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Hormone receptor status and family history in female breast cancer

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***Abstract*---**The objectives for this study are to find the relationship between; breast cancer with hormone receptors, family history with breast cancer and family history with hormone receptors. A prospective data are collected from 251 mastectomies female patients due to breast cancer. The data analyzed regarding the age, weight of patient , family history for Ca breast , parity of the patient , site, size of tumor and hormone receptor status. the total patients with breast cancer 5.57% of them are from young age group(20-29years) and 21.51% of them are from premenopausal age group (30-50 years). ER is positive in 20.23% of the total patients, HER2 is positive in 22.0% of the total patients, and 29. 88% of them are positive to PR .The percentage of patients whom were negative to all receptors was very high (48.60 %).The percentage of patients with positive family history of Ca breast is 22.70%, while 50% of the young age group have positive family history.

***Keywords*---**breast cancer, family history, hormone receptor status.

Introduction

Breast cancer is the first forms of cancer affecting women. Breast cancer is the commonest malignancy of females all over the world. and the second leading cause of death due to malignancy among females. There is a variation in its incidence among multicultural populations, which suggests the etiologic factors differ in their biological expression and impact on the disease outcome. The prognosis and management of breast cancer is influenced by classic variables as the histological type, grade and stage, status of estrogen receptor

(ER) ,and progesterone receptor (PR) and more recently, human epidermal growth factor receptor 2, (H E R 2/neu) status [1].The patient who show hormone receptor positive have a lower risk of mortality and have survival advantage by treatment with hormonal therapy and by chemotherapy

The Hormen Estrogen is necessary for the development of the ductal system, and progesterone is responsible for lobular development. Therefore, the etiology of breast cancer has a strong hormonal component. HER2 is a key contributor to normal cell growth and differentiation..[2] However, when over expressed , it is associated with neoplastic transformation of cells. Approximately 15% to 20% of breast cancers show HER2 overexpression by immunohistochemistry (IHC).and/or amplification of the HER2 gene . HER2-positive malignancies have a significantly more aggressive course and lead to a worse clinical outcome,, including shortened overall survival (OS), compared with those that do not overexpress HER2.[3]

Invasive or infiltrating duct carcinoma (IDC), was the commonest form of breast cancer accounting for 84 to 90% of all cases. These phenomena signify the important role of estrogen in the development of breast cancer [4].Estrogen and progesterone hormone help regulate growth and differentiation of normal breast tissue, and they are considered important in the development and progression of breast cancer *[5].* Estrogen receptor (ER) and progesterone, and affect hormone-dependent organs [6] . Determination of estrogen receptor (ER) status of invasive e receptor (PR) are nuclear receptors; estrogen and progesterone bind specifically to these receptors breast carcinoma is useful as a prognostic and predictive factor and has become standard practice in the management of this neoplasm., ER positivity predicts for response to endocrine therapy, such as antiestrogen (tamoxifen) administration or ovarian suppression.

Similarly, human epidermal growth factor receptor 2/herceptin (HER2) positivity is useful for selecting targeted therapy with monoclonal antibody, (trastuzumab) against HER2 [7] .Recently microarray profiling of invasive breast carcinoma has identified 5 distinct subtypes of morphologically ,similar breast cancers (luminal A, luminal B, normal breast-like, HER2-overexpressing, and basal-like).[8] The basal-like subtype,, accounting for about 15% of breast cancer cases and characterized by negativity for HER2, ER and PR associated with aggressive histology, poor prognosis, and unresponsiveness to the usual endocrine drug therapies, shorter survival and BRCA1- -related breast cancer.[9–10-_11].

The basal-like are HER2-ve , ER-ve and PR-ve, they are sometimes called triple negative so it should be noted that only about85% of triple negative phenotypic breast cancers are deemed to be basal-like, when tested by appropriate Immunohistochemical study.[10,12]

Patients and methods part

The study were prospective method of 251 mastectomies female patients attended AL Sader medical city-Najaf from January 2009 to December 2011due to breast cancer .The specimen sent for histopathology and hormonal receptor status study . A data analysis was done regarding the age of patient, menarche,

parity of the patient , family history for breast cancer , weight, smoking , site, size of tumor hormone receptor status, histological staging. In this study the patients were selected from twenty years to eighty two years old, then divided into four groups, a young age group (20-29years old) , premenopausal old group (30-50years old),postmenopausal age group (51-70years old) and old age group (71 and more). TNM staging was used in this study to classify the tumor. Results were compared using interactive chi square calculator, p-value <0.05 was regarded as significant .

Results part

Hormone receptor distribution among age groups

The hormone receptors that studied in this research were ER and PR and HER2 (Table 1) . There are eight groups of distribution for hormone receptors, from all hormonal receptor positive to all negative or mixed positive and negative. Most of our patients were negative for all hormone receptor (122 patients), and this accounted for 48.6% from the total, but the percentage of hormone receptor negative (HR –ve) is 50.0% from young age group (20-29years), 45.38% from premenopausal age group (30-50years) , 51.57% from postmenopausal age group (51-70years) and 55.33% from old age group (71-more) .

The number of all hormone receptors positive (HR+ve) patients are only 7 patients which form 2.78% from all patients , with peak percentage in premenopausal age group (30-50 years) which was 57.14% , then postmenopausal age group (51-70 years) which was 42% from all HR+ve .There was no patient have all HR+ve in young age group (20-29 years).

The percentage of patients which have ER+ve and PR +ve only (E+P+H-)was 9.16 % from all patients (23 patients), with peak percentage in premenopausal and postmenopausal age groups which was 47.8% for each of them. The percentage of patients which have only HER2 +ve (E-P-H+) was 17.30% from all patients (43 patients) and the peak percentage was in premenopausal age group which was 55.23% from this group .

Distribution of the positive hormone receptor among age group

ER+ve was common in postmenopausal age group (51-70 years) which was 24.21 % , while PR+ve is more common in premenopausal age group (30-50 years) which was 29.23 % . In other hand the HER2 +ve is more common in old age group (71 - more years) which was 33.33% , then premenopausal age group(30-50 years) which was 25.38% (Table 2). As whole the percentage of positive hormone receptor in this study is 20.23% for ER+ve , 29.88% for PR+ve and 22.70% for HER2 +ve.

Table 1 The distribution of hormone receptor among age groups

Age	Young age group (20-29 years)	Premenopausal age group (30-50 years)	Postmenopausal age group (51-70 years)	Old age group (71 - more years)	Total

Hormone receptors status	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%
E_P+H_	**2**	7.14%	19	67.86	7	25%	0	0%	28	100%
E+P_H+	0	0%	3	60.0	2	40.0	0	0%	5	100%
E+P+H+	0	0%	4	57,14	3	42.85	0	0%	7	100%
E+P+H_	1	4.3%	11	47.8	11	47.8	0	0%	23	100%
E+P_H_	0	0%	7	46.66	7	46.66	1	6.66	15	100%
E_P_H_	7	5.73	59	48.36	49	40.16	7	5.73	122	100%
E_P_H+	3	6.97	24	55.81	13	30.23	3	6.97	43	100%
E_P+H+	1	12.5	3	37.5	3	37.5	1	12.5	8	100%
Total	14	5.57	130	51.79	95	37.84	12	4.78	251	100%

Table 2 The relationship between the positive hormone receptor (E/ P/ HER2) and the age

Hormone receptors	ER +ve		PR +ve		HER2+ve	
Age group	No. of patients	%	No .of patients	%	No. of patients	%
20-29	1	7.14%	4	28.57%	3	21.42%
30-50	25	19.23%	38	29.23%	33	25.38%
51-70	23	24.21%	22	23.15%	17	17.89%
71-more	1	8.33%	1	8.33%	4	33.33%
Total	50	20.23%	65	29.88%	57	22.70%

P-value= 0.62

Distribution of family history of Ca breast among the patients age

Positive family history is more common in young age group (20-29 years) which was 50 %. Also there is a significant relation between family history and premenopausal age group(30-50 years) where 30.0% of this group have positive family history , but percentage is less in old age group(70 & more years)which was 8.33% only (Table 3).

Table 3 Relationship of breast Ca to family history

Age groups	F H +ve		F H -ve		Total	
	No. of patients	%	No. of patients	%	No. of patients	%
20-29	7	50%	7	50%	14	100%
30-50	39	30%	91	70%	130	100%
51-70	10	10.52	85	89.48	95	100%
71-more	1	8.33	11	91.67	12	100%
Total	57	22.70	194	77.30	251	100%

P=0.004

F H +ve = positive family history for breast cancer

F H –ve= no family history of breast cancer

Tumor stage among age group

The distribution of the tumor according to the stage of the disease and the age group . Most cases are in stage (III) 39% (98 patients) and stage (II) 37.45 % (94 patients), while stage (I) form 13.14% (33 patients), and stage(0) form 2.78% (7 patients)of the total cases. The stage (I) was most common in premenopausal age group 45.45 % of the total and form 36.36 % in postmenopausal age group (51-70 years), 12.12% in young age group (20-29 years) and 6.06% in old age group (71- more). The distribution of stage (II) according to age group was (54.25%),(35.10%), (6.38%),and (4.25%) from premenopausal age group (30-50years), postmenopausal age group (51-70years) , old age group (71-more years), young age group (20-29 years) respectively . The distribution of stage (III) was more common in premenopausal age patients group (30-50years) which was 52.04% from this group and the less of all groups was old age group (70-more) which was 4.08% . The distribution of stage (IV) was more common in premenopausal age group (30-50 years) which was 52.36%, then it was 42.10% from postmenopausal age group (51-70 years) , with no reported case from old age group(70-more years).

Relationship between family history and hormone receptor status

Table 4 shows the relationship between family history and hormone receptor status . It shows that 19.67 % (24 patients) from receptor negative group (E_,P_,HER2_) , 30. 23 % (13 patients) from (HER2+ve only)group , 26.67% (4 patients) from (ER+ve only)group and 25% (7 patients) from (PR+ve only) group have positive family history .

Table 4 Relationship between HR status and family history

H R status	Family History				Total	
	Positive history		Negative history			
	No. of the patients	%	No. of the patients	%	No. of the patients	%
E_P_H_	24	19.67	98	80.32	122	100%
E_P_ H+	13	30.23	30	69.76	43	100%
E_ P+ H+	2	25.0	6	75.0	8	100%
E+P_H_	4	26.67	11	73.33	15	100%
E+P+H_	3	13.04	20	86.96	23	100%
E+P_H+	3	60.0	2	40.0	5	100%
E_P+H_	7	25.0	21	75.0	28	100%
E+P+H+	1	14.28	6	85.72	7	100%
Total	57	22.7	194	77,3	251	100%

P-value =0.055

Hormone receptors and the tumor stags

Table 5 shows the percentages of HR among the stage of the tumor. HR was negative in 2.45% of stage (0) , 15.57% of stage (I), 41.80% of stage (II) , 33,60% of stage (III) and 6.55% of stage (IV) . HR was positive in 28.57% of stage (I), 28.57% of stage (II), 28.57% of stage(III) and 14,28% of stage (IV) ,with no

reported case have HR positive in stage (0). The peak percentage of stage (0) was 6.66% in the (E+P_H_)group , while the peak percentage of stage (I) was 28.57 in the (E+P+H+) group and stage (II) was 75.0% in the (E_P_H+) group and stage (III) was 80% in the(E+P_H+) group and stage (IV) was 14.28 in (E+P+H+)group .

Table 5 Relationship between hormone receptors and Ca stage

Hormone receptors	Stage 0		Stage I		Stage II		Stage III		Stage IV		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
E_ P_H_	3	2.45	19	15.57	51	41.80	41	33.60	8	6.55	122	100%
E_ P_H+	2	4.65	5	11.62	18	41.86	15	34.88	3	6.96	43	100
E_P_H+	0	0%	0	0%	6	75.0	2	25.0	0	0%	8	100
E+ P_H_	1	6.66	2	13.33	5	33.33	7	46.66	0	0%	15	100
E+P+H_	1	4.34	4	17.39	6	26.08	9	39.13	3	13.04	23	100
E+P_H+	0	0%	0	0%	1	20.0	4	80.0	0	0%	5	100
E_P+H_	0	0%	2	7.14	6	21.42	16	57.14	4	14.28	28	100
E+P+H+	0	0%	2	28.57	2	28.57	2	28,57	1	14.28	7	100
Total	7	2.78	34	13.54	95	37.84	96	38.24	19	7.56	251	100%

P-value = 0.055

Discussion

In our study, we found a high percentage (48.60 %) of hormone receptor negative patient , this was most clearly observed in young age group (20-29 years) and in premenopausal age group which was 50.0% in each group . our study differ from those of other similar studies from European and North American populations, compared to breast cancer cases reported in western parts of the world where the majority of cases were hormonal receptors positive. and the majority of cases in our study were hormonal receptors negative .But our study is consistent with the findings from(Desa Moonim) (2000)studies done in India [13], which also found a very high proportion of hormonal receptors negative cases.whil

Similar results are found from other countries in Asia (Pakistan) (Ahmad R,Shaikh H 1997) [14] , (China) (Chow LW 2000)[15] and Japan (Nomura Y,Tashira H 1984) [16] .One of the reasons for this observation has been younger age at presentation among Iraqi women and Indian women[13] , although this may not be the only responsible factor. Another factor that might be affecting this shift in proportion of cases is perhaps a reduced exposure to exogenous estrogens, such as hormone replacement therapy, and oral contraceptive pills, which leads to a higher occurrence of HR positive tumors when compared to HR negative tumors.[17].It is known from previous Indian studies (Huang WY) [18]. That breast cancer due to causes that act through mechanisms that are independent of hormonal exposures tends to be hormonal receptor negative [18].

Among genetic risk factors, BRCA1 tumors tend to be more likely HR negative than HR positive [19] . Another studies done in Pakistan shown that consanguinity is a risk factor for breast cancer because of the inheritance of

breast cancer susceptibility genes.(20). Liede et al.(2002) (21) found significant associations of consanguinity with early-onset breast cancer in the Pakistani population. (MacGrogan et al (1996)(22) showed that the presence of hormonal receptors, (ER and PR) were not associated with nodal status and so did we in our study . Some researchers speculate that breast tumors progress from hormonal receptors positive to hormonal receptors negative ,, (and from hormonal receptors negative to hormonal receptors positive) over time (23)

The percentage of patients whom have positive family history was low as 22.70% (57 patients), while whom have negative family history was high as 77.30% (194 patients). And that mean the positive family history was statistically insignificant in all carcinoma patients in our study, but still high in young age group (20-29 years) it was 50 % and about 31.48 % in (30-39 years)group . So there is significant relationship between positive family history and young age women whom affected by breast cancer. In our study the peak age incidence of breast cancer are (40-49) years which form 30.27% of total cases and the second group affected was middle age that form 21.51 % from the total , while in Malcolm M bilimoria study (23) it was above 50 years . So in Iraq the affected women by breast cancer are earlier (young and middle age) .

In our study the +ve family history of breast cancer seem to increase liability for hormonal receptors positive and hormonal receptors negative tumors similarly. The increased risk associated with a positive family history may reflect many different heritable factors, some of which affect risk for ER positive tumors and others for ER-negative tumors . Identification of families with multiple affected member whose tumors show concordant receptor expression may permit the elucidation of specific mechanisms that distinguish receptor-positive from receptor-negative cancers. elevations for both receptor categories.(21)

Early age at menarche, nulliparity, and late age at first full-term pregnancy may contribute to the development of PR+ve and ER+ve breast cancer as a result of increased exposure to estrogen and progesterone from the ovaries.(22-23). In our study we found a high percentage (35.0%)of women whom affected have early menarche and this my reflect a strong relationship between, early menarche and Ca breast , and this relation are more clear in young age women (20-29 year,) which was 50.0% of the total Ca breast , also there was no significant relationship between stage of the tumor and hormonal receptor status and also there was no significant relationship between the stag of the tumor and the age , however we found that stage (I) is more common in (20-29 years) group which form 28.58% .In our study , 37.45% (94 patients) and 39.04% (98 patients) of the total cases have been diagnosed when thy are in stage (II) and stage (III)respectively .

Conclusion

There is an obvious relationship between breast cancer in young age and family history, but this relationship is less clear and less significant on the elderly age group. There is no clear relationship between the positive hormonal receptors and family history among patients with breast cancer. The negative hormonal receptors is more common than positive hormonal receptors in these patients.

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