

The Relative Distribution Frequency of Hormonal Factors (Estrogen and Progesterone Receptors) In Patients with Breast Cancer Referred To Ahvaz Golestan Hospital during 2001-2011

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ABSTRACT

Breast cancer is one of the most common cancers among women. Estrogen and progesterone receptors status plays an important role in determining disease prognosis and choosing appropriate type of treatment for this disorder. Therefore, this study aimed to investigate the prevalence of estrogen and progesterone receptors in patients with breast cancer. This is a retrospective and descriptive study conducted on the medical records of 3593 patients with breast cancer referred to the radiotherapy and oncology department of Ahvaz Golestan Hospital during the years of 2001-2011. The relevant data were reviewed and information such as ER, PR, HER₂, age, gender and cancer grade were extracted for further evaluation. Among the 3593 cases, hormone receptor status was determined in 2019 cases that among these, 1331 patients (66%) had positive ER and 1209 (60%) had positive PR. Hormone receptors connection with age of menopause was like this way that the number of positive ER (in age of premenopausal) was 1110 patients (64%) and in ages after menopause was seen in 203 patients (76%), respectively. Positive PR before menopause was also in 1010 patients (56%) and after menopause was in 182 patients (68%) (P: 0.0001). In patients with grades 2 and 1 the positive ER frequency is more than grade 3 (72% in Grade 1 and 2 and 55% in grade 3) (P: 0.000) among all types of HER2, HER2 + 3 frequency was higher in the patients (43%). The Luminal A amount (PR + ER +, HER2-) was 23% and B Luminal (ER +, PR +, HER2 +) was 19% and Triple negative (- HER2, ER-PR-) was 10% of HER2 + (ER-PR-HER2 +) was 18 percent. The hormone receptors frequency in Khuzestan patients is similar to their frequency in Saudi Arabia and European countries and white Americans patients and is more than its frequency in India, African-American and Tanzania patients. Triple negative incidence form in Khuzestan patients is also less than the region countries (Saudi Arabia and India), and is similar to the European countries statistics (Germany and Italy).

Key words: Breast cancer , estrogen Receptor, progesterone receptor,

INTRODUCTION

Breast cancer is a major health problem for women around the world that is the most common cancer in women and the most common cause of death in the United States. In 2009, 27 percent of cancer cases and 15 percent of deaths from cancer was due to breast cancer. Also in Europe in 2006, breast cancer was the most

common form of cancer. According to provided statistics from Iran Bureau of cancers, in the year (2009-2008), among the 10 most common cancer in Iranian women, with 25 percent cases, was ranked first related to breast cancer. In Khuzestan province also breast cancer by 27 percent of cases is the most common form of cancer among the 10 most common cancers in this province¹⁻².

The survival rate of patients who are not treated is 2.7 years after diagnosis and in recent decades the survival rate of 5-years has increased approximately 15 percent due to the diagnosis and treatment of patients³. Mathematical models show that screening with mammography and adjuvant chemotherapy and tamoxifen were equally effective in this disease⁴. Industrialization in developing countries is associated with a rapid increase in breast cancer risk⁵.

Several factors are related to the increasing risk of breast cancer, such as: old age, family history, contact with female reproductive hormones (Endogenous and Exogenous), dietary factors, obesity, alcohol consumption, radiation treatment, benign breast disease, first pregnancy at older ages and related environmental factors. Many of these factors cause a mild to moderate increasing risk of breast cancer in women (7, 8, 6 and 1). Breast cancer has a prognostic factor Such as: tumor size, histologic grade, axillary lymph node status, histologic subtype, hormone receptor status, increased expression of HER₂ and P₅₃ and KI₆₇. Determination of prognostic and predictive factors is very important. Prognostic factor is associated with invasion risk and metastasis in the absence of a cure for patients and predictive factor is effective in determining the sensitivity or resistance to treatment. The best example of predictive factors, in the whole oncology is the presence and absence of estrogen receptors in breast cancer and response to anti-estrogen therapy (3). Many studies show that patients with hormone receptors have a higher survival. Tumors that have estrogen receptor and progesterone receptor, get great benefits from hormone therapy and those who only have one (estrogen receptor or progesterone receptor) also respond well. Two types of estrogen receptors (ER_α, ER_β) and two types of progesterone receptor (PR and B PR) is detected. In other words, these results showed that most patients who have not hormone receptor, responding to hormone therapy is very low in them⁹⁻¹⁵. Many breast cancers have direct connection with estrogen exposure and changes in estrogen receptors¹⁶. Tumors with estrogen and progesterone receptors are sensitive to hormonal therapy and respond to adjuvant hormonal treatment¹⁷. The HER₂ statue is also effective for the benefit of Antracyclin-based

chemotherapy⁵. Studies also show that by measuring the HER₂ in the patient's serum, before the appearance of a clear metastasis, it can be discovered¹⁸.

In a study by Kaul et al (2011), the hormone receptor status of the patients was investigated. 55 patients with breast cancer were studied that 34.5 % of patients were with estrogen receptor (ER) and 36.4% with the progesterone receptor (PR), respectively. According to this study the tumors, which have hormone receptors in this region are low¹⁹.

Several studies in the field of relation between breast cancer and biomarkers have investigated the relation between ER and PR with HER₂. The results of these studies have reported a significant correlation between them and others did not²⁰⁻²².

Breast cancer is one of the most common cancers among women worldwide including in the Khuzestan province (Iran). Estrogen and progesterone receptors status plays an important role in determining disease prognosis and choosing appropriate type of treatment for this disorder. Therefore, this study aimed to investigate the prevalence of estrogen and progesterone receptors in patients with breast cancer referred to the radiotherapy and oncology department of Ahvaz Golestan Hospital during the years of 2001-2011.

MATERIALS AND METHODS

This is a descriptive and retrospective epidemiological study based on hospital information and patient records respectively. The sample of the study has been all patients with breast cancer since the beginning of 2001 until the end of 2011 that were referred to the Radiotherapy and Oncology section of Ahvaz Golestan Hospital and included 3593 cases. Intended information such as ER and PR factors, age, gender, grading and HER₂ factor was extracted and used based on available checklists. Used items, including ER and PR and HER₂ and Grading tumor as well as the age and gender were extracted from the patients' files, then the results were analyzed by using SPSS statistical software, version 17 and chi Manthle Hansel square test.

RESULTS

In this study, 3593 patients' file was reviewed with breast cancer during the years of 2001 to 2011 that were referred to the department of radiotherapy and oncology of Ahvaz Golestan Hospital, of which 3515 were females (98%) and 78 patients (2%) were males. Among the 3593 cases which were under investigation, ER and PR statue in 2019 cases was clear that 1331 (66%) were ER+ and 688 patients (34 percent) were ER-. And 1209 (60%) were PR+ and 810 patients (40%) were PR- (Table 1).

In Table 2 different receptors statues and in Table 3 hormone receptor status is shown by the breakdown of age groups.

The Chi square test showed a significant relation between the frequency of hormone receptors and patients' age groups (P: 0.0001).

In addition, hormone receptor status was separately studied in men and women, by age breakdown (Tables 4 and 5).

The frequency of ER and PR in women, in

the age before and after menopause was reviewed and due to lack of termination age of menstruation in many cases, the definition of Age of menopause at NCCN was used in this field. Among these, 1726 patients (87%) were in the age before menopause, and 267 patients (13%) were in post-menopausal, respectively. In premenopausal, positive ER patients were 1110 (64%) and positive PR patients were 1010 (59%), respectively. In early postmenopausal, ER positive patients were 203 (76%) and positive PR patients were 182 (68%) (Tables 6 and 7).

The Chi square test showed a significant relation between the levels of ER and PR and pre/post- menopausal status (P: 0.0001). In addition, among the total 3593 cases, only 863 cases had clear grading of which 348 patients (40%) had grade 1 and 2, and 515 patients (60%) had grade 3.

Among of 348 patients with Grade 1 and 2, only in 205 cases the hormone receptor status was determined that 147 patients (72%) had positive ER and 58 patients (28%) had negative ER and also 135 patients (66%) had positive PR and 70 patients (34%) had negative PR. Among of 515 patients with grade 3, in 356 cases, hormone

Table 1: Prevalence of hormone receptors

ER+	ER-	PR+	PR-
1331	688	1209	810
-66%	-34%	-60%	-40%

Table 2: Frequency of different types of hormonal receptors

ER+PR+	ER+PR-	ER-PR+	ER-PR-
1190	141	19	669
-59%	-7%	-1%	-33%

Table 3: The frequency of hormone receptors versus the patient's age groups

Age Receptors	20-Oct	21 – 30	31 – 40	41 – 50	51 - 60	61 – 70	71 – 80	81 – 90
ER+PR+	2	30	241	432	296	131	54	4
	-0.10%	-1%	-12%	-21%	-15%	-6%	-3%	-0.10%
ER+PR-	0	70	20	50	42	15	7	0
		-0.30%	-1%	-2%	-2%	-1%	-0.30%	
ER-PR+	0	0	7	6	5	1	0	0
			-0.30%	-0.20%	-0.20%	-0.04%		
ER-PR-	0	48	161	228	165	48	19	0
		-2%	-8%	-11%	-8%	-2%	-1%	
Total	2	85	429	716	508	195	80	4
	-0.10%	-4%	-22%	-35%	-25%	-10%	-4%	-0.10%

receptor statue was known and 196 patients (55%) had positive ER and 190 patients (53%) had positive PR positive (Table 8).

The Chi square test showed a significant relation between the frequency of receptors and different grades of breast cancer (P: 0.0001).

Among of 3593 cases, the HER₂ statue was registered in 1543 cases and among their 662 patients (43%) were HER₂+3 and 216 patients (14%) were HER₂+2 and 110 patients (7%) were HER₂+1 and 555 patients (36%) were negative HER₂ (Table 9).

Table 4: The frequency of hormone receptors in men by age breakdown

Age Receptors	ER+PR+	ER+PR-	ER-PR+	ER-PR-	Total
10 – 20	0	0	0	0	0
21 – 30	1 -4%	0	0	1 -4%	2 -8%
31 – 40	2 -8%	0	0	2 -8%	4 -16%
41 – 50	4 -15%	1 -4%	0	0	5 -19%
51 – 60	2 -8%	0	0	1 -4%	3 -12%
61 – 70	3 -12%	0	0	4 -15%	7 -27%
71 – 80	4 -15%	0	0	0	4 -15%
81 - 90	1 -4%	0	0	0	1 -4%

Table 5: The frequency of hormone receptors in women by age breakdown

Age Receptors	ER+PR+	ER+PR-	ER-PR+	ER-PR-	Total
10 – 20	2 -0.10%	0	0	0	2 -0.10%
21 – 30	29 -1%	7 -0.30%	0	47 -2%	83 -6%
31 – 40	239 -12%	20 -1%	7 -0.30%	159 -8%	425 -21%
41 – 50	428 -21%	49 -2%	6 -0.30%	228 -11%	711 -36%
51 – 60	294 -15%	42 -2%	5 -0.20%	164 -8%	505 -25%
61 – 70	128 -6%	15 -1%	1 -0.05%	44 -2%	188 -9%
71 – 80	50 -3%	7 -0.30%	0	19 -1%	69 -3%
81 - 90	3 -0.10%	0	0	0	3 -0.10%

Table 6: The Frequency of hormone receptors in pre and postmenopausal

Receptor Number (%)	ER+	ER-	PR+	PR-
premenopausal	1110 -64%	616 -36%	1010 -59%	716 -41%
postmenopausal	203 -76%	64 -24%	182 -68%	85 -32%

Table 7: The Frequency of different statuses in pre and postmenopausal hormone receptors

Receptor Frequency	ER+ PR+	ER+ PR-	ER- PR+	ER- PR-
premenopausal	992 -57%	118 -6%	18 -2%	598 -35%
postmenopausal	181 -68%	22 -8%	1 -1%	63 -23%

Table 8: The frequency of Receptors in various grades

Receptor Frequency	ER+	ER-	PR+	PR-
I, II	147 -72%	58 -28%	135 -66%	70 -34%
III	196 -55%	160 -45%	190 -53%	166 -47%

Table 10: The Frequency of different types of hormonal receptors and HER2

Receptor Frequency	ER+PR+	ER+PR-	ER-PR+	ER-PR-
HER ₂ +3	287 -19%	48 -3%	20 -1%	271 -18%
HER ₂ +2	144 -10%	20 -1%	4 -0.20%	43 -3%
HER ₂ +1	70 -5%	12 -1%	1 -0.06%	22 -1%
HER ₂ -	347 -23%	42 -3%	9 -1%	143 -10%
HER ₂ +/-	417 -28%	54 -4%	10 -1%	165 -11%

Table 9: The frequency of all kind of HER₂

HER2 +3	HER2 +2	HER2 +1	HER2 -
662 -43%	216 -14%	110 -7%	555 -36%

Among of 1543 cases which have been registered, only in 1483 cases, hormone receptor status was known and Luminal A and Luminal B and Triple negative group status and HER₂ were as follows (Figures 1 and 2):

- 1- Luminal A (ER+PR+HER₂-) → 347 patients (23%)
- 2- Luminal B (ER+PR+HER₂+) → 287 patients (19%)
- 3- Triple Negative (ER-PR-HER₂-) → 143 patients (10%)
- 4- HER₂ + (+ HER 2 ER-PR-) → 271 patients (18%)

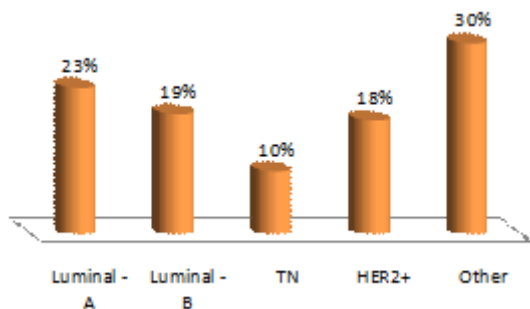


Fig. 1: The Frequency of different groups

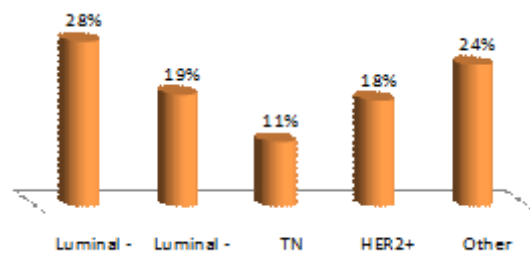


Fig. 2: The frequency of different groups versus +/-HER2

Because of the lack of performing FISH for patients, the HER₂+2 group was evaluated separately and there was no possibility of adding statistics to HER₂+3 or negative HER₂ groups (Table 10).

If we consider the sum of HER₂+1 and the negativeHER₂ as a negative HER, in this case:

Luminal A * (ER+PR+HER₂-) → 417 patients (28%)

Triple Negative * (ER+PR+HER₂-) → 165 patients (11%)

The Chi square test showed a significant relation between the frequency of receptors and levels of HER2 among the breast cancer patients (P: 0.0001).

DISCUSSION

In Khuzestan province, among of 2019 case study patients, 1331 patients (66%) had a positive ER and 1209 patients (60%) had a positive PR that was similar to the result of a study conducted in Saudi Arabia, but positive ER in Khuzestan province was more than various studies that had been done in India (7,24,19,23). In contrast, in a similar study conducted in Tanzania the number of positive ER patients (33%) and positive PR (18.3%) were lower compared with Khuzestan²².

The patient number with ER+PR condition were 59% in Khuzestan province and patients with ER-PR-were 33% compared with a study conducted in Spain, the number of ER+PR+was lower in this study, but was similar to a study that was conducted in the United States (Chicago) (15,11).

In our study, the number of tumors with positive ER in premenopausal is (64%) which means the positive ER in post-menopause is more, while Petricevic et al reported no significant

differences between them in the ages before and after menopause. Therefore, Khuzestan province's statistics was not consistent with the country's (Iran) statistics¹². In Khuzestan province, the majority of patients were with grade 3 tumors, respectively (60% grade 3 and 40% grades 2 and 1) that is similar to the statistics that obtained in the study of Liukkonen¹⁰. In Khuzestan patients, positive ER in grades 1 and 2 is more than grade 3. In the Liukkonen study, 65% of patients with Grade 3 had negative ER, which is different from Khuzestan (45%) statistics from this point is different ((21). In the Khuzestan's patients the Luminal A is (23%) and Luminal B is (19%) and Triple negative is (10%) and HER2 + is (18%).

Compared with Cardarella et al's study where the Luminal A is (70.3%) and the Luminal B is (15.6%) and TN is (8.1%) and HER2 + is (6%), in Khuzestan the Luminal A is less and Luminal B and TN and + HER2 are more than Italy (13). Also the amount of TN in Khuzestan is less than its amount in Ghosh et al's study in India (29.8%) and Satti et al's study in Saudi Arabia (24%) but showed no significant difference with the findings of the Elswaf study in Germany (24-10%) and Cardarella et al's study in Italy (8.1%) (13, 23- 25). Among the patients of this study, the HER₂+3 is (43%) and HER₂+2 is (14%), which compared with Ghosh's study in India the HER₂+3 is (16.7%) and HER₂+2 is (8.1%), these figures are more in Khuzestan patients (23). Further studies on the effects of hormone receptor status on the overall survival and local recurrence of breast cancer are recommended. In addition, the findings of this study can be used in developing novel techniques of early diagnosis (24) and also efficient treatments of breast cancer disorders (25).

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