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Correlation of Estrogen and Progesterone Receptor expression in Breast Cancer

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ABSTRACT: - Breast cancer is the most common malignant tumor among women. It accounts for 22% of all female cancers; more than twice the prevalence of cancer in women at any other site. Immunohistochemistry (IHC) is now the globally accepted methodology for detection of estrogen (ER) and progesterone (PR) receptors in breast carcinomas. The present study is designed for further insight into age and biology of ER and PR expression pattern in breast cancer patient of Bihar, India. Samples were obtained from biopsy and analyzed for ER/PR expression through Immunohistochemistry (IHC). Data were collected and statistically analyzed. It was observed that mean age of ER+ positive breast cancer patients were 47 years, while mean age of PR positive patient were 44 years. Two third patients had either ER or PR is positive while one third had both negative. In our study we observed 6.4 % patients with ER negative and PR positive. Thus it is concluded that two third of breast cancer patients was positive for hormone receptor. ER/PR positive indicates over-expression of estrogen and progesterone in carcinoma breast. ER negative and PR positive group was also observed in significant number of breast cancer patients. ER negative were observed in early age group of breast cancer while PR negative were observed in higher age group patients.

***Key Words:** Immunohistochemistry, Carcinoma, ER, PR.*

I. INTRODUCTION

Breast cancer is the most common malignant tumor among women. It accounts for 22% of all female cancers; more than twice the prevalence of cancer in women at any other site [1]. It has a varied spectrum of molecular, pathological and clinical features with different prognostic and therapeutic implications [2].

Invasive breast cancer is still the most common female malignancy worldwide and more than 1 million women are diagnosed with breast cancer each year [3]. Currently, it is believed that the invasive carcinoma derives from an in situ component; because of its frequent coexistence and histological similarity [4]. This linear process would occur through several steps, where the normal epithelium modifies to Ductal Carcinoma *in situ* (DCIS), progressing to invasive carcinoma and then metastasis [5].

Immunohistochemistry (IHC) is now the globally accepted methodology for detection of estrogen (ER) and progesterone (PR) receptors in breast carcinomas [6]. Both ER and PR show nuclear expression in positive cases. ER content, in particular, is correlated with prolonged disease-free survival and increased likelihood of response to hormonal therapy.

Estrogen and its receptor (ER) play important roles in the genesis and malignant progression of breast cancer. ERα regulates the transcription of various genes as a transcription factor, which binds to estrogen response elements (ERE) upstream of the target genes. The expression of ERα is closely associated with breast cancer.

Thus, despite the fact that ER and PR evaluation have played central roles in breast cancer diagnostics and research since the 1970s, it is currently not well established if the joint assessment of ER and PR stratifies breast cancers into four biologically meaningful and clinically useful subgroups (ER+/PR+, ER+/PR-, ER-/PR-, and ER-/PR+).

The present study is designed for further insight into age and biology of ER and PR expression pattern in breast cancer patient of Bihar, India.

II. METHODS

The study has been carried out on 350 breast cancer patients diagnosed and treated at Mahavir Cancer Institute and Research Centre and were classified according to their ER/PR expression. The study was approved by the ethics committee of Mahavir Cancer Institute and Research Centre, Patna, Bihar, India. All the patients were involved voluntarily in this study. The IHC assays for ER and PR were performed on 3 μm sections unstained slide from paraffin block and float mounted on plus-coated glass slides. The methodology for ER and PR were same as for each antibody and each batch, positive and negative controls were used. Human endocervix was used as a positive control because of its easy availability and relatively stable reactivity. The negative control consisted of non-immune mouse IgG substituted for the primary antibody.

Samples were obtained from biopsy and analyzed for ER/PR expression through Immunohistochemistry (IHC). Data were collected and statistically analysis was performed according to statistical package of Graph pad Prism. The blood group frequencies were compared using Chi- square test. Power of study was 80% while confidence Interval (CI) was 95%.

III. RESULTS

It was observed that mean age of ER+ positive breast cancer patients were 47 years, while mean age of PR positive patient were 44 years (Graph -I). ER was positive in 60.1% patients while ER is negative in 39.9% patients. PR is positive in 55.67 % while PR was negative in 44.33% patients. Two third patients had either ER or PR is positive while one third had both negative. In our study we observed 6.4 % patients with ER negative and PR positive (Graph –II, Table - 1).

IV. DISCUSSIONS

The biologic, prognostic and predictive importance of assessment of estrogen receptor (ER) expression in breast cancer is well established; however, the added value of progesterone receptor (PR) assessment is controversial [7, 8]. Since the 1970s, it has been hypothesized that PR expression is associated with response to hormonal therapies in ER+ breast cancer, as it is thought that ER and PR co-expression demonstrates a functionally intact estrogen response pathway [9, 10]. Analyses from observational studies showed that loss of PR expression was associated with worse overall prognosis among ER+ breast cancers [11, 12, 13, 14, 15].

These results suggested that evaluation of PR status in ER+ breast cancer might be used to help guide clinical management, as high levels of PR expression may identify a subset of ER+ patients most likely to benefit from hormonal therapy [16].

The presence of ER, as detected by IHC, is a weak prognostic marker of clinical outcome in breast cancer [17] but a strong predictive marker for response [18] to tamoxifen-based therapy. Recent studies have demonstrated that ER expression is present in approximately 70% of breast cancers, [19] so an accurate and reliable ER result is critical for hormone therapy.

One of the interesting results in our study observed was that ER-/PR+ was found only in one case out of 137 malignant cases. Such findings were also reported by Olivotto, et al.,[20] as they found only one case out of 192 with ER- have PR+ with weak positive immune-staining. These results were strongly challenged by [21] Colomer, et al., reported ER+/PR+, ER+/PR–, ER–/PR+, and ER–/PR– in 46%, 19%, 7% and 28%, respectively.

In the present study we also observed 6.4% cases of ER-ve and PR+ve group, which indicates that this group is also a important subtypes of breast cancer patients.

It has further been suggested that PR status is independently associated with disease-free and overall survival, that is, patients with ER-positive/PR-positive tumors have a better prognosis than patients with ER-positive/PR-negative tumors, who in turn have a better prognosis than patients with ER-negative/PR-negative tumors. [22]

Thus it is concluded that two third of breast cancer patients were positive for hormone receptor. ER/PR positive indicates over-expression of estrogen and progesterone in carcinoma breast. ER negative and PR positive group were also observed in significant number of breast cancer patients. ER negative was observed in early age group of breast cancer while PR negative were observed in higher age group patients.

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REFERENCES

[1]. Lal P, Chen B. Correlation of HER-2 status with estrogen and progesterone receptors and histological features in 3,655 invasive breast cancers. American Journal of Clinical Pathology, 2005, 123 (4): 541-6,

[2]. Carey L A, Perou C M, Livasy C A,et al. Race breast cancer subtypes and survival in the Carolina breast cancer study. JAMA, 2006, 295: 2492- 502,

[3]. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics-2002. CA Cancer J Clin 2005; 55: 74-108.

[4]. Allred DC, Wu Y, Mao S, et al. Ductal carcinoma in situ and the emergence of diversity during breast cancer evolution. Clin Cancer Res 2008; 14: 370-8.
[5]. Mario CS, Jose´ LP, Ricardo FS, Cla´udio GZ. Are the pure in situ breast ductal carcinomas and those associated with invasive carcinoma the same?. Appl Immunohistochem Mol Morphol 2010; 18:51-4.
[6]. Harvey JM, Clark CM, Osborne CK, Allred DC. Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer. J Clin Oncol. 1999. 17: 1474 – 1481.
[7]. Colozza M, Larsimont D, Piccart MJ: Progesterone receptor testing: not the right time to be buried. J Clin Oncol 2005, 23:3867–3868.
[8]. Fuqua SA, Cui Y, Lee AV, Osborne CK, Horwitz KB: Insights into the role of progesterone receptors in breast cancer. J Clin Oncol 2005, 23:931–932.
[9]. Horwitz KB, McGuire W: Estrogen control of progesterone receptor in human breast cancer, correlation with nuclear processing of estrogen receptor. J Biol Chem 1978, 253:2223–2228.
[10]. Horwitz KB, McGuire WL: Estrogen control of progesterone receptor induction in human breast cancer: role of nuclear estrogen receptor. Adv Exp Med Biol 1979, 117:95–110.
[11]. Dunnwald LK, Rossing MA, Li CI: Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. Breast Cancer Res 2007, 9:R6.
[12]. Grann VR, Troxel AB, Zojwalla NJ, Jacobson JS, Hershman D, Neugut AI: Hormone receptor status and survival in a population-based cohort of patients with breast carcinoma. Cancer 2005, 103:2241–2251.
[13]. Bardou VJ, Arpino G, Elledge RM, Osborne CK, Clark GM: Progesterone receptor status significantly improves outcome prediction over estrogen receptor status alone for adjuvant endocrine therapy in two large breast cancer databases. J Clin Oncol 2003, 21:1973–1979.
[14]. Cancello G, Maisonneuve P, Rotmensz N, Viale G, Mastropasqua MG, Pruneri G, Montagna E, Iorfida M, Mazza M, Balduzzi A, Veronesi P, Luini A, Intra M, Goldhirsch A, Colleoni M: Progesterone receptor loss identifies luminal B breast cancer subgroups at higher risk of relapse. Ann Oncol 2013, 24:661–668.
[15]. Prat A, Cheang MC, Martin M, Parker JS, Carrasco E, Caballero R, Tyldesley S, Gelmon K, Bernard PS, Nielsen TO, Perou CM: Prognostic significance of progesterone receptor-positive tumor cells within immunohistochemically defined luminal A breast cancer. J Clin Oncol 2013, 31:203–209.
[16]. Horwitz KB, McGuire WL: Predicting response to endocrine therapy in human breast cancer: a hypothesis. Science 1975, 189:726–727.
[17]. Hahnel R, Woodings T, Vivian AB. Prognostic value of estrogen receptors in primary breast cancer. Cancer. 1979; 44: 671 – 675.
[18]. Allred DC, Harvey JM, Berardo M, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. Mod Pathol. 1998. 11: 155 – 168.
[19]. Nadji M, Gomez-Fernandez C, Ganjei-Azar P, Morales AR. Immunohistochemistry of estrogen and progesterone receptors reconsidered: experience with 5,993 breast cancers. Am J Clin Pathol. 2005; 123: 21 – 27.

Table – 1: ER and PR expression and Breast Cancer

Marker	Positive		Negative		P- Value
	Number	**Percent**	**Number**	**Percent**	
ER	122	60.10	81	39.90	**0.0003**
PR	113	55.67	90	44.33	**0.0025**

Graph- I: Age of Breast cancer Patients