study procedures, the samples were read at 450 nm using a microplate ELISA reader to calculate the concentrations. Serum Galectin-3 concentrations were measured using Cusabio ELISA kits (Cusabio Biotech Co., LtD. P. R. China).

Statistical Analysis

The study data were analyzed statistically using SPSS for Windows, Version 20.0. Chicago, SPSS Inc. The preoperative and postoperative Galectin-3 levels in the oncology group were compared using a repeated measures analysis of variance (ANOVA), while the serum Galectin-3 levels of the patient and the healthy controls were compared using a Student's t-test. $P<0.05$ was considered to indicate statistical significance.

Results

The mean age of patients newly diagnosed with non-metastatic breast cancer was 55.9 years, ranging from 36 to 80 years. The mean BMI was 28.2585 kg/m^2. Of the study patients, 16 (40%) had stage 1 disease, 15 (37.5%) had stage 2 disease and nine (22.5%) had stage 3 disease. In terms of tumor grade, two patients (5%) had grade 1 tumors, 25 (62.5%) had grade 2 tumors and 13 (32.5%) had grade 3 tumors. The mean tumor grade was 2.28

Ki-67 values were in the 0–10 range in 13 patients (32.5%), the 10–20 range in 13 patients (32.5%), and above 20 in 14 patients (35%). The demographic data, disease stages, tumor grades and Ki-67 levels of the patients and their frequencies are presented in Table 1.

In a comparison of preoperative and postoperative serum Galectin-3 levels of the patients with newly diagnosed non-metastatic breast cancer, the mean preoperative serum Gal-3 level was 21.76 and the mean postoperative serum Gal-3 level was 21.20. There was no statistically significant difference between the groups (p=0.690). The mean serum Gal-3 level was 19.88 in the healthy control group, and a comparison of this with the preoperative serum Gal-3 levels of the newly diagnosed non-metastatic breast cancer patients revealed no statistically significant difference, with a p=0.477 (Table 2).

Table 1. Demographic data of the patients

Characteristics	Patient group (n=40) n (%)
Age, years (mean±SD)	55.9±11.33
Stage (TNM)	
I	16 (40)
II	15 (37.5)
III	9 (22.5)
Histological Grade	
I	2 (5)
II	25 (62.5)
III	13 (32.5)
Hormone Receptor Status	
ER/PR-positive	30 (75)
ER/PR-negative	3 (7.5)
ER-negative/PR-positive	1 (2.5)
ER-positive/PR-negative	6 (15)
Cerb-B2 Status	
Positive	13 (32.5)
Negative	27 (67.5)
Ki-67	
0–10	13 (32.5)
10–20	13 (32.5)
>20	14 (35)
Her-2 Status	
Positive	6 (15)
Negative	34 (85)

Table 2. Serum Galectin-3 levels of the groups

	GALECTIN-3 (ng/ml)		GALECTIN-3 (ng/ml)
Preoperative patient group (n=40) mean±SD	21.76±11.57	Preoperative patient group (n=40) mean±SD	21.76±11.57
Postoperative patient group (n=40) mean±SD	21.20±9.53	Control group (n=40) mean±SD	19.88±8.52
p	0.690	p	0.477

*SD: Standard Deviation; **N: Number of patients.

Discussion

The present study found no significant difference between the preoperative and postoperative serum Galectin-3 levels of the patients newly diagnosed with non-metastatic breast cancer, and between preoperative serum Galectin-3 levels of the patients and those of the healthy controls.

In a series of studies conducted on human tissues, Galectin-3 was implicated in malignant transformations in various organs, including the stomach, colon, central nervous system and thyroid.[23] Galectin-3 has also been reported to play a role in invasion and metastatic processes in malignant lesions.[24–27] leading to suggestions that the presence of Galectin-3 could be useful in differentiating malignant lesions, and further studies exploring its role in carcinogenesis.[24–28] Idikio et al.[29] evaluated Galectin-3 levels using immunohistochemical methods while considering the histological grades of patients diagnosed with invasive breast cancer, and observed a decrease in the expression of Galectin-3 with increasing tumor grade. In an in vivo study conducted by Shekhar et al.[30] using the co-culture method, an increase was observed in Galectin-3 levels in normal breast tissues and benign breast lesions, although the authors reported a decrease in Galectin-3 levels in low-grade ductal carcinoma in situ. Castronova et al.[31] on the other hand, reported a significant increase in Galectin-3 expression in normal breast tissue and benign breast lesions, and a decrease in Galectin-3 expression in in situ carcinomas and breast cancer with axillary metastasis. In another study, Lu et al.[21] investigated the relationship between Gal-3 status and colorectal cancer progression, and found Gal-3 expression to be upregulated in colorectal cancer tissues and cells, reporting a correlation between Gal-3 levels and the progression of colorectal cancer. Studies of colon, gastric and thyroid cancers have reported a correlation between serum Galectin-3 levels and tumor presence and progression, while there are no studies identifying such a correlation in breast cancer. The present study found no correlation between serum Galectin-3 levels and the presence of a mass lesion, indicating that Galectin-3 is expressed independently of the presence of a tumor in breast cancer. It should be noted that the sustained release of Galectin-3 from healthy breast tissue in patients with breast cancer may have contributed to the observed insignificant findings in this study.

The present study may have certain limitations related to the potential variability of Galectin-3 levels in tissue and serum samples, the relatively small number of patients and the lack of evaluation of Galectin-3 levels in the tissues. In contrast to previous studies suggesting that Galectin-3 may play a key role in malignancies and carcinogenesis in various cancer types, the findings of the present study raise questions regarding its role in breast cancer.

Conclusion

In conclusion, current evidence fails to allow a comprehensive understanding of the role of Galectin-3 in the pathogenesis of breast cancer and other malignancies, highlighting the need for further research in this area.

Disclosures

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Ethics Committee Approval: Approval for the study was granted by the Interventional Clinical Studies Ethics Committee prior to the launch and upon the submission of our application.

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