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Original Article

Alteration of saliva and blood ghrelin, obestatin, leptin and weight based on adjuvant chemotherapy treatment in early-stage operated breast cancer patients

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Abstract

Aim: To evaluate the weight change and ghrelin, obestatin and leptin levels in operated early stage breast cancer patients receiving adjuvant chemotherapy.

Material and Methods: This study was conducted with 22 operated breast cancer patients (examined before and after adjuvant chemotherapy) and 33 BMI-matched two different healthy controls (of 33 healthy controls, 17 BMI-matched control was used to compare before adjuvant chemotherapy, 16 BMI-matched control was used to compare after adjuvant chemotherapy). Age, anthropometric measurements (weight, BMI, waist circumference), and blood biochemistry were recorded. Blood and salivary total ghrelin, obestatin and leptin levels are measured by using ELISA.

Results: The mean ± SD weight (67.2 ± 12.3 and 72.9 ± 11.8 kg., p<0.001), BMI (27.3 ± 4.7 and 29.61 ± 4.4 kg/m2, p<0.001) and waist circumference (88.6 ± 10.8 and after adjuvant chemotherapy, (93.4 ± 11.0 cm., p<0.05) values increased significantly when compared to pre-treatment values. Acyl ghrelin (74.05 ± 50.85 and 186.47 ± 89.61 pg/ml., p<0.001 and 59.28 ± 45.74 and 151.74 ± 94.88 pg/ml., p<0.01) and des-acyl ghrelin (347.59 ± 241.95 and 936.76 ± 446.93 pg/ml., p<0.001 and 295.40 ± 241.44 and 765.38 ± 471.74 pg/ml., p<0.01) serum levels were significantly lower in breast cancer patients compared to the control group in both pre-treatment and post-treatment periods.

Conclusion: In conclusion, our study confirms that adjuvant chemotherapy causes significant weight gain in early stage breast cancer patients but does not indicate a concomitant treatment related change in ghrelin, leptin or obestatin levels. The fact that serum ghrelin levels were lower in breast cancer patients compared to BMI-matched control group, independent from treatment, might indicate that ghrelin-specific weight or adjuvant chemotherapy may be a regulatory mechanism for cancer etiopathology in breast cancer patients.

Keywords: Breast cancer; adjuvant chemotherapy; ghrelin; obestatin, leptin

INTRODUCTION

Breast cancer is the most common type of cancer among women worldwide and accounts for about 25% of all newly diagnosed cancer cases (1). In early stage breast cancer patients, curative surgery followed by adjuvant chemotherapy application is a widespread treatment approach which has proven to have positive effects on recurrence and survival (2).

Increased survival rates due to progressions in screening programs and treatment protocols have led to the increasing importance of adverse metabolic effects due to adjuvant chemotherapy, of which has an application rate reaching up to 60% (3).

Adjuvant chemotherapy related weight gain is a frequently reported complication with long-term consequences in breast cancer patients and besides its negative effects on quality of life, it is known to have possible relation with cardiovascular disease and diabetes development risk, as well as higher disease recurrence (4,5).

Obesity is a risk factor for the development of breast cancer and in addition to this, increased susceptibility to obesity in patients after diagnosis and weight gain

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after chemotherapy are observed in early stage patients and also it has been reported that pathological complete response rates might be lower in patients, who happen to be obese at the time of adjuvant chemotherapy initiation (6).

Even though weight gain caused by adjuvant therapy is a known complication in breast cancer patients, its mechanism has yet to be clarified. The current results of the factors, which might play a potential role in this metabolic deterioration, such basal metabolic rate, thermogenesis, physical activity and food intake, are far from providing satisfactory evidence for none of them (7).

Leptin, ghrelin and adiponectin play a direct role in food intake and weight control and may increase the risk of cardiovascular diseases and diabetes development. Body mass index (BMI) values have been shown to have a positive correlation with plasma concentrations of adipokines such as leptin, adiponectin and ghrelin. However, in spite of the fact that there are studies about the possible role of adipokines and insulin and insulin-like growth factors on metabolic disorder in breast cancer patients, there has not been a consensus on this issue (7, 8).

While being a peptide containing 28 amino acids, ghrelin is suggested to take part in growth hormone secretion, food intake and energy balance control and lipid and glucose metabolism, as well as to have an anti-cachectic and appetite-enhancing effect (8-11). It has been shown that ghrelin levels are high in breast cancer patients.

Obestatin, which is encoded by the same gene as the ghrelin hormone, is an anorectic peptide comprised of 23 amino acids and by its adverse effect to ghrelin, obestatin is claimed to suppress appetite and weight gain by way of creating central saturation sensation (9, 12-14). While it is a protein with 167 amino acids, leptin has effect on hypothalamic receptors by means of increase in energy expenditure and decrease in food in take, as being a major regulator of fat and energy storage in mammals (15). It has been shown that, the adults with leptin deficiency have increased appetite and obesity that is responsive to leptin treatment (16). The leptin-signaling pathway has been shown to stimulate the growth of human breast cancer cells in addition to close association with obesity and leptin levels have been shown to be high in breast cancer patients (17).

In this study, it was aimed to evaluate the effects of adjuvant chemotherapy application on anthropometric measurements, blood biochemistry (glucose, lipid profile and thyroid function) and obesity hormones (leptin, ghrelin, obestatin levels) in early stage breast cancer patients, compared to pre-treatment values, age and BMI-matched controls.

MATERIAL and METHODS

Study population

This study was conducted with 22 operated breast cancer patients and 33 healthy controls with indications for adjuvant chemotherapy. The patient group (n = 22) examined before and after adjuvant chemotherapy (BAC-breast cancer group) and after (AAC-breast cancer group) and before and after adjuvant chemotherapy (BAC-control group; n = 17) (AAC-control group; = 16) BMI-matched two different control groups; a total of 4 groups were formed. In order to eliminate the effect of weight changes of individuals on obesity hormones, the control group was composed of two seperate groups of healthy individuals in this study. The criteria to be included in the control group were determined as being between 18-70 years of age, being at close ages of patient group and having BMI, being a teetotaler and a nonsmoker, not having any gastrointestinal disorder diagnosis history of himself or his family, not having undergone gastrointestinal system surgery, being euthyroid and not using thyroid drugs, not being diagnosed with DM, not being involved in programs that requires walking more than 1 km/day or different weight loss programs and not having any health complaints within the last month. In addition to the control group criteria in patient group were having been operated for newly diagnosed breast cancer, having neither other cancer diagnosis nor metastasis, not having received any chemotherapy, radiotherapy or hormone therapy in the past and having survival expectancy of longer than 3 months.

All patients were informed about the study and informed consent was obtained. This study, which was carried-out within the framework of the ethical principles specified in the Helsinki Declaration, was approved by the Ethics Committee of Firat University Faculty of Medicine. (Date: 01.31.2008, Decision No: 11).

Study parameters

Age, anthropometric measurements (weight, BMI, waist circumference), blood biochemistry (glucose, cholesterol, triglyceride, High-density lipoprotein (HDL), Lowe-density lipoprotein (LDL), fT3, fT4, Thyroid stimulating hormone (TSH) and serum and salivary obesity hormone (total ghrelin, obestatin and leptin) levels were recorded in the study groups and compared. Hormone levels were also analyzed according to tumor clinicopathologic characteristics.

Anthropometric measurements

Height and body weight of the patient control group were measured by Nan Tarti INC. brand scale device and the waist circumferences of the same group were measured with a tape measure in meter unit. Height, body weight, and waist circumference were measured after fasting overnight, standing merely with underwear and without shoes, after a normal expiration. Waist circumference was measured at the narrowest diameter between the archus costarum and the anterior superior of the iliac spine. Height and waist circumference were recorded in CM and body weight was measured in KG. BMI body weight was calculated with (kg)/neck squared (m2) formula.

Collection of Blood and Saliva Samples

2 blood and 2 saliva samples were collected from the patient group, one being before treatment (basal) and the other being post-treatment; Control group has provided only 1 sample of each. Samples were collected upon overnight fasting, simultaneously between 09:00 am -10:00 am as 5 ml. venous blood and 2 ml. saliva. Blood and saliva samples were placed into epandorf tubes with 20-30 µl aprotin, in order to prevent breaking of peptides by proteases. After blood samples were centrifuged at 4000 RPM for 5 minutes and saliva samples at 4000 RPM for 10 minutes, the blood and the supernatants that were acquired have been stored at-20 ºC until the study.

Hormonal and Biochemical Measurements

Glucose, cholesterol, triglyceride, HDL, LDL, sT3, sT4, TSH parameters in venous blood were measured by AU2700 device (Optical Co., Ltd., Tokyo-Japan) in biochemical laboratories. As for the blood and saliva samples, ELISA kit (catalog number A05106) of Bretonneux Company from Tokyo Japan was used for acyl ghrelin and ELISA kit (catalog number A05119) of the same company was used for des-acyl ghrelin and for both of them Elexsus 800 was used for reading. And total ghrelin level has been determined by mathematically adding up acyl ghrelin and des-acyl ghrelin values.

Blood and salivary obestatin levels were measured by using BACHEM brand Human Obestatin ELISA kit with catalog number S-1285 (Peninsula Laboratories, Inc., BACHEM group, California, USA) in medical biochemistry laboratory. Blood and salivary leptin levels were measured in medical biochemistry laboratory using the DRG leptin kit No. 2395.

Statistical analysis

Statistical analysis was performed using SPSS Statistical Software for Windows version 22.0 (IBM Corp., Armonk, NY). Chi-square (x2) test was used for the analysis of categorical data and Independent Samples T Test and Mann-Whitney U Test were used for the analysis of numerical data. Data were expressed as mean ± standard deviation (SD) and n(%). P<0.05 was considered statistically significant.

RESULTS

Age and anthropometric measurements

There was no significant difference between control and patient groups in terms of age, BMI and waist circumference. In breast cancer patients, mean ± SD weight (67.2 ± 12.3 and 72.9 ± 11.8 kg., p<0.001), BMI (27.3 ± 4.7 and 29.61 ± 4.4 kg/m2, p<0.001) and waist circumference (88.6 ± 10.8 and 93.4 ± 11.0 cm., p<0.05) values were significantly increased after adjuvant chemotherapy compared to pre-treatment values (Table 1).

Table 1. Anthropometric measurements, biochemical and blood and saliva hormone analysis results in control and patient groups before and after treatment

	Control group (n=33)		Patient Group (n=22)	
Median (SD)	**BAC-control (n=17)**	**AAC-control (n=16)**	**BAC-patient**	**AAC-patient**
Age (year)	38.6±9.7	38.6±8.4	44.8±6.2	
Anthropometric Measurements				
Weight (kg)	66.1±4.8	77.2±16.2	67.2±12.3	72.9±11.8**
BMI (kg/m^2)	25.0±1.7	29.0±5.7	27.3±4.7	29.61±4.4**
Waist Circumference (cm)	89.41±11.0	97.6±14.0	88.6±10.8	93.4±11.0*
Biochemical Analysis				
Glucose (mg/dL)	87.58±15.21*	91.31±11.53	100.04±12.79	96.50±9.36
Total Cholestrol (mg/dL)	191.94±36.47*	197.06±34.10	213.95±31.87	206.31±24.41
HDL (mg/dL)	55.24±9.69	54.00±9.27	51.14±10.67	47.68±8.15
LDL (mg/dL)	115.71±25.79	119.06±30.16	115.05±39.26	112.04±30.10
Triglyceride (mg/dl)	102.24±42.15*	122.00±45.25	142.64±35.67	139.81±24.30
TSH (uIU/mL)	2.67±1.68	2.34±1.66	2.12±1.94	2.01±1.37
sT3 (pg/mL)	2.92±0.58	3.25±0.60	2.65±1.05	2.52±0.92
sT4 (ng/dL)	1.27±0.31*	1.28±0.55	1.77±0.74	2.05±0.60
Blood hormone levels				
Acyl ghrelin (pg/ml)	186.47±89.61**	151.74±94.88q	74.05±50.85	59.28±45.74

Des-acylghrelin (pg/ml)	936.76±446.93**	765.38±471.74q	347.59±241.95	295.40±241.44
Obestatin (pg/ml)	4.15±1.32	4.78±1.33	7.33±14.15	2.56±1.53
Leptin (pg/ml)	39.65±30.68	57.25±36.94	60.66±29.89	54.59±29.28
Saliva Hormone Levels				
Acyl ghrelin (pg/ml)	5.11±2.13	7.96±6.71	3.72±0.88	4.56±1.26*
Des-acyl ghrelin (pg/ml)	23.68±9.31	40.42±20.25	17.14±1.55	19.10±4.03*
Obestatin (pg/ml)	3.65±4.71	7.39±6.1	14.61±11.35	8.78±6.7.68
Leptin (pg/ml)	0.11±0.48	0.62±0.80	0.71±1.77	0.25±0.74

BAC: Before Adjuvant Chemotherapy; AAC: After Adjuvant Chemotherapy; BMI: Body Mass Index, HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; TSH: Thyroid Stimulating Hormone *p<0.05 and **p<0.001; BAC-according to patient group qp<0.01; AAC- according to patient group

An average of 5.7 kg (7.4%) weight gain, 8.8% increase in BMI, and 5.6% increase in waist circumference were observed in breast cancer patients at the end of the treatment.

Blood biochemistry analysis

Pre-treatment glucose (100.04 ± 12.79 and 87.58 ± 15.21 mg/dl, p<0.05), total cholesterol (213.95 ± 31.87 and 191.94 ± 36.47 mg/dl, p<0.05), triglycerides (142.64 ± 35.67 and 102.24 ± 42.15 mg/dl, p<0.05) and sT4 (1.77 ± 0.74 and 1.27 ± 0.31 ng/dl, p<0.05) values were significantly higher in breast cancer patients compared to the control group.

In terms of biochemical measurements, no significant difference was observed between the pre-treatment and post-treatment values in the patient group (Table 1).

Blood and salivary hormone analysis

Acyl ghrelin (respectively, 74.05 ± 50.85 and 186.47 ± 89.61 pg/ml., p<0.001 and 59.28 ± 45.74 and 151.74 ± 94.88 pg/ml., p<0.01) and des-acyl ghrelin (respectively, 347.59 ± 241.95 and 936.76 ± 446.93 pg/ml., p<0.001 and 295.40 ± 241.44 and 765.38 ± 471.74 pg/ml., p<0.01) blood levels were significantly lower in breast cancer patients compared to the control group in both pre-

Table 2. Blood, saliva ghrelin, obestatin ve leptin levels in breast cancer patients according to their hormonal status and tumor characteristics.

Breast Cancer Patients (n=22)	n (%)	Blood Levels			Saliva Levels		
		Ghrelin	Obestatin	Leptin	Ghrelin	Obestatin	Leptin
Menopausal Condition							
Premenopause	15(68.2)	78.81	8.68	57.17	3.53	13.50	0.91
Postmenopause	7(31.8)	63.66	4.57	61.57	4.11	17.00	0.31
Histopathology							
Invasive Ductal	14(63.6)	82.66	6.10	7.08	3.63	19.12	0.98
Invasive Lobular	2(9.1)	60.00	0.66	100.00	3.75	12.51	0.05
Mucinous	4(18.2)	63.00	12.38	46.00	4.10	7.20	0.52
Medullary	1(4.5)	70.00	1.00	8.50	2.80	0.01	0.00
Papillary	1(4.5)	30.00	25.00	97.00	4.10	0.01	0.00
T Stage							
T1	2(9.1)	135.00	17.15	100.00	4.00	38.50	0.90
T2	13(59.1)	74.25	7.33	50.65	3.61	8.89	0.94
T3	7(31.8)	56.29	4.67	61.44	3.83	18.43	0.27
N Stage							
N0	7(31.8)	63.03	4.98	54.86	3.27	11.45	1.41

N1	7(31.8)	83.43	10.90	66.14	4.11	11.13	0.33
N2	2(9.1)	62.50	1.60	25.75	3.15	33.50	0.05
N3	6(27.3)	79.83	7.98	65.02	3.95	16.09	0.60
Grade							
Grade I	2(9.1)	78.00	0.01	55.00	3.85	0.66	4.00
Grade II	15(68.2)	66.01	10.36	58.10	3.65	19.26	0.39
Grade III	5(22.7)	96.60	1.38	61.42	3.86	6.28	0.40
Vascular invasion							
Yes	13(59.1)	78.62	3.24	54.55	3.51	10.50	1.08
No	9(40.9)	67.47	13.35	64.39	4.01	20.56	0.21
Lymphatic invasion							
Yes	8(38.4)	71.40	4.80	63.00	3.26	14.14	1.46
No	14(63.6)	75.57	8.85	56.04	3.96	14.89	0.30
ER status							
Negative	10(45.5)	77.12	1.07	62.30	3.71	14.64	0.43
Positive	12(54.5)	71.50	12.63	55.47	3.72	14.60	0.47
PR status							
Negative	11(50.0)	73.36	8.80	60.77	3.94	19.48	1.09
Positive	11(50.0)	74.75	5.95	56.37	3.46	9.76	0.35
C-Erb B2 status							
Negative	15(68.2)	73.95	7.14	67.20	3.60	9.90	0.94
Positive	7(31.8)	74.29	7.89	40.09	3.96	24.72	0.26

T: Tumor, N: Nod, ER: Estrogen Receptor, PR: Progesterone Receptor. p>0.05

treatment and post-treatment periods. There was no significant difference in blood obestatin and leptin values and salivary ghrelin, des-acyl ghrelin, obestatin and leptin values between the control and patient groups neither before nor after the treatment (Table 1). In patient group, blood ghrelin, leptin and obestatin levels did not change significantly after the treatment compared to the pre-treatment values. In patient group, salivary acyl ghrelin (3.72 ± 0.88 and 4.56 ± 1.26 pg/ml., p<0.05) and des-acyl ghrelin (17.14 ± 1.55 and 19.10 ± 4.03 pg/ml., p<0.05) levels were significantly increased compared to pre-treatment values (Table 1).

Patients' blood and salivary ghrelin, obestatin and leptin levels according to their hormonal status and tumor characteristics

The majority of the study populations were premenopausal (68.2%), with invasive ductal histopathology (63.6%), at stage T2 (59.1%), at stage N0/N1 (63.6%) and at Grade II (68.2%), with non-vascular invasion (59.1%), with lymphatic invasion tumor (63.6%), with positive estrogen receptor (54.5%), with positive progesterone receptor (50.0%) and with C-ErbB2 negative (68.2%) breast cancer patients (Table 2).

There was no statistical difference among patients' blood and salivary ghrelin, obestatin and leptin levels according to their tumor clinicopathologic characteristics (p> 0.05) (Table 2).

DISCUSSION

Our findings pertaining to the metabolic effects of adjuvant chemotherapy in operated early stage breast cancer patients were found to be higher in breast cancer patients before the treatment compared to the control group's levels of glucose, total cholesterol, triglyceride and sT4; Yet, it was observed that blood acyl-ghrelin and des-acyl ghrelin levels were lower in both pre-treatment and post-treatment periods compared to control. After adjuvant therapy, there was a significant increase in weight, BMI and waist circumference and salivary ghrelin levels in breast cancer patients compared to pre-treatment values, while no significant effect observed neither on any of the biochemical parameters nor on the blood obesity hormones studied in the patient group. There was no statistical difference between blood and salivary ghrelin, obestatin and leptin levels according to tumor clinicopathologic characteristics.

Our observation of average 5.7 kg (7.4%) weight gain, 8.8% BMI increase and 5.6% waist circumference increase in our breast cancer patient group after adjuvant chemotherapy as opposed to the pre-treatment values is consistent with common complication of %50 to %96 weight gain and median increase value changing in between 2.5 to 6.2 kg. in early stage breast cancer patients receiving chemotherapy (18). Considering the fact that the majority of our patients are premenopausal, the average weight gain of 5.7 kg during the course of treatment supports the opinion that adjuvant chemotherapy might be associated with higher weight gain in premenopausal breast cancer patients as opposed to postmenopausal patients.

Moreover, our finding that shows 5% or more weight gain in early stage breast cancer patients during adjuvant chemotherapy is also noteworthy in regard to the opinion suggesting its pertinence to decrease in survival rate (19).

In a study conducted with 176 early stage breast cancer patients in Turkey, prior to adjuvant chemotherapy, by completion and 1-year after weight (respectively, 68.9 kg., 70.6 kg. and 71.9 kg.) and BMI (respectively, 27.1, 27.8 and 28.3 kg/m2) values have been reported to have increased significantly compared to pre-treatment values (20). Likewise, in another study conducted on 81 early stage breast cancer patients in Turkey, weight gain after adjuvant chemotherapy has been observed in %89.8 of the patients, while 38 of them (43.2%) have gained 3 kg. or more; And, it is concluded that >3 kg. weight gain has a negative effect on well-being and overall survival (21).

Even though our findings show that operated early stage breast cancer patients have significant weight gain caused by adjuvant therapy, no indication of treatment-related change has been observed on ghrelin, obestatin and leptin levels, which are known to have potential effect on weight control. In this study, in order to eliminate the effect of the weight difference between the patient and control groups on the results, blood obesity hormones were compared with two BMI-matched control groups before and after treatment. Blood ghrelin level was lower in breast cancer patients before and after treatment compared to BMI-matched control individuals. Plasma ghrelin levels show negative correlation with obesity, while showing increase with weight loss (8, 22). Yet, in terms ghrelin decrease, the lower course of ghrelin levels in breast cancer patients before and after treatment when they are compared to BMI-matched control individuals and absence of significant variation of ghrelin levels in patient group before and after treatment in our study, point out to a mechanism specific to cancer etiopathology rather than having any relevance with adjuvant chemotherapy or weight gain. Based on the fact that both forms of ghrelin trigger the growth hormone release, which has a strong effect on carcinogenesis, ghrelin level decrease might have an inhibitory role as a compensatory mechanism on neoplastic cells' proliferation by way of down-regulation of growth hormones (23,24). On the other hand, while there are studies in the literature which report that ghrelin has antineoplastic or antiapopitotic effects (25-27), the effect of ghrelin level increase or decrease on neoplastic development has not been fully elucidated.

Cisplatin-based chemotherapy exhibited significant drop in total plasma ghrelin level in esophageal cancer patients, as well as reduced food intake and deteriorating nutritional condition (28). Yet, guinea pig studies that investigate chemotherapy-induced dyspepsia have presented plasma ghrelin level (29) increase as well as improvement of symptoms by ghrelin treatment (30). Also it has been asserted that the elevation in ghrelin level due to chemotherapy might be a defensive reaction to correct impaired gastrointestinal motility against the toxic effects of chemotherapy on the basis of prokinetic effect (31).

In a comparison study between breast cancer patients and their healthy relatives, there was no significant difference between the two groups in terms of plasma leptin, adiponectin and ghrelin levels. Likewise, no significant difference was observed in plasma leptin levels between premenopausal patients with in-situ breast carcinoma and healthy control groups (32).

While an increase in leptin levels has been observed with obesity and weight gain (33,34),

a significant positive correlation between leptin levels and BMI has been shown in breast cancer patients. Yet, there was no significant difference in leptin levels compared to control or before and after treatment. Likewise, there are also studies showing that chemotherapy does not have any significant effect on leptin levels, in breast cancer patients (18,35).

Actually, it has been claimed that the slower course of weight loss in patients with breast cancer, compared to lung and prostate cancer patients might lead to more vague variations of adiponectin, ghrelin and leptin levels, by means of a potential adaptation mechanism, in breast cancer patients (22).

While glucose and lipid profiles were higher in breast cancer patients compared to pre-treatment control, neither was there significant difference compared to BMI-matched control group nor was there significant variation in these biochemical parameters during treatment.

This is coherent with the notion that the glucose and insulin metabolism changes in patients who are receiving chemotherapy are metabolic changes that are secondary to weight gain and/or dyslipidemia (7, 36). At the same time, low ghrelin levels as opposed to higher glucose and thyroid hormone levels, in breast cancer patients compared to control group is notewhorthy in terms of ghrelin's negative correlation with glucose and thyroid hormone levels (37, 38).

Even though its mechanism has yet to be clarified, it might be possible that the weight gain due to adjuvant chemotherapy has negative effect on quality of life as well as on glucose and insulin metabolism and it might also be a causing factor for the increase of cardiovascular disease and deterioration in cancer prognosis (6,7, 39).

Therefore, there is a necessity for large-scale and long-term well designed studies and development of treatment approaches to prevent or restrict metabolic deterioration in this field (7).

CONCLUSION

In conclusion, our study confirms that adjuvant chemotherapy causes significant weight gain in operated early stage breast cancer patients, yet does not display any change in ghrelin, leptin or obestatin levels in concurrent with a treatment. Being independent from treatment, lower blood ghrelin levels in breast cancer patients compared to BMI-matched control group, suggests that breast cancer patients might possibly have a cancer etiopathology oriented mechanism which happens to have no connection with ghrelin-specific weight or adjuvant therapy. We are in need of larger scale longitudinal studies in order to comprehend the mechanisms of weight gain and correlative metabolic changes related to adjuvant chemotherapy in early stage breast cancer patients and to be able to eliminate this complication, which has negative effect on quality of life, cardiovascular disease development and disease prognosis and also to find its treatment.

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Ethical approval: This study, which was carried-out within the framework of the ethical principles specified in the Helsinki Declaration, was approved by the Ethics Committee of Firat University Faculty of Medicine. (Date: 01.31.2008, Decision No: 11).

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