



IRAQI
Academic Scientific Journals



العراقية
المجلات الأكاديمية العلمية

ISSN:1813-1638 (Print)
The Medical Journal of Tikrit University

Journal Homepage: <http://mjtu.tu.edu.iq>

MJTU

The Medical Journal
of Tikrit University

Evaluation of resistin, prolactin, and aromatase in women with breast cancer

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Received: 05/04/2024
Accepted: 05/05/2024
Available online: 15/12/2024

ABSTRACT

Cancer is a group of diseases characterized by uncontrolled cell division leading to growth of abnormal tissue, it is a common term for tumors that affect the body's organs, which are the two types of benign tumors and malignant tumors (which are known as carcinoid tumors). A distinction is made between them by examining the tissue (taking a sample). Breast cancer (BC) is formed due to a change in the functioning and growth of cells that make up breast tissue without the ability to control it, which turns them into cancer cells with the ability of these cells to spread. The aims of the study were to evaluate serum levels of resistin (RST), prolactin (PRL), aromatase (ARO), in women with breast cancer and compared with apparently healthy women (control). 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 December 2022 to the end of May 2023. The subject enrolled in the study were divided into (44) breast cancer women and (42) apparently healthy women as control In Kirkuk city. The highest percentage of age for women with BC equal to (34.1%) in the age group (50-59) years, with mean age, was 48.7 years and the statistical tests data obtained showed: highest significant elevation of RST, PRL, and ARO level in women with BC were 6.8 ± 1.8 ng/ml, 58.7 ± 8.4 ng/ml, and 1.5 ± 0.4 pg/ml as compared to control group 4.4 ± 0.5 ng/ml, 24.4 ± 7.2 ng/ml, and 0.4 ± 0.2 pg/ml respectively at ($p < 0.001$). The present study conclude that levels of resistin, prolactin, and aromatase dismutase were significantly higher in women with breast cancer compared to the control.

KEY WORDS:

Breast Cancer; Resistin;
Prolactin; Aromatase.

DOI: <http://dx.doi.org/10.25130/mjotu.29.1.9>



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INTRODUCTION

The most common malignancy cancer among women all over the world is breast cancer. Approximately 25% of cancers in women and 15% of cancer deaths are caused by breast cancer. It has been estimated that the prevalence of breast cancer in the world will reach 2.3 million by 2030 [1-3]. Breast cancer has a strong proclivity for spreading to lymph nodes, the lungs, the bones, and the liver, early local invasion occurs in close proximity of adipocytes at the invasive front^[1-3]. Resistin is 12.5 kDa, a cysteine-rich peptide hormone (similar to a cytokine) derived from adipose tissue that in humans is encoded by the RETN gene, whose physiologic role has been the subject of much controversy regarding its involvement with obesity and type II diabetes mellitus (T2DM) [4].

Aromatase is the enzyme synthesizing estrogens from androgens. In estrogen-dependent breast tumors, estrogens induce the expression of growth factors responsible for cancer cell proliferation. In situ estrogen synthesis by aromatase "is thought to play a key role in the promotion of BC growth" [5]. Aromatase inhibitors (AIs) provide new approaches for the prevention and treatment of breast cancer by inhibiting estrogen biosynthesis. Through reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemical techniques, aromatase has been found to be expressed in many endocrine tissues and tumors originating from these tissues. Unexpectedly, this enzyme is now known to also be expressed in liver and colon cancers. Such findings suggest a potential role for endocrine manipulation of these types of cancer using aromatase inhibitors [6].

EXPERIMENTAL PART

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 December 2022 to the end of May 2023. Verbal consent was taken from each woman included in this study whether considered as a case or control. Around seventy three women with breast cancer were screened to participate in the present

study. Women with breast cancer who attended to Oncology Center were enrolled in this study. The diagnosis of breast cancer was made by the histopathological examination of a breast mass which was removed by surgery from each woman included in this study, which means that the diagnosis of breast cancer was according to the discussion of the histopathologist. Women ages were between 29 to 68 years, and they were from the center and periphery of Kirkuk City. Forty-four women with breast cancer were considered as a study group, twenty-one women did not meet the inclusion criteria and eight women refused to participate in this study due to the agreement of their families. Sixty-one apparently healthy women without breast cancer were interviewed to participate in this study, nineteen women were refusing to participate in this study therefore Forty two apparently healthy women without breast cancer and with negative family history for the first and second-degree relatives of breast cancer and other types of cancer were considered as a control group, their ages were from 31 to 64 year.

The main objectives of the study are to clarify the importance of the tests for Resistin (RST), Prolactin (PRL), Aromatase (ARO), and some biochemical criteria for early detection of breast cancer patients and their severity. Data was analyzed using unpaired t-test. $P < 0.05$ was considered to be statistically significant and $P < 0.001$ was taken as statistically highly significant. Each woman included in this study was measured for her weight and height and the body mass index was calculated by using the following formula: weight in kilograms divided by height in squared meters. The quantifying obesity by the body mass index classification of WHO, and international obesity task force.

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 (34.1%) in the age group (50-59) years, with a mean age was 48.7 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 (63.6%), while it was for women who reside in the urban areas (36.4%), see

figure(6). The study also included calculating the average body mass index through body weight (kg) and height (meters). The study showed that the vast majority of women with breast cancer suffering from obesity. The mean BMI \pm SD was 29.8 ± 8.4 versus 25.1 ± 5.0 kg/m² for casualties and intact, respectively.

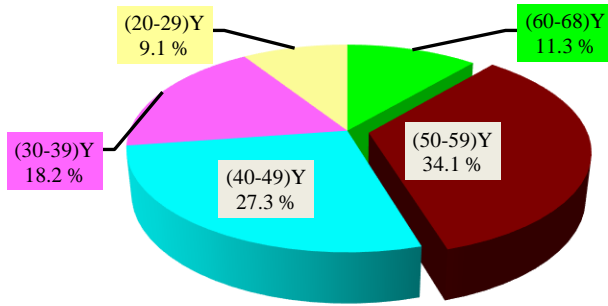


Figure (1): Distribution of breast cancer women according to age.

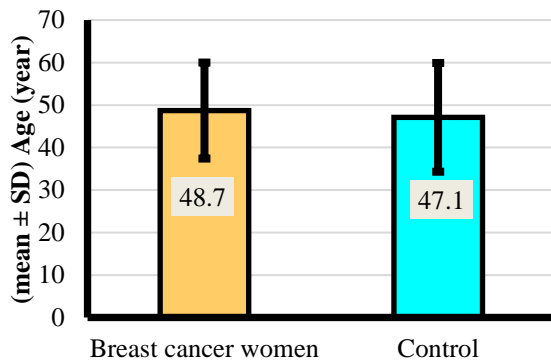


Figure (2): Relation of breast cancer women and control groups to age.

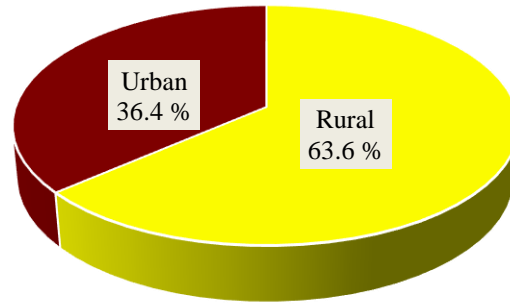


Figure (3): The distribution of breast cancer cases according to residence

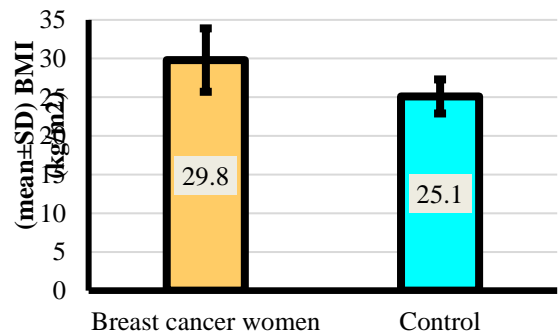


Figure (4): Comparison of BMI (kg/m²) of breast cancer women and controls

Table (1) relieved that the mean \pm SD serum value of resistin, prolactin, aromatase, were higher in women with breast cancer of compared to control. However the differences were significant for resistin, prolactin, and aromatase. Table (2) relieved that the mean serum value of RST, ARO, were higher in urban areas of compared to rural areas. In addition, PRL serum value were about equal in both areas. Table (3), shown the correlation coefficients (r) value between the biochemical parameters tests that is used in the study for women with breast cancer. The diagnostic tests in Table (4) shoes the percentage value of diagnostic tests (sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and accuracy) of serum biochemical tests for breast cancer women.

Table (1): The serum biomarkers level in women with breast cancer compared to control.

Variable	Mean ± SD Breast cancer	Mean ± SD Control	t-test	P. value
RST (ng/ml)	6.8 ± 1.8	4.4 ± 0.5	0.44	0.0033
PRL (ng/ml)	58.7 ± 8.4	24.4 ± 7.2	0.12	0.0042
ARO (pg/ml)	1.5 ± 0.4	0.4 ± 0.2	0.35	0.0045

Table (2): Mean serum of biomarkers in women with breast cancer in relation to residence.

Variable	Mean ± S D Urban area	Mean ± S D Rural area	t-test	P. value
RST (ng/ml)	5.1 ± 2.1	7.4 ± 2.7	0.48	0.0031
PRL (ng/ml)	51.5 ± 7.7	60.1 ± 7.8	0.18	0.0047
ARO (pg/ml)	1.1 ± 0.2	1.4 ± 0.4	0.37	0.0043

Table (3): correlation coefficients (r) value between the biochemical tests that used for women with breast cancer serum.

Verbal	RST	PRL	ARO
Resistin	-	-	-
Prolactin	0.69	-	-
Aromatase	0.61	0.63	-

Table (4): Comparison of diagnostic tests of the studied Parameters tests for breast cancer women

Verbal	Sn%	Sp%	PPV%	NPV%	LR+	LR-	Accuracy
Resistin	91	90	87	90	0.885	8.913	0.145
Prolactin	93	91	89	93	0.885	7.309	0.109
Aromatase	95	92	85	94	0.828	4.345	0.189

Figure (5): The diagnostic tests diagram

Biochemical tests	test +ve thinks it's a case test -ve thinks isn't a case	Diseased	non-diseased	PPV NPV
		TP FN Total disease	FP TN Total healthy	

DISCUSSION

Evaluates status biochemical tests for breast cancer women become after studies diagnostic tests by Sensitivity (Sn) it was a test ability to identify a condition correctly, Specificity (Sp) it was a test ability to exclude a condition correctly [7], Positive Predictive Value (PPV) it was the proportion of positive tested persons have the disease, it was directly related to prevalence, Negative Predictive

Value (NPV) it was the proportion of negative tested persons have not the disease, it was inversely related to prevalence, Positive Likelihood Ratio (LR+) it was the Ratio of the proportion that tests positive among those with the target condition compared to the proportion that tests positive among those without the target condition, Negative Likelihood Ratio (LR-) it was the ratio of the proportion that tests negative

among those with the target condition compared to the proportion that tests negative among those without the target condition [8]. Accuracy was the quality of being correct or true to some objective standard, it is the proximity of measurement results to the true value. Accuracy is occasionally referred to as

True positive (TP)

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

True negative (TN)

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

True positive (TP)

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

True negative (TN)

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

TP + TN

TP + TN

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{Total populations}} = \frac{\text{TP} + \text{TN} + \text{FP} + \text{FN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}}$$

TP / (TP+FN)

$$\text{Positive Likelihood ratio (LR+)} = \frac{\text{TP} / (\text{TP} + \text{FN})}{\text{FP} / (\text{TN} + \text{FP})}$$

FP / (TN+FP)

FN / (TP+FN)

$$\text{Negative Likelihood ratio (LR-)} = \frac{\text{FN} / (\text{TP} + \text{FN})}{\text{TN} / (\text{TN} + \text{FP})}$$

TN / (TN+FP)

Breast cancer is one of the commonest causes of cancer mortality in females. It is responsible for the death of millions of women worldwide every year. It is a disease which usually begins as a localized proliferation of cells, which over the course of time, spreads to regional lymph nodes and then to distant tissues in the body (bones, liver, lungs, etc.) Resistin is involved in inflammatory processes such as atherosclerosis as well as various cancers such as colorectal, prostatic, and endometrial cancers [9]. In a previous study, serum resistin level was found to be significantly higher in breast cancer patients as compared with that in normal subjects [10,11].

"diagnostic accuracy" or "diagnostic effectiveness" and is expressed as the proportion of correctly classified subjects among all subjects [7]. The diagnostic value measures from the above equations, the presentation of diagnostic exam results is often in 2x2 tables, such as figure (5).

Furthermore, it has been reported that high resistin expression in breast cancer tissue is associated with malignancies, postmenopausal breast cancer, and poor cancer prognosis. Although accumulating evidence suggests that resistin plays an important role in the progression of cancers, the molecular mechanisms by which it acts have not been fully evaluated [12-14]. Our findings show a decrease in prolactin in breast cancer women in comparison with control. These results agree with previous reports [15,16]. One potential alternative mechanism may be through the JAK2-nuclear factor 1-C2 (NF1-C2) pathway. PRLR activates JAK2 that in turn can

activate NF1-C2 in the nucleus, independent from STAT5 activation^[16].

This study reveals the highest sensitivity and specificity value of blood RST, PRL, and ARO levels in Breast Cancer women. that mean RST, PRL, and ARO tests are very good to use in the diagnosis of breast cancer Numerous results obtained by WANG^[17] founds the specificity of RST for breast cancer women was 87%, with a sensitivity of 64 % reported results indicated that the RST test may be useful in the diagnosis of breast cancer. However, the low sensitivity but it's a high specificity. Also, Mujagić^[18] found the specificity of PRL for Breast Cancer women was 85.5 %, with a sensitivity of 80 % reported results indicated that the PRL test is useful in the diagnosis of breast cancer. Dekker^[19] founds the highest sensitivity and specificity value of ARO was testing for breast cancer, with an overall sensitivity and specificity of 99.7 and 95.4 %, respectively.

CONCLUSION

The mean serum levels of resistin, prolactin, and aromatase dismutase were significantly higher in women with breast cancer compared to the control. Women with breast cancer from the rural areas had a significantly higher serum level of resistin, prolactin, and aromatase compared to women with breast cancer from the urban areas.

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