

Determination of Some Biochemical Markers for Breast Cancer Women in Baghdad

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Abstract

The most important tumor that develops from breast tissue is breast cancer: signs may have , mass in the breast; variation in shape; skin dimpling; bloody discharge from the nipple. The present study was conducted to have a clearer integrative idea on the impact of expression of estrogen and progesterone receptor. In addition CA15-3, CA-125 in sera of women with breast cancer in baghdad is compared with a healthy normal population.

The paper studies two groups including 100 breast cancer women by using immunohistochemical analysis for evaluation of the Estrogen receptor (ER) and progesterone receptor (PR). Moreover, the sera of samples have been quantitatively measured for CA15-3, CA-125 by using ELISA method.

This study statistically showed increased level of CA-125 among the patients group (54.07 ± 7.19 U/ml) in comparison with healthy control group (8.57 ± 4.93 U/ml) with a highly significant increase between them ($p < 0.0001$). While CA15-3 in sera of patients groups revealed that there was a significant increased between its level of patients (17.28 ± 8.38 U/ml) in comparison with healthy control groups (11.45 ± 8.36 U/ml) ($P=0.001$). Analysis of data showed a trend toward increasing ER and PR expression with age. Especially in menopausal age between 47-57 years compared to other age groups.

The conclusion of this study indicated that ER &PR is overexpressed in breast cancer women especially in age between (47-57) years and elevated level of CA125 and CA15-3 in breast cancer women.

Keywords: estrogen receptor(ER), progesterone receptor(PR), ca125.ca15-3,immunohistochemistry (IHC).

تقدير بعض العلامات البايوكيميائية للنساء المصابات بسرطان الثدي في بغداد

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المستخلص :

وضحت الدراسة تأثير ابراز او عرض مستقبل الاستروجين ومستقبل البروجسترون لدى النساء المصابات بسرطان الثدي في بغداد مقارنة بالأصحاء. حددت مجموعتي الدراسة والتي تتضمن (١٠٠) عينة لنساء مصابات بسرطان الثدي تم استخدام اختبار المناعي النسيجي الكيماوي IHC في تقييم مستوى مستقبل الاستروجين والبروجسترون في الخلايا النسيجية المسرطنة . فضلا عن ذلك فقد اختبر مصل المرضى للتحري عن مستوى الضد الجيني السرطاني (١٢٥) بطريقة مقياس المر المناعي للانزيم المرتبط ELISA .

كشفت التحليل الاحصائي ارتفاع في مستوى الضد الجيني السرطاني (١٢٥) في مصل النساء المصابات بسرطان الثدي (54.07 ± 7.19) مقارنة بمصل الاصحاء (8.57 ± 4.93) وبفارق احصائي عالي المعنوية ($p < 0.0001$) بينما بين مستوى الضد الجيني السرطاني (١٥-٣) ارتفاعاً طفيفاً في مصل المصابات بسرطان الثدي (17.12 ± 8.38) مقارنةً بالنساء غير المصابات (11.45 ± 8.36) وبفارق احصائي معنوي ($P=0.001$) وكذلك بين التحليل احصائيا عن ارتباط مهم بين زيادة عرض او ابراز مستقبل الاستروجين وبروجسترون وعمر النساء المصابات بسرطان الثدي بدون فارق احصائي يذكر . خصوصا في عمر انقطاع الطمث (٤٧-٥٧) سنة مقارنةً بالأعمار الاخرى .

بينت هذه الدراسة اهمية ابراز مستقبل البروجسترون ومستقبل الاستروجين لدى النساء المصابات بسرطان الثدي وخصوصا في الاعمار (٤٧-٥٧) وارتباطه المهم بارتفاع مستوى الضد الجيني السرطاني (١٢٥) وال ضد الجيني السرطاني (١٥-٣) لدى النساء المصابات بسرطان الثدي.

Introduction

Breast cancer is cancer that grows from breast tissue. Malignant mammary tumor was carcinomas: type of tumor that start in cell ,that mark organ and tissue similar to the breast,which start in glandular tissues [1]. Other types of malignancy can occur in breast similar sarcomas, start in the cells of muscle; fat or connective tissues. The universal importance of cancer were irrefutably, considered the 2nd cause of death worldwide, as risk factor results of elevating exposure in life expectancy create different cancer elevated both in advanced and in developing countries [2]. Over 1,300,000 cases and 450,000 deaths each year worldwide from are caused breast cancer [3].The greatest breast masses are not malignant , they are not dangerous in effect (benign). Benign breast masses are unusual growths, but then they do not disseminate outside the breast and they are not life threatening,. Nevertheless, some benign breast lumps are able to increase a woman's risk of developing breast cancer. It affects 1/9 of women, which include variable in breast such as lump, thicken, dimpling or alteration on the nipple. Personal history of breast cancer creates women high risk at the age above 50 years old, nulliparous and obese. A monthly self-check was suggested for all women and base line mammogram was recommended for all females between the ages of 35 and 40years with a follow mammogram every 1 or 2 years. Therapy usually included surgical resection, irradiation, endocrine or chemotherapy therapy [4].

Tumor markers(TM) are molecules arising in tissue or blood that are secreted by a tumor or by the host in response to the tumor whose measurement or identification is beneficial for clinical diagnosis or patient managing. TM can be used for showing a high risk population for tumor, creating prognosis and diagnosis in specific tumor and checking the course of

treatment for patient to reduction or getting surgery, radiation, or chemotherapy. The ideal marker would be blood test for tumor in which positive end result would arise only in patient with the malignancy, one that would correlate with stages and responses to drugs and that could be simply and reproducibly measure[2].

A Cancer antigen 15-3 (CA 15-3) is murine monoclonal antibody made by normal breast cell (molecular weight: 300–450 kDa). In numerous patients with cancerous breast cancer, there is an elevated creation and molting of CA 15-3 by the cancer cells. As it passes in the blood stream, is determined in blood makes it beneficial as a tumor marker to monitor the course of the tumor. In well subjects the upper limit of CA 15-3 is 25 U/ml. CA15-3 may be elevated in person with other tumors, illnesses, or conditions ,such as lung tumor colorectal tumor, cirrhosis, hepatitis, and benign breast disease [5].

A Carbohydrate antigen 125 (CA125) is carbohydrate-related to high molecular mass glycoproteins (molecular weight: >200 kDa) found in 80 % of non-mucinous ovarian carcinomas. It is distinct by a monoclonal antibody (OC125) that is produced by vaccinating laboratory mice with cell line recognized from human ovarian carcinoma. In healthy individual the upper concentration of CA125 is 35 U/ml. The CA125 is increased in additional cancers including breast, lung, endometrial, colon and pancreas and in menstruation, endometriosis, pregnancy and gynecologic and non-gynecologic condition [2].Further tumor marker possibilities exist for use in estimating breast tumor than for most other cancers. Serum markers include CEA, CA125, 3CM, CA549, CA15-3, MCA, CK-BB and Ferritin. Tissue can be examined for estrogen and progesterone receptor, cathepsin D, epidermal growth factor receptor (HEGR-2) , and collagenase [1]. Estrogen receptor (ER) and progesterone receptor (PR; also

called PgR) may be found in breast cancer cells. tumor cells with these receptors depend on estrogen and correlated hormones, such as progesterone, to develop. Estrogen and progesterone affect many endocrine function in women, like breast growth .If breast tumor cells have ER, the tumor is called ER-positive breast cancer. If breast cancer cells have PR, the cancer is called PR-positive breast cancer. If the cells do not consume either of these two receptors, the cancer is called ER/PR-negative. About two-thirds of breast tumors are ER and/or PR positive[6,7,8]. Although this improbability, the American Society of Clinical Oncology and the College of American Pathologists recommend testing for both ER and PR on all recently detected cases of invasive breast tumor [5].

Analysis for ER and PR was made to discover out if a tumor is likely to be effectively treated by endocrine therapy that ends these hormone from assisting. Examples of endocrine therapy used for metastatic breast tumor include the following: Aromatase inhibitor [9]. Selection of therapy is influenced by the effects of these assay. Multiple markers can be used at the time of analysis to assiste in prognosis. There is today a 90% survival percentage for this disease, if the tumor has not yet invaded adjacent tissues and lymph node the survival percentage approaches 100% [10].

Material and methods

The study comprised one hundred Iraqi women patients with breast cancer visiting hospital of tumors in Baghdad city for diagnosis and treatment. The diagnosis was made by the consultant medical staff, and it was based on clinical examination and laboratory evaluation.

Hundrad breast cancer women were included in this study to estimation of CA125, CA15-3, ER and PR. In addition to forty apparently healthy control group (non-cancerous

women). 5ml of venous blood samples have been collected from each patients and control groups for serological examination by enzymatic method (ELISA) for quantitative determination of CA125, CA15-3 . Tissue biopsy was taken from breast cancer women to express the estrogen and progesterone receptor by immunohistochemistry assay. The age group were range between (25-68) years.

Statistical analysis

The SPSS version 18.0 was used for the statistical analysis, one- way ANOVA test was used in this study for serum CA 125& CA15-3, while chi-square test was used for immunohistochemistry changes. Statistically a P-value of ≤ 0.05 was considered as significant.

Results:

Figure (1) shows the positive estrogen receptor (ER) and positive progesterone receptor (PR) of patients with breast cancer tissue by immunohistochemistry technique (IHC).

Figure(1): Estrogen Receptor (ER) Testing using IHC (brown). Progesterone Receptor (PR) Testing using IHC (brown).

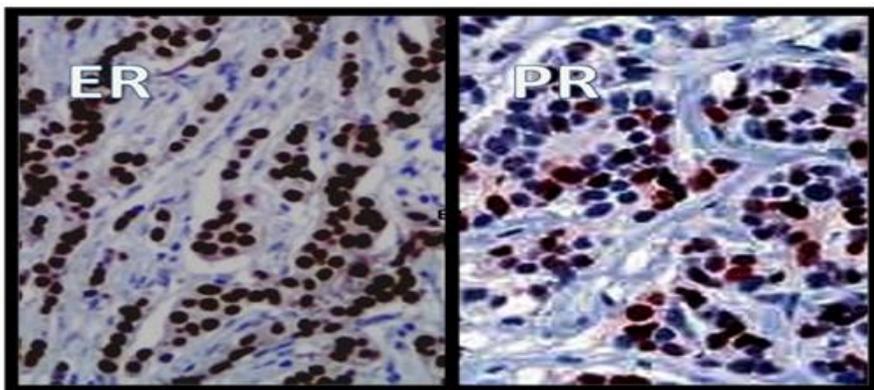


Table (1) showed a trend toward positive increasing ER and PR expression(26%) with young women especially at age between (47-57)years .The average age of menopause was between 47-57 years of age. One important aspect of the role of pathology in the evaluation of breast cancer was biomarker testing, specially the accurate assessment of the estrogen receptor (ER),and progesterone receptor (PR).

Table (1). Distribution of patients group according to age group and percentage of progesterone /estrogen receptor .

Age of studied groups/ years		Progesterone receptor				Estrogen receptor			
		+1	+2	+3	-ve	+1	+2	+3	-ve
25-35	Count	6	2	4	4	0	4	2	10
	% of Total	6.0%	2.0%	4.0%	4.0%	0.0%	4.0%	2.0%	10.0%
36-46	Count	6	6	12	8	0	6	10	16
	% of Total	6.0%	6.0%	12.0%	8.0%	0.0%	6.0%	10.0%	16.0%
47-57	Count	6	12	8	10	8	12	6	10
	% of Total	6.0%	12.0%	8.0%	10.0%	8.0%	12.0%	6.0%	10.0%
58-68	Count	0	2	4	10	2	4	0	10
	% of Total	0.0%	2.0%	4.0%	10.0%	2.0%	4.0%	0.0%	10.0%

Table (2) shows that the concentration of CA15-3 is significantly ($P=0.0001$) increased in patients groups (17.12 ± 8.38 U/ml) in comparison with healthy control groups

(11.45±8.36 U/ml), on other hand the level of CA125 was highly increased in patients groups (54.07±7.19U/ml) when compared with healthy control groups(8.57± 4.93U/ml).

Table (2) Estimation level of CA15-3, CA125 in patients with breast cancer women and healthy control.

studied groups		N	Mean	Std. Deviation	t-test for quality of means	
					Sig (2- tailed)	C.S
CA15-3 U/ml	Patient	100	17.12	8.38	.000	S
	healthy group	40	11.45	8.36	.001	S
CA125 U/ml	Patient	100	54.07	7.19	.000	HS
	healthy group	40	8.57	4.93	.000	HS

Discussion

The present study shows over expression of estrogen/progesterone receptor (ER/PR) positivity in women especially at age (47-57) years because the average age of menopause was between 47-57 years .Declining levels of the natural hormones estrogen and progesterone in a woman's body during and after the completion of menopause at this time lead to increased releasing of estrogen and progesterone receptor and epidemiologic studies suggest that ovarian hormones contribute to the development of breast cancer at all stages.Early menopause and premenopausal reduce the risk while postmenopausal and menopausal estrogen replacement therapy increases the risk[11] as shown in table (1) so the

result is in agreement with a study in Iran[12] from 2007 to 2011 in Shahid Beheshti Hospital which showed the mean age of the patients was 40.2 ± 2.3 (ranged 19-82 years). Other study showed increasing ER and PR expression with rising age [13].

The level of CA15-3 and CA 125 is significantly increased in breast cancer women due to increased secretion of carbohydrate antigen(CA 125) and cancer antigen (CA15-3) in the blood stream from cancer cell , which is beneficial as a tumor marker to monitor the course of the tumor. This result is in agreement with a study in Norwegian[14] Radium Hospital(2001) which examined 221 breast cancer women and showed elevated level of CA125 tumor marker. It also agrees with other and the study in Canada 2010 [15] elevation of CA 15-3, and/or CA 125 was documented in the majority of patients with metastatic breast cancer with CA 15-3 occurring most commonly. And it is in agreement a with study in India [16].

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