



OBSERVATION ON HORMONE RECEPTOR STATUS OF BREAST CANCER AT PATNA MEDICAL COLLEGE & HOSPITAL, PATNA

Surgery

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ABSTRACT

AIMS and OBJECTIVES: Aim is to study the prevalence of hormones receptor among the patients of carcinoma breast and its co-relation with several factor like tumour size, tumour histology, stage, grade, nodal status, menstrual status etc. and to asses the role of hormone receptor as prognostic factor at Patna Medical College & Hospital, Patna.

MATERIAL AND METHODS: The study was performed among the patients attending surgery out patients department follow up clinic and all patients admitted in indoor ward with carcinoma breast during July 2011 to June 2013 all together data of 30 patients work collected.

RESULTS AND CONCLUSION: The prevalence of positive ER and PR was found in 53.33% and 43.33% respectively. In pre menopausal and post menopausal patients the figures are (33.33%, 22.22%) and (83.33%, 75%) respectively. Age of the patients ranges from 30-80 years (mean as =47.8 years) average size of tumor 4.62 cm tumors size has an inverse correlation with ER/PR positivity which is statistically significant ($p < 0.05$). Most of patients belong to well differentiated group. Almost all patients presented with IDC (infiltrating Duct Carcinoma). The prognostic implication of ER/PR receptors assessed by notingham prognostic index. Implies good prognosis for ER/PR positive as oppose to negative receptor status.

KEYWORDS

Carcinoma breast, Infiltrating ductal carcinoma, ER/PR receptor, Notingham prognostic index.

INTRODUCTION

The importance of steroid hormone receptors to the biology of breast cancer was recognized over 40 years ago, when it was observed that radiolabeled estrogens concentrated preferentially in the estrogen-influenced target organs of both animal and human breast cancers. These findings gave rise to the concept of an estrogen receptor (ER), it has since become clear that human breast cancers are dependent upon estrogen and/or progesterone for growth and that this effect is mediated through ERs and progesterone receptors (PRs). Not surprisingly, ER and PR are both overexpressed in malignant breast tissue.

The determination of estrogen receptor (ER) and progesterone receptor (PR) activity in breast cancer is a standard medical practice nowadays. It is an important predictor of response to hormonal therapy and overall prognosis of the patients. The tumors that are estrogen receptor (ER) positive and/or progesterone receptor (PR) positive have lower risks of morbidity and mortality after their diagnosis as compared to women with ER and/or PR negative disease.

A cancer is called estrogen-receptor-positive (or ER+) if it has receptors for estrogen. This suggests that the cancer cells, like normal breast cells, may receive signals from estrogen that could promote their growth. The cancer is progesterone-receptor-positive (PR+) if it has progesterone receptors. Again, this means that the cancer cells may receive signals from progesterone that could promote their growth.

By late 1960s and early 1970s, several investigators, most importantly Elwood Jensen and William McGuire observed that ER status might be a predictor of response to hormone therapy in advanced breast cancer. A consensus conference met in 1974 to study and analyze the predictive value of ER, the cumulative results are now more than 25 years old, they stand essentially unchanged and many subsequent larger and better controlled studies have confirmed the accuracy and validity of these original observations. Overall results indicate that 50% to 60% of all ER+ tumors can benefit from first line hormone therapy (only 5% to 10% of patients with ER- tumors benefit).

Although ER status is clinically most valuable as predictive factor, it can also be used as a prognostic factor. Women after ER+ tumors who do not receive any systemic therapy after surgery have a chance of recurrence by 5 years that is 5-10% lower than ER-ve tumors.

The usefulness of PR status as a prognostic factor is not as clear; some evidence supports its usefulness whereas other data do not. Unlike ER, PR is more likely to be higher or positive in young or premenopausal women, probably as a result of greater estrogen stimulation. PR status is probably a weak prognostic factor, even weaker than ER status and this probably accounts for variability in study results. Also, because of this weakness, it has not achieved any clinical usefulness based solely on its prognostic value.

MATERIALS AND METHODS

The study was performed among the patients attending surgery out patients department follow up clinic and all patients admitted in indoor ward with carcinoma breast during July 2011 to June 2013 all together data of 30 patients work collected.

Any patients to the surgical department with clinic-pathological diagnosis of carcinoma breast who was operated and specimen sent for histopathology and receptor status has been included in the study.

Detailed clinical history taken and clinical examination of all patients done methodically and the findings were recorded. Also the data collected about preoperative clinical findings in those patients who were met in follow up for the first time.

TNM staging was done according to clinical findings and available preoperative investigations. FNAC (preoperative) and detailed histopathology (postoperative) were noted. Operative procedures were also noted.

Among the post-operative patients routine clinical follow up were done at initially every month and then 6 months interval (after 1 year).

ER and PR receptor status was determined by immunohistochemistry (IHC) method from paraffin embedded histopathology specimen. As results vary according to method of fixation, procedure employed and antibody used, so scoring and cut off values are different in different laboratories. Receptor analysis of all cases was done from a single laboratory to maintain uniformity and minimize technical variability. During IHC, >20% positively stained cells in the slide considered to be positive for both ER and PR status according to the standardization of the particular laboratory concerned.

RESULT AND ANALYSIS METHOD:

The data of all 30 patients according to their ER/PR status were divided according to the percentage of different combinations. The correlation of hormonal receptors with several factors like tumor size, tumor histology, stage, grade, nodal status, menstrual status etc. determined. The statistical significance of the correlations was determined by applying Chi-square test.

Since the duration of the study is just two years and since all the patients were not included in the study at same time, it is unsuitable to assess the prognostic importance of receptors directly. The prognostic implication of ER and PR receptors were assessed indirectly with the help on Nottingham Prognostic Index (NPI).

NPI is calculated with the help of following formula-

$$NPI = (\text{tumour size in cm} \times 0.2) + \text{lymph node stage} \quad (1 = \text{no node}, 2 = 1 \text{ to } 3 \text{ nodes}, 3 = 4 \text{ or more nodes} + \text{grade} (1, 2, 3))$$

RESULTS:

Total No. of cases 30 all (female)

Age of the patients ranges from 30-80 years (mean age 47.8 years)

Distribution of the patients according to age and ER/PR status shown in table 1A and 1B

Table- 1A

Age (Years)	ER+	ER-	PR+	PR-
<=39	2	5	2	5
40-49	5	7	4	8
50-59	6	1	4	3
60-69	0	1	0	1
70-79	2	0	2	0
>80	1	0	1	0

Table- 1B

Age (Years)	ER+	ER-	PR+	PR-
<=50	7	12	6	13
>=50	9	2	7	4

By applying Chi-square test, the differences are significant at P<0.05 for age and ER but not for age and PR.

MENOPAUSAL STATUS:

Pre menopausal=18 (60%)

Post menopausal=12(40%)

Distribution of the patients according to menopausal status and ER/PR status shown in table -2

TABLE 2

	ER+	ER-	PR+	PR-
Pre menopausal	6	12	4	14
Post menopausal	10	2	9	3

By applying Chi-square test, the differences are significant at P<0.05

TUMOR SIZE:

Average size of tumor=4.62 cm

Distribution of the patients according to tumor size and ER/PR status shown in table 3

Tumor size (cm)	ER+	ER-	PR+	PR-
<=2.9	0	2	2	2
3-3.9	6	0	3	3
4-4.9	7	1	4	4
5-5.9	0	7	0	7
6-6.9	0	3	0	3
7-7.9	0	2	0	2
>=8	1	1	0	2

By applying Chi-square test, the differences are significant at P<0.05

TUMOR GRADE

Tumors were graded as well differentiated (w), moderately differentiated (m), poorly differentiated (P)

Distribution of the patients according to tumor grade and ER/PR status

Table 4

Tumor grade	ER+	ER-	PR+	PR-
W	13	0	12	1
M	3	10	1	11
P	0	4	0	5

By applying Chi-square test, the differences are significant at P<0.05.

Distribution of the patients according to NPI and ER/PR status shown in table 5

Table 5

NPI	ER+	ER-	PR+	PR-
<=2.4	0	0	0	0
2.5-3.4	9	0	9	0
3.5-4.4	5	2	4	3
4.5-5.4	2	1	0	3
>=5.5	0	11	0	11

By applying Chi-square test, the differences are significant at P<0.05.

DISCUSSION:

Estrogen receptor positivity predicts clinical response to endocrine therapy and as progesterone receptor is induced by estrogen- the presence of both is associated with 80% chance of endocrine response. ER negative patients derived, increased benefit from chemotherapy because they contain higher S-phase fraction and more genetic abnormality. Estrogen receptor is also a prognostic factor.

The prevalence of positive ER and PR was found in 53.33% and 43.33% respectively, in pre menopausal and post menopausal patients the figures are (33.33%, 22.22%) and (83.33%, 75%) respectively Tabei S et al (2002) found that the prevalence of positive ER and PR was 46% and 41% respectively. Mehrdad Nadji et al (2005) found the prevalence of positive ER and PR in 75% and 55% respectively in patients of invasive breast cancer. Panda (2004) found the corresponding figures as 49% and 47% respectively.

Age of the patients ranges from 30-80 years (means age=47.8 years). Majority of patients belongs to 40s and 50s. patients's age has no statistically significant correlation with PR status but has a statistically significant correlation with ER status-ER positivity significantly increases after the age of 50 years. This is probably related to age related hormonal changes in human body.

Average size of tumor= 4.62 cm. size of tumor ranges from 2.5-8 cm. most of tumors were about 3-5 cm in size. Tumors size has an inverse correlation with ER/PR positivity which is statistically significant (P<0.05). smaller tumors have greater ER/PR positivity than larger tumors. Onitilo et al(2009) found similar result. But probably tumor size is not an independent factor for ER/PR status.

Most of patients belongs to well differentiated group (13) followed by moderately differentiated (12) and poorly differentiated (5). Tumor grade has an inverse correlation with ER/PR positivity which is statistically significant(P<0.05) the poorly differentiated tumors are less likely to express ER/PR. Tabei S(2002) found similar results in his study. Since tumor grade is a well established prognostic factor for carcinoma breast, a strong correlation with it makes ER/PR a good prognostic factor likely.

Almost all patients 28(93.33%) presented with IDC (Infiltrating Duct Carcinoma). Only 2 patients presented with mucinous carcinoma. Tabei S (2002) found that the highest and lowest positivity of receptors was due to lobular carcinoma (66.7%) and medullary carcinoma (21.4%) respectively. Due to huge preponderance of IDC in our study, it is difficult to assess the relationship of ER/PR status with tumor histology. However, a bigger study with larger sample size may be required.

Total number of positive axillary lymph nodes ranges from 0 to 7. Average number of positive lymph node is 2.4. Number of positive lymph nodes has an inverse correlation with ER/PR positivity which is statistically significant. Once again, correlations with axillary lymph node, strongest prognostic factor of breast cancer establish the role of ER/PR as a good prognostic factor.

Since the duration of the study is just two years and since all the

patients were not included in the study at same time, it is unsuitable to assess the prognostic importance of receptors directly. However, we have noted few cases of recurrence- both loco-regional and distant, during follow up but they are not recorded in the study since only a fraction of patients actually turned up in the follow up clinic. Panda (2004) found that both in ER+PR+ and ER-/PR- groups, 38.9% had recurrence. On statistical analysis, no difference was found.".... isolated ER/ PR status didn't prove to be any significance in predicting recurrence."

The prognostic implication of ER and PR receptors were assessed indirectly with the help of Nottingham prognostic Index (NPI), since NPI, which is a standardized measure of prognosis of breast cancer, has already well established relation with survival, correlation of NPI with ER/PR positivity has a statistically significant correlation with Nottingham prognostic Index (NPI)- higher the NPI, the positivity of both ER and PR status decreases. Hence positive receptor status implies good prognosis as opposed to negative receptor status. Therefore ER/PR status can act as a reliable prognostic marker.

CONCLUSION

The present study was carried out to know the prevalence of hormonal receptors among the patients of carcinoma breast, the correlation of hormonal receptors with several factors like tumor size, tumor histology, stage, grade, nodal status, menstrual status etc., and to assess the role of hormonal receptors as prognostic factor and also to know which type of adjuvant therapy should be given-hormonal or chemotherapy.

In this study total of 30 patients ER and PR positivity found in 53.33% and 43.33% cases respectively. Patients' age has no statistically significant correlation with PR status but has a statistically significant correlation with ER status- ER positivity significantly increases after the age of 50 years. Menopausal status has statistically significant correlation with ER/PR status- positivity is more in postmenopausal patients. Tumors size has an inverse correlation with ER/PR positivity which is statistically significant. Tumor grade has an inverse correlation with ER/PR positivity which is statistically significant. Number of positive lymph nodes has an inverse correlation with ER/PR positivity which is statistically significant. ER/PR positivity has a statistically significant correlation with Nottingham Prognostic Index (NPI)- therefore ER/PR status can act as reliable prognostic marker.

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