Altered Serum Marker of Adipokines Profile in Breast Cancer Women

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Abstract

Introduction and Objective:Breast cancer is a heterogeneous cancer with diverse clinical symptoms and an ambiguous molecular spectrum. This study is designed to determine level changes in the leptin, ghrelin, chemerin, and adiponectin in sera of breast cancer patients. Blood samples were obtained from all women with PCOS and healthy between 8 and 11 AM, after fasting overnight. Serum leptin, and ghrelin, chemerin, adiponectin concentrations were analyzed by enzyme-linked immune-sorbent assaykit.Results: The results of this study showed that the mean and standard deviation of serum TSP-1,chemerin ,andadiponectin concentration have increased significantly in patients with BC (16.1±8.87 vs 8.169±4.60 ng/ml), (261 ± 83.3 vs 536 ± 94.6µg/l: P < 0.001),and (9 ± 1.82 vs 20.4± 2.1: P<0.001) respectivelythan in the control group. The mean and standard deviation of leptin, and ghrelin in patients with BC were (27.6±3.4 vs 42±4.6ng/ml: P<0.001), and (336.2±80.97 vs155±57.4 ng/mL)respectively while it was 42±4.6ng/ml: P<0.001), and (155±57.4 ng/mL)in the control group. It was significantly higher in people who had breast cancer than in the healthy group (P<0.001).Conclusion:The serum Leptin, and Ghrelin, chemerin, adiponectin may have a potential role as a biomarker in the pathogenesis, development, and metastasis of BC.

Keywords: *Serum; Adipokines; Breast Cancer; Women*

Introduction

Cancer is characterized by loss of control of cellular growth and development leading to excessive proliferation and spread of cells[(1)].Breast cancer(BS) is the most commonly diagnosed cancer in women worldwide(2.1 million newly cases in 2018) and it still remains one of the major causes of death for cancer in over 100 countries[(2-3)].Its etiology and causative factors are complex and interlinked which includes family history, gene susceptibility, hormone, diet, lifestyle factors and environmental exposures[(4,5)].In breast cancer, early local invasion occurs in close proximity of adipocytes at the invasive front. Still, the cellular and molecular interactions between adipocytes and breast epithelial cells, along with the role of adipocytes in tumor progression remain incompletely understood[(6)].

Adipose tissue is a complex, essential, and highly active metabolic and endocrine organ. that secretes a variety of cytokines and hormones, termed adipokinessuch as leptin, adiponectin, interleukin-6, VEGF, TNF-α, these secreted factors are able to influence tumor cell survival and behavior[(7-9)].

Materials and Methods

Sixty one women with BC, aged 25–60 years were recruited from Kirkuk Teaching Hospital / Kirkuk / Iraq, from tenth of January 2019 to tenth of March 2020. Sixty one healthy women matched for age with the patients agreed to participate to this study as controls. These women were clinically, mammographically and/or cytologically confirmed to be clear of BCa. The study was approved by the local ethics committee, and all

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subjects gave written informed consent before taking part in the study.

Venous blood samples obtained from participants after overnight fasting of at least 12 h. All tubes were centrifuged at 4 °C (1000 rpm, 15 min) and stored at -80°C until required for analysis. An enzyme-linked immune sorbent assay (ELISA) were used to determine concentrations of ghrelin ,chemerin,adiponectin and leptinin serum (Uscn Life Science Inc., Wuhan, China).

Statistical analyses were conducted using SPSS for Windows, version 20 (Chicago, IL, USA).The data are expressed as mean ± SD for continuous variables. The differences among the means were considered significant if $P < 0.05$.

Results

The baseline demographic characteristics and biochemical variables of cases and controls are summarized in [Table 1]. From the 122 study participants, 61 in BC group and61 in control group were studied. Both groups were comparable regarding to age, PON-1chemerin,adiponectin and leptin[Table 1].

Table 1 shows the mean and standard deviation of serumchemerin , and adiponectinwere significantly raised in breast cancer patients (261 ± 83.3 µg/l **), and (9 ± 1.82)respectively than the normal Controls group (536 ± 94.6µg/l: P < 0.001), and (20.4± 2.1: P<0.001) respectively. Leptin and Ghrelin showed significant increased values in breast cancer patients than the controls group (27.6±3.4 vs 42±4.6ng/ml: P<0.001), and (336.2±80.97 vs155±57.4 ng/mL) respectively (Figures 1-4).**

Table1: Demographic characteristics of cases and controls

Clinical Characteristics	Group A(Control)	Group B	P value
No. of subjects	60	60	------
Age (yr)	43.50 ± 0.80	45.14 ± 0.80	0.152

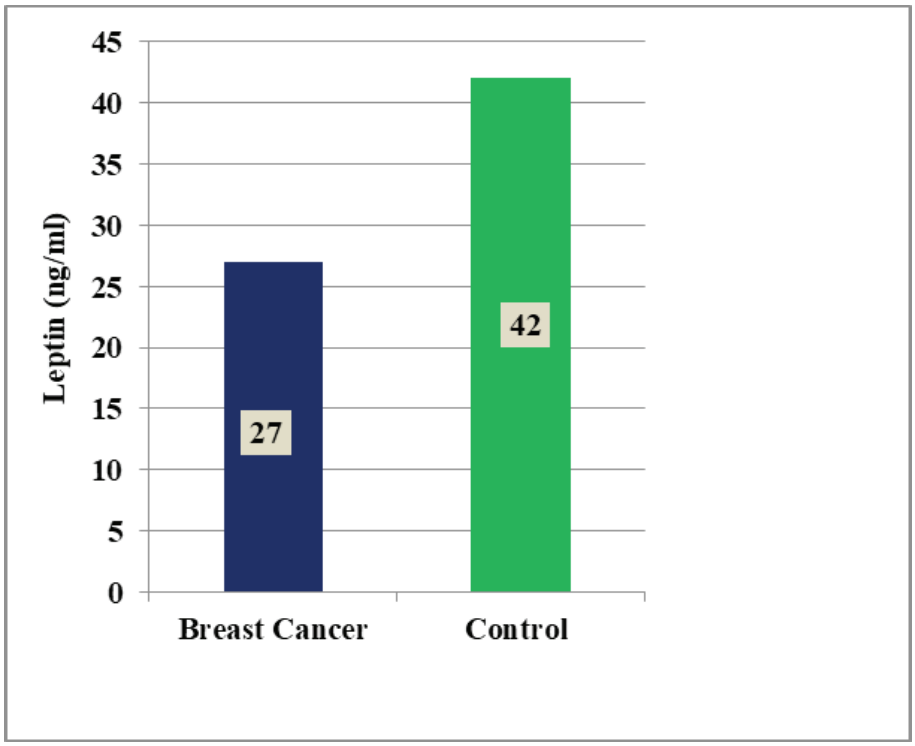

Figure (1):-The level of Serum Leptin (ng/ml)in study groups.

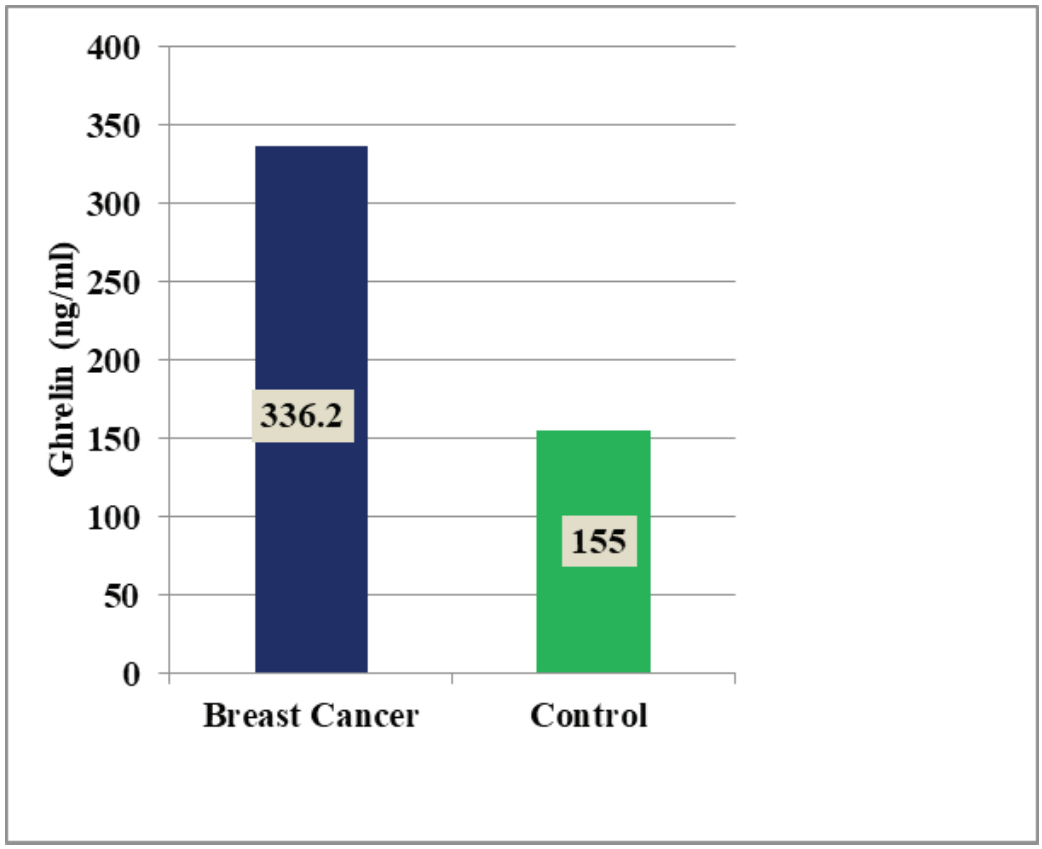

Figure (2):-The level of serum ghrelin (ng/mL) in study groups.

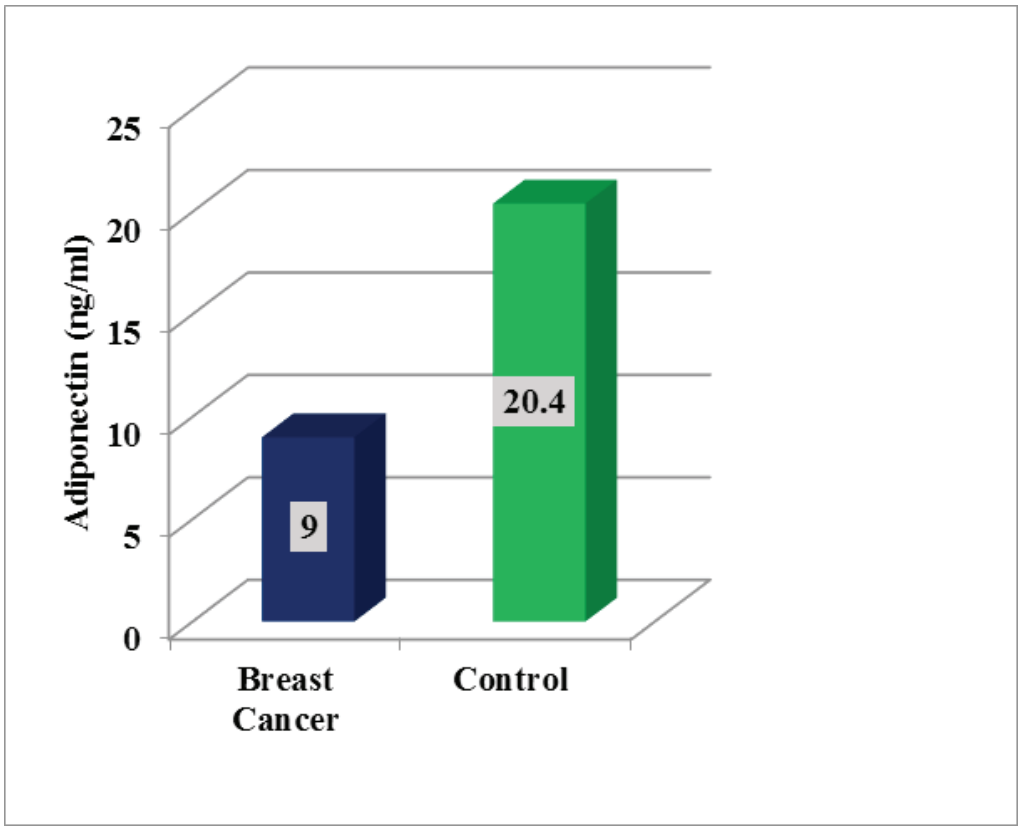

Figure (3):-The level of serum adiponectin (ng/mL) in study groups.

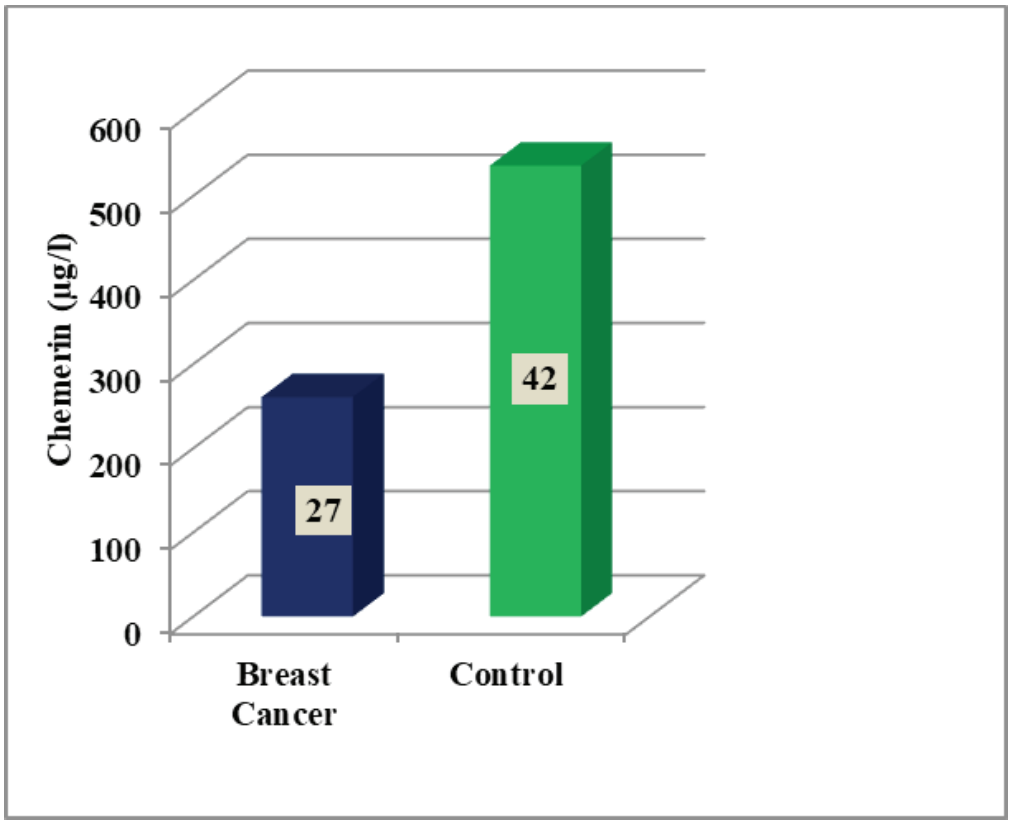

Figure (4):-The level of serum chemerin (µg/l)in study groups.

Discussion

Leptin, a polypeptide hormone, 16 KDa protein consisting of 167 amino acid peptide hormone synthesized predominantly Ob gene from adipocytes, that acts as a sensor to the hypothalamus, circulates in serum either in a free or a bound form , influencing appetite control and energy expenditure through its actions on the hypothalamus and other regions in the brain[10-13].Leptin impacts the body's obstruction parts, including Immune system microorganisms, macrophages and endothelial cells. Thusly, a couple of masters have named it a cytokine[14].Leptin activated via signaling pathways activated include the mitogen-activated protein kinase (MAPK) signaling cascades ,cytokine Janus kinase/ signal transducer phosphoinositide 3-kinase (PI3K), and activator of transcription (STAT), which increase cancer cell proliferation, motility and overall cancer progression [15].leptin may enhance growth and proliferation of breast cancer cells through activation of various through several signal transduction pathways and by altering cell-cycle checkpoints via upregulation of cyclin D1 and cyclin-dependent kinase 2[16,17].

Adiponectin inhibits Nuclear Factor NF-κB activation, which is a key pathway in breast cancer development. In the present study, serum Adiponectin of study group was significantly lower than control group, due shown to contribute to tumorigenesis through down regulation of PTEN activity[18].

Insulin and C□peptide are the products of the enzymatic cleavage of proinsulin and secreted into the circulation in equimolar concentrations. C-peptide, initially considered an inactive molecule, has, currently, been shown to be a bioactive molecule when it binds to the surface of several cell types, and activates the calcium-dependent intracellular signaling pathway(19,20).

Insulin may upregulate the expression of vascular endothelial growth factor (VEGF), a potent angiogenic agent that is secreted by breast cancer cells, may synergize with the mitogenic effects of estrogen. Adiponectin inversely correlated with estrogen levels may effect breast cancer risk by altering circulating

estrogen levels

Chemerin, also known as retinoic acid receptor responder 2 (RARRES2) encoded by the RARRES2 gene is a newly identified adipokinesecreted by adipose tissue characterized as a potent chemoattractant protein[21].known for its roles in adipogenesis, angiogenesis, skin function, metabolic activity, and, recently, tumorigenesis[22].Chemerin derived peptides plays a crucial role in regulation of immune response, insulin resistance, and adipose maturation, differentiation, and metabolism as well as exhibits both pro-inflammatory and anti-inflammatory effects, that may be involved in both initiation and resolution of inflammation[23,24],chemerin as a chemoattractant protein may contribute to recruitment of macrophages into adipose tissue and has a role at an early stage of adipose tissue inflammation.

Chemerin promotes tumorigenesis by triggering the production and activity of matrix metalloproteinase, which plays a crucial role in angiogenesis, while the antitumor role for high chemerin levels has been reported to be through recruitment of natural killer (NK) cells which would help the immune system to recognize and fight the cancer cells[25].

Ghrelin is a multifunctional peptide with 28 amino acids hunger-stimulating peptide, Principally secreted by the stomach, and has been characterized as the ligand of the growth hormone secretagogue receptor (GHSR) with physiological actions ranging from hormonal secretion, regulation of food intake, modulation of insulin secretion, adipogenesis and gastrointestinal motility, energy homeostasis, body mass regulation through mechanisms independent from growth hormones.and one of the most important orexigenic peptides currently known[26-28].It was implicated in various processes of cancer progression including cell proliferation, cell migration and invasion, angiogenesis, and apoptosis, probably via an autocrine/paracrine mechanism[29]. Serum ghrelin levels were significantly higher than normal control indicated a compensatory mechanism triggered by cachectic catabolic–anabolic imbalance[30].

Conclusion

The results of this analysis suggested that leptin and adiponectin could be a potential biomarker for breast cancer risk in women, In addition , leptin will provide useful information for a therapeutic target to treat BC.Serum Chemerin promises to be a novel biomarker of diagnostic and prognostic value. Larger prospective studies are required to confirm our findings.

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Ethical Approve: We declare that the study does not need ethical approval.

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