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Serum Levels of Vimentin and Oxyntomodulin in Women with Breast Cancer. Comparative Study

[1]Maryam A. faiq, [2]Salam S. Ahmed, [3]Thaer J. Mohammed

Abstract

Background*: Breast cancer is the most frequent malignancy among women worldwide, accounting for 25 % of all cancers.(1) The incidence rates of breast cancer have been increasing almost in all countries to reach more than two million cases in 2018.(2) Vimentin (VIM), is a 57 KDa protein is one of the most widely expressed and highly conserved proteins of the type III intermediated filament protein family.(3) VIM plays a significant role in holding the organelles in the cytosol it has a flexible nature, allowing it to respond to mechanical stress and by interacting with other structural proteins, like microtubules, it makes the cell rigid and sturdy.(4) Oxyntomodulin (OXM) is a 44.499 KDa peptide hormone produced by the neuroendocrine cells of the ileum.(5) Oxyntomodulin characterized by, ability to interact with and modulate the gastric oxyntic gland.(6)*

Materials & Methods*: This is a cross sectional hospital based study. This study was carried out at the Oncology Center in Kirkuk City-Iraq from the1st of November 2019 to the end of May 2020. Forty-five women with breast cancer were considered as a study group. Forty-tow apparently healthy women without breast cancer and with a negative family history for the first and second degree relatives of breast cancer were consider as a control group. By using a sterile disposable syringe 5 mls of venous blood sample was drawn from each woman and was kept in a plain tube and allowed to clot at room temperature, then each sample was centrifuged at 3000 rpm to obtain serum. Serum of the patients and controls had assay for Vimentin and Oxyntomodulin by ELISA.*

Results*: The mean serum level of vimentin was significantly higher in women with breast cancer compared to control at a P value of 0.006, while the mean serum level of oxyntomodulin was lower in women with breast cancer as compared with the control group, this result was highly significant at a P value of 0.003. This study found that there was a negative correlation between S.OXM and S. VIM level in breast cancer women (r = -0.135).*

Conclusion*: This study reveals that there was a negative correlation between S.OXM and S. VIM level in breast cancer women r = -0.135.*

Key Wards: *Breast cancer**,** Vimentin, and Oxyntomodulin.*

[1] Kirkuk General Hospital, Ministry of Health, Iraq
[2] Clinical & Medical Biochemistry, Pediatrician, College of Medicine, University of Tikrit, Iraq
[3] Clinical & Medical Biochemistry, Pediatrician, College of Medicine, University of Tikrit, Iraq

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I. Introduction:

Breast cancer is the most common cancer worldwide and the leading cause of death among women in developing countries.[7] BC is a malignant tumor that starts in the ductal epithelial cells of the breast. A malignant tumor is a group of cancer cells that can grow into surrounding tissues or spread to distant areas of the body. Most breast cancers begin in the cells that line the ducts (ductal cancers). Some begin in the cells that line the lobules (lobular cancers), while a small number start in other tissues.[8] The incidence rates of breast cancer have been increasing almost in all countries to reach more than two million cases in 2018.[9]

Vimentin is comprised of 466 amino acids, with a highly conserved α-helical rod domain that is flanked by non-α-helical N-terminal head 77 residues and C-terminal tail 61 residues regions.[10] Vimentin is intermediate filament protein that is widely distributed in the cytoplasm of many cells. The expression of vimentin variants showing high sequence homology and similar expression in major tissues in organisms down to shark, indicates that vimentin has an evolutionary role.[11]

Oxyntomodulin (OXM) is a 37 amino acids peptide hormone produced by the neuroendocrine L-cells of the ileum.[12] No specific OXM receptor has been identified. OXM does activate the glucagon receptor, though less potently than native glucagon due to the octapeptide tail. The same tail allows OXM to activate the GLP-1 receptor, but also less potently than native GLP-1.[13] Additionally, the octapeptide tail slows clearance of OXM from the circulation when compared to glucagon.[14] OXM is produced by the action of proprotein convertase subtilisin/kexin type1(PCSK1) on the proglucagon peptide. OXM is co-secreted from the intestine with GLP-1 in response to nutrient intake. All current available obesity treatments – dietary, pharmacological and surgical – reduce food intake. However, the initial weight loss from the food intake reduction is associated with a fall in energy expenditure, which limits overall weight loss.[15]

II. Patients Materials & Methods:

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 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 1st of November 2019 to the end of May 2020. A verbal consent was taken from each women included in this study whether considered as a case or control. Forty-five women with breast cancer were considered as a study group, their ages were between 31 to 75 years, and they were from the center and periphery of Kirkuk City, while 42 apparently healthy women without breast cancer and with negative family history for the first and second degree relatives of breast cancer were consider as a control group, their ages were from 30 to 73 year.

By using a sterile disposable syringe, 5 mls of venous blood sample was drawn in a centrifuge tube from each women included in this study, and allowed to clot at room temperature, then the tubes were centrifuged at 3000 rpm and the supernatant serum was aspirated then divided into aliquots in eppendrof tubes and stored at ⁻20 ^{0}C until the time of estimation. Serum of the patients and controls had assay for

1. vimentin by ELISA.

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2. oxyntomodulin by ELISA.

III. Statistical analysis:

All the date collected in this study were analyzed by using the student t-test, the mean, standard deviation, and P-value was also considered. The significance was considered at a P value of less than 0.05. While the correlation was considered as follow:

Interpretation of R value (correlation coefficient)

- 0.70. A strong negative correlation.

- 0.50. A moderate negative correlation.

- 0.30. A weak negative correlation.

- 0.3<R <0.3: no correlation.

+ 0.30. A weak positive correlation.

+ 0.50. A moderate positive correlation.

+ 0.70. A strong positive correlation.

IV. Results:

The highest rate of breast cancer (40 %) was in women within the age group 41 - 50 years, followed by those within the age group of 51 - 60 years (20 %). The least rate of breast cancer (4.4%) was in women within the age group of more than 70 years, as see in the figure 1

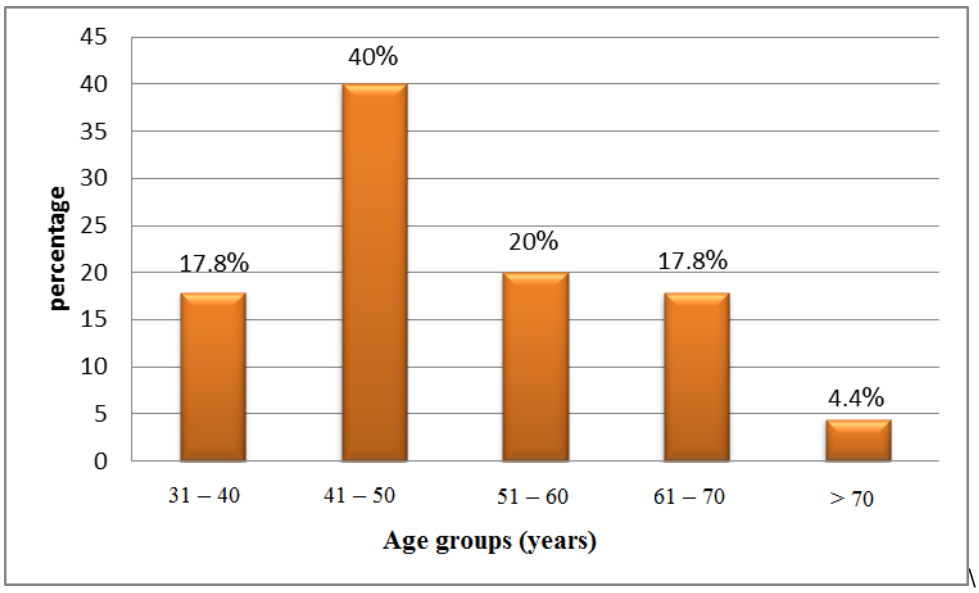

Figure (1): Relation of breast cancer with age.

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This study showed that maximum rate of breast cancer 71.1% in women was where from the urban area, while 28. 9% of breast cancer women were from the rural area, see figure (2).

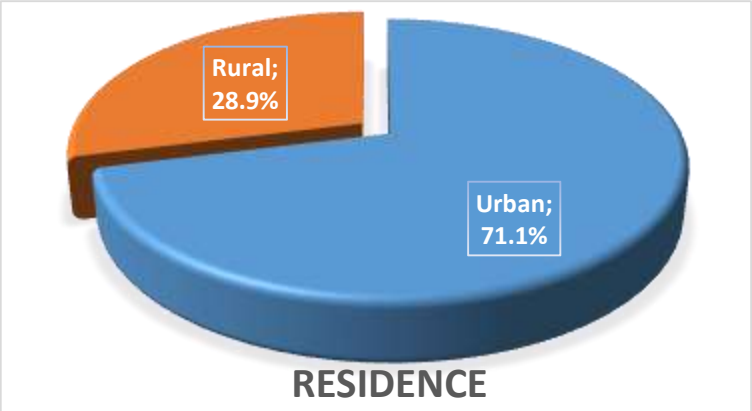

Figure (2): Distribution of breast cancer according to residence.

This study demonstrated that the BMI was significantly higher at a P value of 0.054 in women with breast cancer compared to control women 31.55 ± 4.04 versus 29.75 ± 5.09 Kg/m^2 respectively , as shown in table (1).

Table (1): The mean and standard deviation of BMI for women with breast cancer and the control group.

Study groups	**No.**	**BMI (Kg/m^2) Mean ± SD**	**T-Value**	**P-value**
Breast cancer women	45	31.55 ± 4.04	1.91	0.054*
Control	42	29.75 ± 5.09		

This present study reveals that the mean serum level of vimentin in breast cancer women 338.6 ± 61.9 ng/mL, was significantly higher than that of the control women 129.7 ± 33.9 ng/mL, as evident in the following table.

Table (2): Serum Level of Vimentin in breast cancer women and the control group**.**

Study groups	**No.**	**Vimentin level (ng/mL) Mean ± SD**	**T-value**	**P-value**
Breast cancer women	45	338.6 ± 61.9	19.70	0.006**

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Control	42	129.7 ± 33.9		

This study also shows that the mean serum level of oxyntomodulin in women with breast cancer 4.71 ± 1.51 ng/mL was significantly lower than that of the control 6.12 ± 2.64 ng/mL, as evident in the following table.

Table (3): Serum level of oxyntomodulin in breast cancer women and the control group.

Study groups	**No.**	**Oxyntomodulin level (ng/mL)Mean ± SD**	**T-value**	**P-value**
Breast cancer women	45	4.71 ± 1.51	-3.04	0.030*
Control	42	6.12 ± 2.64		

The present study showed that there was negative correlation between S.OXM and S. VIM level in breast cancer women (r = -0.135), as shown in flowing figure.

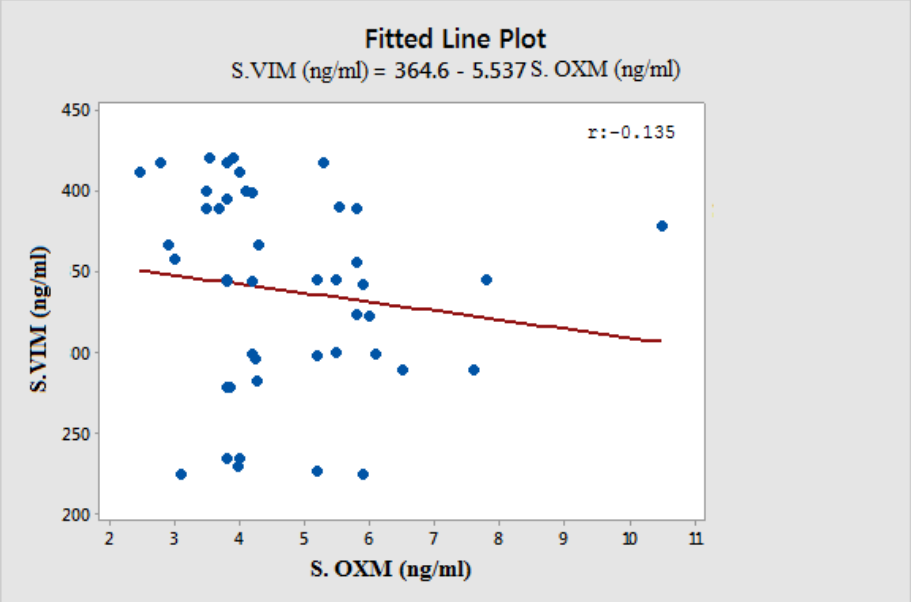

Figure (2): Correlation between S.OXM level and S. VIM level in B.C women.

V. Discussion:

This study reveals that, the highest rate of breast cancer in women was within the age group 41 - 50 years and the least was within the age group of more than 71 years. Numerous results obtained by other studies were focused on the age of women with breast cancer, e.g. the study that carried by Mishra S *et al*, [16] who found that the mean age of breast cancer women was 42.2 ± 10.41 years, while the study by Armstrong K [17] who found that the mean age was 50.4± 12.45 years.

This the study reveals that the majority of women with breast cancer were from the urban area while the minority were from rural area. This result was in agreement with Majid *et al*[18], that they found in their study that the urban exceeding the rural rate by 2:1,concerning the incidence of breast cancer in women. This finding could be attributed to the migration of some peoples in Iraq from the rural to the urban area in the last decades. Previous study found that malignant lesions of breast cancer were more common in rural areas as compared to urban.[19] This could be due to poor medical aid in rural areas, lower socioeconomic status, and illiteracy.[20] The result of this study does not agree with this study since that there were no migration of people in that country

In the present study it was found that there were an increase in the BMI of women with breast cancer more than that of the control women. BMI was significantly higher at a P value of 0.054 in women with breast cancer compared to control women, this finding was consistence with Platet N *et al* [21] and Rebbeck R. *et al* [22] who reported a high prevalence of overweight and obesity in women with breast cancer.

The mean serum concentration of VIM in breast cancer women was significantly higher than the control women, there were significant differences between the protein levels in the breast cancer women and the control women at a P value of 0.006. Similar findings were also observed by Arko-Boham, Benjamin, *et al*,[23] Earlier reports also suggest that there were elevated expression of the protein in breast cancer cells and tissues and also in several aggressive breast cancer cells.[24]

In this study the serum levels of oxyntomodulin were determined in sera of breast cancer women and apparently healthy control women. The mean serum concentration of the OXM in breast cancer women was significantly lower than the control women, there were significant differences between the hormone levels in the breast cancer women and the control at a P value of 0.03. Oxyntomodulin used to reduced body weight by reduces food intake, suppresses gastric emptying, and facilitates lipolysis with reduced side-effects, also shows excellent receptor-activating effects.[25] Thus, oxyntomodulin play an important role in both; the decrease of the chance of initiation of breast cancer since that obesity is one of risk factor for breast cancer, otherthing that may be used in future for treatment or in the control measures of breast cancer since that oxyntomodulin control the body weight and is one of the risk factors that prevent obesity.

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