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Evaluation of the level of leptin, visfatin and some biochemical in women with breast cancer

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Abstract
Background: Breast cancer (BC) happens when cells in the breast grow in an uncontrolled way and form a lump called a tumor (primary cancer). Sometimes, cancer cells spread to other parts of the body through the blood and lymphatic system. This is called secondary cancer. There are different types of breast cancer, but they are treated in similar ways. Breast cancer is not infectious and cannot be passed on to other people. The stage of breast cancer means how big it is and if it has spread, and the grade of breast cancer is how quickly the cancer may grow.
Objective: The aims of the study were to assess the clinical utility of serum Leptin, and visfatin, in women with breast cancer for diagnostic and prognostic purpose.
Methods: Forty clinically and histopathologically confirmed female patients of the age group of 30-70 years served as cases and 40 normal healthy females in the same age group served as controls. The parameters were estimated by standard biochemical methods.
Results: The highest percentage of age for women with BC equal to (32.58%) in the age group (56-65) years, with mean age, was 51.19 years and the statistical tests data obtained showed: highest significant elevation of leptin, visfatin, level in women with BC were 40.35±7.11 ng/ml, 51.26±9.05 ng/ml, as compared to control group 31.14±5.07 ng/ml, 21.60±4.62 ng/ml, respectively at (p<0.001).
Conclusion: The study showed that breast cancer patients had significantly higher levels of Leptin, Visfatin.

Keywords: Breast cancer, endocrine tissue, leptin, visfatin

Introduction

Breast cancer (BC) is a malignant neoplasm characterized by abnormal cell growth of breast tissue in an uncontrolled pattern and their ability to infiltrate and invade normal tissue locally. It is a form of cancerous tumor that affects the breast tissue and appears in the ducts of the tubes that carry milk to the nipple and milk glands [1, 2]. Breast cancer (BC) is the second most common cancer worldwide and the most frequent malignant disease, with an estimated 2.3 million cases and 685,000 deaths in 2020, and the cases are expected to reach 4.4 million in 2070. Its etiology and causative factors are complex and interlinked which includes family history, gene susceptibility, hormone, diet, lifestyle factors and environmental exposures [3, 4]. Adipose tissue is an endocrine tissue that secretes many peptides that are adipocytokines including leptin, adiponectin, resistin and visfatin [5, 6].

Leptin is a 167-amino acid protein including a 21 amino acid signal peptide.It is found in number of tissues & organs like but mostly articulated in the visceral adipose tissue [7]. LEP acts through the activation of its receptor (ObR) located in the hypothalamus in the central nervous system and at the peripheral level [8].

Visfatin is a large 52 kDa protein made of 167 amino acids involves various metabolic pathways within mammalian cells, such as oxidation of fatty acids, growth, apoptosis, and angiogenesis. Visfatin functions as both an extracellular secretory factor and an intracellular enzyme in mammalian cells. Visfatin is also known as nicotinamide phosphoribosyl transferase (NAMPT), named after its role as a rate-limiting enzyme in the biosynthesis of nicotinamide adenine dinucleotide (NAD) and accountable for cellular homeostasis of NAD that regulates cell viability including the survival of breast cancer cells [9, 11].

Materials and Methods

This study is a cross-sectional, hospital-based study, the protocol of this study was approved by the scientific committee of Tikrit University College of Medicine, and the agreement of the attendance to Kirkuk Oncology Center, Kirkuk general hospital to collect the sample from the patients was approved by the Kirkuk Health Directorate. This study was carried out at the Oncology Center in Kirkuk city-Iraq from the beginning of January 2017 to the end of May 2017. The subjects enrolled in the study were divided into (40) breast cancer women and (40) apparently healthy women as controlled in Kirkuk city.

Results

The study included age and its class of groups, so the statistical tests show the highest percentage of age for women with breast cancer equal to (32.58%) in the age group (56-65) years, with a mean age of 51.19 years, see figure (1)&(2). And the study included the geographical distribution of samples in terms of their areas of residence (the urban or the rural area) and showed that the highest rate of disease was among women living in rural areas (62.88%), while it was for women who reside in the urban areas (37.12%), see figure (3). The study also included calculating the average body mass index through body weight (kg) and height (m). The study showed that the vast majority of women with breast cancer suffer from obesity. The mean BMI ± SD was 29.55 ± 8.27 versus 25.02 ± 4.86 kg/m^2 for casualties and intact, respectively, see figure (4).

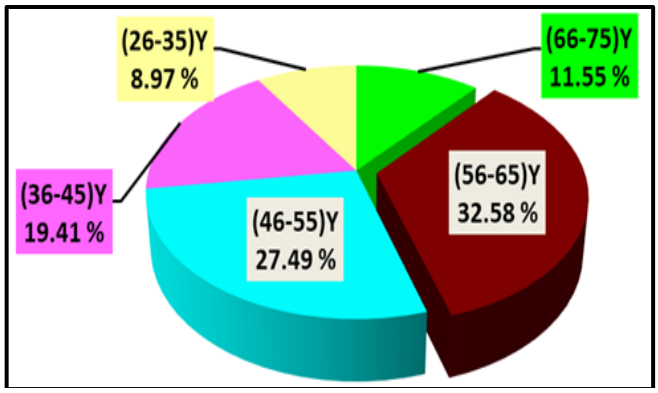

Fig 1: Distribution of breast cancer women according to age.

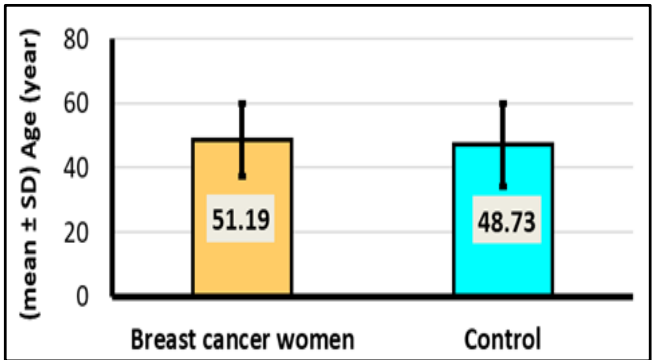

Fig 2: Relation of breast cancer women and control groups to age.

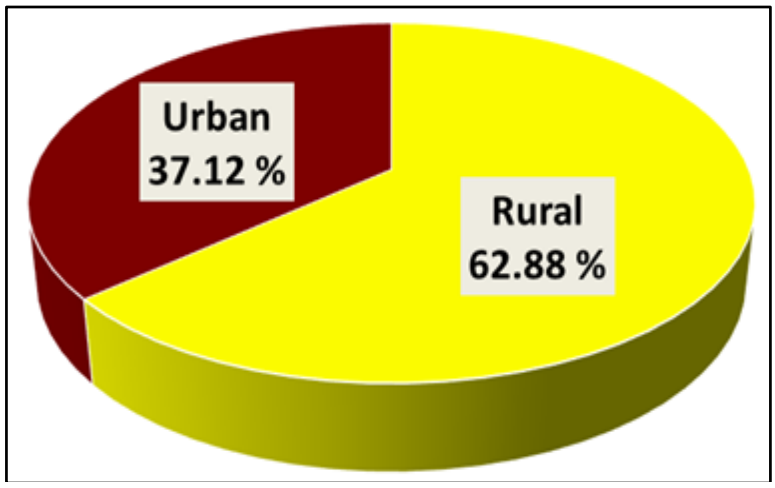

Fig 3: The distribution of breast cancer cases according to residence

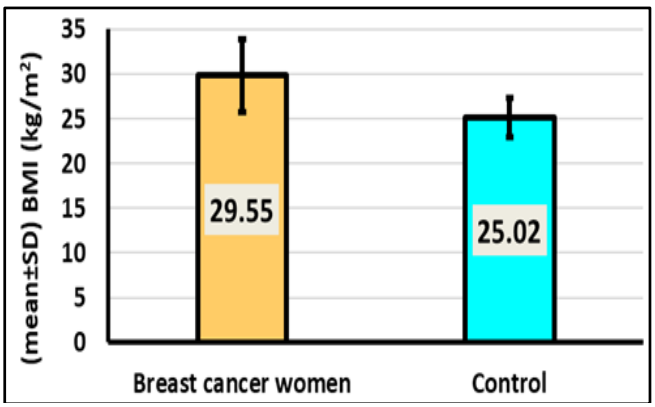

Fig 4: Comparison of BMI (kg/m^2) of breast cancer women and controls

Table 1 relieved that the highly significant increase in mean serum Leptin and Visfatin was observed in carcinoma breast patients when compared to controls (p<0.001).

Table 1: Comparison of serum levels of leptin and visfatin between controls and carcinoma breast cases.

Parameters	Mean ± SD Controls	Mean ± SD cases	P Value
Leptin (NG/ML)	16.98±1.17	19.38±1.37	<0.001
Visfatin (NG/ML)	31.14±5.07	40.35±7.11	<0.001

Diagnostic test

Evaluates status before symptom become definitive, Sensitivity (Sn) & Specificity (Sp) are statistical measures of the performance of the test.

Sensitivity was a test ability to Identify a condition correctly. Specificity was a test ability to exclude a condition correctly

$$\text{Sensitivity (Sn)} = \frac{\text{True positive (TP)}}{\text{True positive (TP) + False negative (FN)}}$$

Specificity was a test ability to exclude a condition correctly

$$\text{Specificity (Sp)} = \frac{\text{True negative (TN)}}{\text{True negative (TN) + False positive (FP)}}$$

Positive Predictive Value (PPV) is the proportion of positive tested persons have the disease, it was directly related to prevalence.

$$\text{Positive Predictive Value (PPV)} = \frac{\text{True positive (TP)}}{\text{True positive (TP) + False positive (FP)}}$$

Negative Predictive Value (NPV) is the proportion of negative tested persons have not the disease, it was inversely related to prevalence.

$$\text{Negative Predictive Value (NPV)} = \frac{\text{True negative (TN)}}{\text{True negative (TN) + False negative (FN)}}$$

PPV likelihood of having the disease when test is positive.
NPV likelihood of not having the disease when test is negative.
Sensitivity (Sn) & Specificity (Sp) are widely used.
Usually not both Sensitivity (Sn) & Specificity (Sp).
High Sensitivity tests are for screening.
High Specificity tests used to make the definitive diagnosis.
Clinicians used multiple moderate to high specificity test
Sensitivity (Sn) & Specificity (Sp) are not related to prevalence, where PPV & NPV are intimately related.
PPV & NPV are so related to prevalence that it is difficult to related results to patients.
Sensitivity (Sn) & Specificity (Sp) refer to the identification of patients with and without the disease. For a test to be useful, it must have high Sensitivity (Sn) & Specificity (Sp).

Table 2: Comparison of diagnostic tests of the studied Parameters tests for breast cancer women

Variable	Leptin	Visfatin
Sensitivity Sn	0.91	0.89
Positive Predictive Value (PPV)	0.81	0.85
Specificity Sp	0.86	0.88
Negative Predictive Value (NPV)	0.90	0.88
Accuracy	0.105	0.101

Discussion

Leptin may specifically amplify estrogen signaling in two different ways, (i) by increasing aromatase gene expression or (ii) by directly transactivating Erα [12]. Leptin has mitogenic effects on epithelial cells, and in breast cancer cell lines it affects their proliferation and migration [13]. The overexpression of leptin detected in triple-negative mammary carcinomas is also in concordance with previous results in triple-negative breast cancer, where leptin signaling is crucial for tumor growth [14].

Present study showed that leptin levels which was significantly higher in women with breast cancer and when compared healthy group. Zeinab *et al.* [15], Manar *et al.* [16] and Adel *et al.* [17] which illustrated that breast cancer patients had significantly higher serum leptin levels than healthy controls. Another similarity to the study's results was shown by Pan *et al.* [18] who presented that leptin levels were found to be higher in breast cancer patients, especially in overweight or obese women.

Visfatin impacts mammary tissues through endocrine and paracrine mechanisms, involving metabolic pathways like fatty acid oxidation, growth, apoptosis, and angiogenesis within mammalian cells [19]. NAMPT, it was a key rate-limiting enzyme in the biosynthesis of NAD^+ ,which partly explained the elevated NAMPT expressions in patients with malignant tumors [20].

In our study a highly significant increase in serum visfatin was observed in carcinoma breast patients as compared controls, (p<0.001). These results were in agreement with the results of Shaoxue [21] and Sarhat *et al* [22]. Possible mechanisms assumed that: First, Visfatin, a proinflammatory molecule produced by adipose tissue macrophages, may inhibit macrophage apoptosis triggered by various endoplasmic reticulum (ER) stressors. Visfatin increases IL-6 protein secretion, activating prosurvival signal transducer and transcription 3, potentially contributing to obesity-associated diseases like inflammation or tumorigenesis. Additionally, The increase in visfatin is directly linked to the rise of Sirt6, which in turn, post-transcriptionally, contributes to the upregulation of TNF-α [23, 24].

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