Study the correlation between hormonal receptors in Iraqi patient women with Breast Cancer

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Abstract

   Breast Cancer is one of common types of cancer in the world and is considered one of the causes of death among Iraqi women . The discovery of the hormone receptors (estrogen and progesterone) a significant impact in the selection of patients for treatment and expected to live after period and to the possibility of recurrence treatment again is because the relationship between tumor grade and the percentage of representation of hormone receptors on the surface cells . The research based on measuring the proportion of ER and PR in tissue and blood serum and note relationship between the level of receptors and the clinical situation in Iraqi women with breast cancer . The study has been started from May 2014 to December 2014 in the Educational Tumor Hospital were selected infected women in the age group (28-68) years as measured by the proportion of their ER and PR in tissue and serum .The results showed that the proportion of women with a family history of patients is 62.5% and that the patients whose ratio to have a tumor of the second degree is 76.7% and the third degree was 13.3% and that the first degree ratio is 10% and that there is no significant difference in the measurement of the percentage ER and PR in ELISA technique and Immunohistochemistry . Sensitivity and Specifity of Immunohistochemistry study is better than ELISA technique because the value of IHC sensitivity and specifity for ER and PR are 70%(1.0)ng/ml and 69%(1.0)ng/ml respectively while in ELISA technique are 38%(0.9)ng/ml and 20%(0.95)ng/ml respectively .
Keywords: Breast Cancer, Estrogen receptors , Progesterone receptors .

Introduction :

   Breast Cancer is the most common cancer in women . Worldwide , more than one million women are affected by this disease every year . In Iraq it constituted 19.59% total cancer cases and alone is accounted for 31% of all new cancer cases among females in Iraq (AL-Khafaji and *etal* 2014). It is now firmly believed that breast cancer commonly starts in the epithelium which lines the terminal ductules within the lobule . Physiologically , the human female breast is under the primary control of different hormones like sex steroid hormones which play a significant role in the physiology of the human breast (Hana 2010; Saeed and Majeed 2011) . Number of tumor associated with hormones and its receptors which has been evaluated for monitoring or detecting breast cancer . Estrogen and Progesterone receptors have been found in normal and malignant tissue (AL-Atrooshi 2014 ; AL-Siagh and *etal* 2012) . Estrogen and Progesterone and them receptors play an important roles in the risk factors for breast cancer (Hayashi and *etal* 2003 ; Lim and *etal* 2014) .The estrogen and progesterone receptors belong to a super-family of nuclear hormone receptors . These receptor proteins function as transcription factors when they are bound to their respective ligands ; these receptors share a common structural and functional organization (AL-Atrooshi 2014) .
Aim of the study :
Our study can be categorized into these point:
(1)Evaluation of IHC markers (ER,PR and Her-2/neu) in Iraqi breast cancer women.
(2)Estimation of serum ER and PR by ELISA kit .
(3)Clinicopathological finding correlated between hormone receptors and Estimation the sensitivity and specifity of IHC and ELISA .

Patients and Methods :
Patient:
   From May 2014 to December 2014 , 64 patients were newly diagnosed as breast cancer with chemotherapy treatment were included in this study . The patients were diagnosed at Educational Tumor Hospital . Blood samples were collected from the 64 patients to estimate ER and PR . The main data and parameter include in our study : patient's age, family history of breast cancer and another cancer, and pattern of menstrual cycle.

Control :
  Twenty patients (women) diagnosed as having breast cancer were also included in this study as a control group .

Samples Collection :
Blood Sampling :
  Three to five ml of blood was collected from 64 patients and from twenty control individuals . Blood samples were drawn from cubital vein . Blood samples were centrifuged at 3000 rpm for 2-5 minutes then serum was separated and stored immediately . Specimen held for longer time by frozen at **-20°C** prior to assay .

Methods:
Immunohistochemistry for ER ,PR and Her-2/neu :
  The Data of Immunohistochemistry for ER ,PR and Her-2/neu were obtained from patient's reports .

Estimation of serum ER and PR (Biochemical) :
   Serum level of ER and PR were determined by Elabscience ELISA kit is an in vitro enzyme linked immunosorbent assay for quantitative measurment .

Statistical analysis :
  Database was examined for errors by using Statistical Analysis System Programe – SAS (2012) in statistical analysis to study Clinicopathological analysis in breast cancer patients , and correlation between clinicopathological assessment and IHC tumor markers ER and PR , and correlation between sensitivity and specifity by IHC and ELISA in 64 patients with breast cancer (SAS 2012) .

Results and Discussion :
Clinicopathological analysis :
  Total group studied was in the age category of (28-68) years accounting for 64 patients . In this study table (1) show 63% of patients had apositive family history weather 77% it is second degree and 43% positive HER2 that agree with Numerous studies which suggest a strong link between the female hormone and the development of breast cancer (AL-Khafaji and *etal* 2014).

Table (1) : Clinicopathological analysis in breast cancer patients

Clinicopathological analysis		
Age group/year(female)	Number	Percentage
<=45	37	57.8
>=45	27	42.2
Family history	Number	Percentage
None	24	37.5
Positive	40	62.5
Total	64	100.0
T	Number	Percentage
1.00	17	26.6
2.00	40	62.5
3.00	3	4.7
4.00	4	6.3
Total	64	100.0
N	Number	Percentage
0.00	1	1.6
1.00	18	28.1
2.00	37	57.8
3.00	7	10.9
4.00	1	1.6
Total	64	100.0
Grade	Number	Percentage
1.00	6	10.0
2.00	46	76.7
3.00	8	13.3
Total	60	100.0
HER2	Number	Percentage
-ve	20	34.5
+	12	20.7
++	1	1.7
+++	25	43.1
Total	58	100.0

Correlation between immunohistochemical Analysis and ELISA ER and PR :

Table (2) show the value of ER ELISA was P<0.05 while PR ELISA was non significant and both ER IHC and PR IHC were non significant so this the first study to investigate the role of ER and PR on the risk of breast cancer in Iraqi postmonopausal women which agree with Lim and *etal* 2014 .

Table (2) : Correlation between clinicopathological assessment and IHCtumor markers ER and PR

Clinico-pathological analysis			
Age at diagnosis	Number	Mean+Std.D.	P-Value
patient	64	45.2969+1.2075	P<0.01
control	20	37.4500+1.5735	P<0.01
ER ELISA	Number	Mean+Std.D.	P-Value
patient	64	0.5397+0.0772	P<0.05
control	20	0.2100+0.0478	P<0.05
PR ELISA	Number	Mean+Std.D.	P-Value
patient	64	0.5175+0.0760	NS
control	20	0.2960+0.06647	NS
ER IHC	Number	Mean+Std.D.	P-Value
-ve	17	0.4165+0.1113	NS
+	21	0.6590+0.1880	NS
++	8	0.5125+0.1402	NS
+++	11	0.5218+0.1548	NS
Total	57	0.5396+0.0840	NS
PR IHC	Number	Mean+Std.D.	P-Value
-ve	19	0.4568+0.1134	NS
+	25	0.6680+0.1550	NS
++	4	0.3175+0.1627	NS
+++	13	0.4538+0.1380	NS
Total	61	0.5336+0.0791	NS

Correlation between sensitivity and specifity by IHC and ELISA :

Table (3) show that the sensitivity of ER IHC and PR IHC were 70% and 69% respectively while the sensitivity of ER ELISA and PR ELISA were 38% and 20% respectively and the specifity of both ER IHC and PR IHC were 1.00 ng/ml and the specifity of ER ELISA was 0.90 ng/ml while PR ELISA was 0.95 ng/ml . Our results show the IHC technique was better than ELISA. And the ER cutoff was 0.6912 ng/ml while PR cutoff was 0.89056 ng/ml which disagreement with Sun and *etal* 2001.

Table (3) : Correlation between sensitivity and specifity by IHC and ELISA in 64 patients with breast cancer

Parameters	ER IHC	PR IHC	ER ELISA	PR ELISA
sensitivity	70%	69%	38%	20%
Specifity ng/ml	1.00	1.00	0.90	0.95

References :
(1)AL-Atrooshi,S.A.M. (2014) .Immunohistochemical Expression of Estrogen and Progesterone Receptors in human colorectal carcinoma (clinicopathological study) .J.Fac.Med.Baghdad,Vol.56,No.3,pp:296-300.
(2)AL-Khafaji ,A.H.; Fadhil,A.M.A. ; and Hameed,M.A. (2014) .Immunohistochemical study of Estrogen , Progesterone Receptor and Her-2neu Oncogene with Her-2neu Biomarker Estimation by ELISA Technique in Primary Breast Cancer before Chemical Therapy . Iraqi Journal of Science , Vol.55, No.1,pp:132-144.
(3)AL-Siagh,T.H.T. ; AL-Bayati, S.A. ; and Ahmed,F.A. (2012). Evaluation of CA15-3,Her-2/neu and estrogen/progesterone status in breast cancer patients treatedby surgical removal and chemotherapy. Iraqi J.Pharm.,Vol.12,No.1,pp:1-7.
(4)Hana,D.B. (2010) . Association of Interleukin 6 with positive Immunohistochemical staining of Estrogen Receptor in Breast Cancer Pattients . AJPS, Vol.7, No.1,pp:106-114.
(5)Hayashi,S.I.; Eguchi,H.;Tanimoto,K.;Yoshida,T.; Omoto,Y.;Inoue,A.;Yosida,N.;and Yamaguchi,Y. (2003).The expression and function of estrogen receptor α andβ inhuman breast cancerand its clinical application. Endocrine-Related Cancer, Vol.(10),pp:193-202.

(6)Lim,V.W.;Li,J.;Gong,Y.;Jin,A.Yuan,J.M.;Young,E.L.;and Koh,W.P.(2014). Serum estrogen receptor bioactivity and breast cancer risk among postmenopausal women . Endocr. Relat Cancer , Vol.21, No.2, pp:263-273.

(7)Saeed ,A.S. and Majeed,A.H. (2011) . Immunohistochemical analysis of estrogen and progesterone receptors expression in gingival lesions. J.Bagh.College Dentistry,Vol.23(1),pp:34-38.

(8)SAS.(2012).Statistical Analysis System , User's Guide.Statistical Version 9.1[th]ed.SAS.Ins.,Inc.Cary.N.C.USA.

(9)Sun,C.F.;Wu,T.L.;Tsoo,K.C.;and Wu,J.T.(2001).Development of two ELISA for estrogen and progesterone receptor with sufficient sensitivity for fine needle aspirate and core biopsy.J.Clin.Lab.Anal., 15(3):pp:138-143.

دراسة علاقة الارتباط مابين المستقبلات الهرمونية في المريضات العراقيات المصابات بمرض سرطان الثدي

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الخلاصة

سرطان الثدي يعتبر أحد انواع السرطان شيوعاً في العالم كما يعتبر احد اهم اسباب الوفاة بين النساء العراقيات . إن لاكتشاف مستقبلات الهرمونات (الاستروجين والبروجستيرون) أثر كبير في اختيار المريضات للعلاج وتوقع فترة العيش بعد العلاج والى امكانية رجوع الورم مرة أخرى ويعود سبب ذلك الى العلاقة بين درجة الورم ونسبة تمثيل مستقبلات الهرمونات على سطح الخلايا . يقوم البحث على اساس قياس نسبة في النسيج ومصل الدم وملاحظة العلاقة بين مستوى المستقبلات والحالة الاكلينيكية في النساء العراقيات المصابات بسرطان الثدي . ER و PR تم بدأ الدراسة من مايس 2014 الى كانون الاول 2014 في مستشفى الاورام التعليمي وتم اختيار المصابات من الفئة العمرية (28-68) سنة في النسيج ومصل الدم وأظهرت النتائج ان نسبة اللواتي لديهن تاريخ عائلي مرضي هي 62,5% وان نسبة ER و PRحيث قيست لهن نسبة المريضات اللواتي لديهن الورم من الدرجة الثانية هي 76,7% اما الدرجة الثالثة فكانت بنسبة 13,3% وان نسبة الدرجة الاولى هي 10% في تقنية الاليزا والدراسة النسيجية المناعية وان حساسية وخصوصية الدراسة ER و PRوان ليس هنالك فروق معنوية في قياس نسبة للدراسة النسيجية هي 70% (1,0) نغم/مل و 69% ER و PRالنسيجية المناعية هي افضل من تقنية الاليزا حيث كانت حساسية وخصوصية (1,0) نغم/مل على التوالي اما في تقنية الاليزا فهي 38% (0,9) نغم/مل و 30% (0,95) نغم/مل على التوالي .

الكلمات المفتاحية : سرطان الثدي , مستقبلات الاستروجين , مستقبلات البروجيستيرون .