

Assessment of ER, PR, p53 and HER2/neu Markers in Breast Carcinoma Patient

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ABSTRACT

Introduction: Breast cancer is reported as one of the most widespread cancers with more than 1,300,000 cases and 450,000 deaths each year worldwide. Hormone receptors and oncoproteins are used to determine prognosis and also predicts response to therapy in breast carcinoma patients. The present study was undertaken to find expression of ER, PR, p53 and HER2/neu in breast carcinoma.

Material and Methods: The study was conducted among 50 cases of breast cancer patients. Specimens received as lumpectomy or mastectomy were subjected to immunohistochemistry for ER, PR, p53 and HER2/neu expression. Data so obtained was analysed using the SPSS Version 17 software and was expressed as percentage and number of respondents.

Results: 18 cases (36%) revealed estrogen and progesterone receptor positivity, 6 cases (12%) revealed HER2/neu positivity, 52% cases showed combined ER and PR negativity and 26% cases were ER and PR positive. p53 positive cases comprised of 16 cases which were ER and PR negative.

Conclusion: It was concluded that inversely proportional relation of p53 to ER PR expression was found. Thus, it can be considered as a marker for prognosis and disease free survival rate.


Keywords: Hormone Receptors; Immunohistochemistry; Tumor Markers.

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INTRODUCTION

Breast cancer is reported as one of the most widespread cancers with more than 1,300,000 cases and 450,000 deaths each year worldwide.¹ Hormone receptors (ER, PR) and oncoproteins (HER2/neu) are used to reveal prognosis as well as evaluates response to treatment in breast carcinoma patients.² Mutation in p53 gene is one of the most common genetic change identified in human neoplasia and p53 mutation in breast cancer, is related with more aggressive disease pattern and worsens the overall survival rate.³ Breast cancer is classified into subgroups by using immunohistochemical markers, which are biologically different and behave differently. According to these immunohistochemical markers, breast cancer can be divided into 4 major subgroups i.e. luminal A and luminal B are characterized by high expression of ER and PR; HER2/neu overexpression is characterized by ER and PR negativity and HER2/neu positivity and triple-negative is characterized by negative expression of ER, PR and HER2/neu.⁴ The present study was undertaken to find expression of ER, PR, p53 and HER2/neu in breast carcinoma.

MATERIALS AND METHODS

The study was commenced among 50 cases of breast cancer in the Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences And Research, Amritsar. Specimens were received as lumpectomy or mastectomy specimens. Ethical clearance was obtained. Informed consent was taken from patients. Medical history of the patient was taken. The tissue was fixed in formalin, embedded in paraffin and Haematoxylin and Eosin sections were prepared. Immunohistochemistry procedure was performed for ER, PR, p53 and HER2/neu expression. Antigen retrieval was carried out and sections were viewed under the microscope. Obtained data was arranged accordingly and was expressed as a number and percentage of respondents and were analyzed using the SPSS Version 17 software.

RESULTS

Table 1 shows positivity of tumor markers in patients with breast carcinoma. 18 cases comprising 36% of the total cases showed

estrogen receptor positivity. Percentage of positive cells varied from 14 to 90% with mild to strong intensity. 18 cases comprising 36% of the total cases showed progesterone receptor positivity. Percentage of positive cells varied from 1 to 90% with mild, moderate and strong intensity. 31 cases comprising 62% of the total cases showed p53 positivity was seen in. Percentage of positive cells varied from 07 to 90% with mild to strong intensity. 6 cases comprising 12 % of the total cases showed HER2/neu

positivity. Percentage of positive cells varied from 06 to 83% with mild to strong intensity.

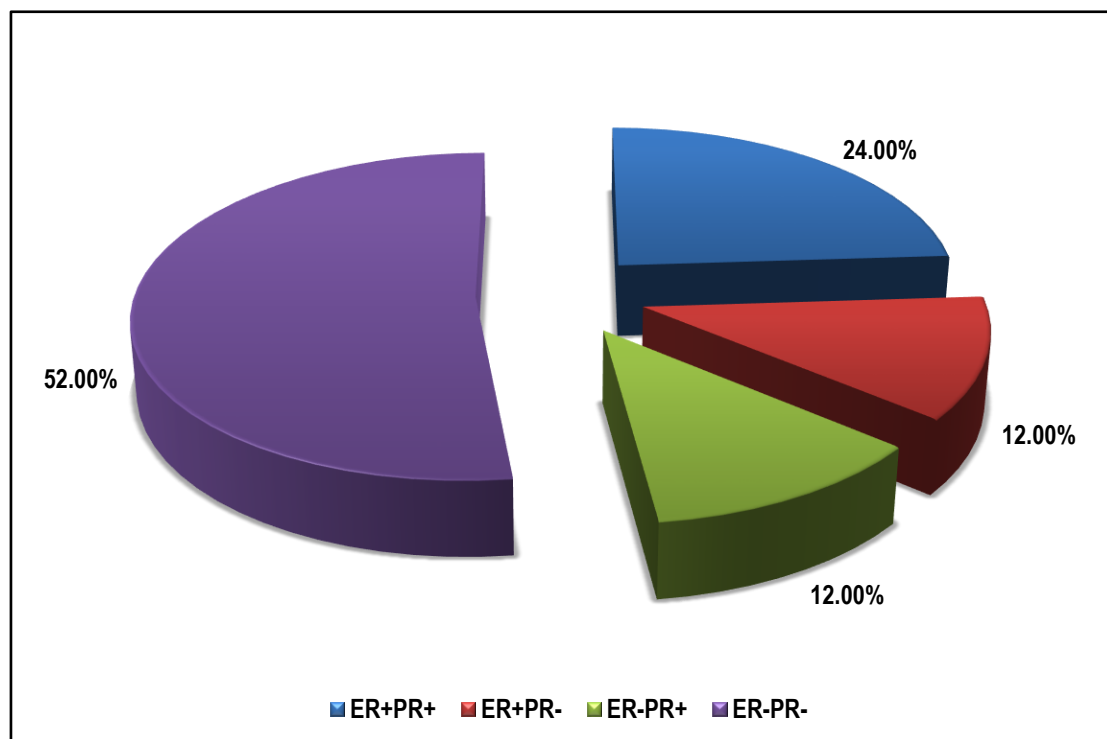
Tumors were separated into four categories according to ER PR positivity,: ER+PR+, ER+PR-, ER-PR+ and ER-PR-. Maximum number of cases were combined ER and PR negative constituting 52% followed by ER and PR positive cases constituting 26% cases (Table 2). p53 positive cases comprised of 16 cases which were ER and PR negative (table 3, graph 2)

Table 1: Assessment of tumor markers in patients with breast carcinoma

Tumor marker	Positive cases	Negative cases	Total
Estrogen receptor	18 (36%)	32 (64%)	50
Progesterone receptor	18 (36%)	32 (64%)	50
P53 Receptor	31 (62%)	19 (38%)	50
HER2/neu	6 (12%)	44 (88%)	50

Table 2: Combination of ER and PR cases

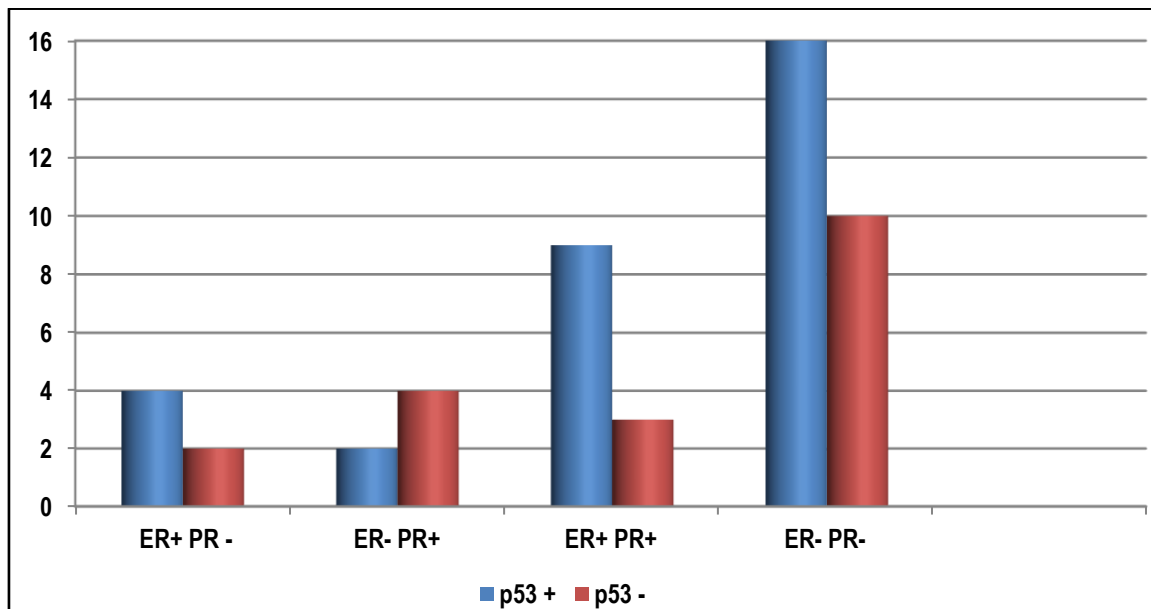
Combination of ER and PR	Number of cases (n=50)	Percentage
ER+PR+	12	24%
ER+PR-	6	12%
ER-PR+	6	12%
ER-PR-	26	52%



Graph 1: Distribution of ER and PR cases

Table 3: Correlation of ER, PR and p53

ER PR status	p53 Positive	p53 Negative	Total
ER + PR-	04	02	06
ER- PR+	02	04	06
ER + PR +	09	03	12
ER- PR-	16	10	26



Graph 2: Correlation of ER, PR and p53

DISCUSSION

Tumor Markers are biochemical substances which are produced by tumor cells due to the cause or effect of malignant processes and, when present in significant amounts, indicates the presence of a cancer. These markers can be a product of newly switched on genes that remained quiescent in the normal cells or can be normal endogenous products that are produced at an increased rate in cancer cells.⁵

Estrogen receptors are specific proteins that are found mainly in the cytoplasm of cells of target tissue for estrogen action.⁶ In the present study, estrogen receptor positivity was shown 36% of the total cases. In the Western and Indian literature Estrogen Receptor positivity varies between 50-70% and 30-50% respectively.⁷

Progesterone receptor is an intracellular steroid receptor that specifically binds progesterone expressed by a single gene.⁸ In the present study, progesterone receptor positivity was revealed in 36% of the total cases. When measured accurately, PR status is an independent predictive factor for benefit from adjuvant endocrine therapy with tamoxifen.⁹

Mudduwa LK,¹⁰ reported a prevalence of 48.3% PR-positive tumours. Patnayak R et al¹¹ reported that the percentage of tumours expressing PR but negative for ER was found to be in 13.1% cases. Desai SB et al¹² and Ambroise et al¹³ reported prevalence of 46.1% and 51% for PR-positivity in breast cancers, respectively.

p53 is the main regulator of genomic stability through regulation of the cell cycle. Overexpression of p53, which is caused by mutation of TP 53, is the most frequent genetic alteration in breast cancer.¹⁴

Lacroix M et al¹⁵ showed that breast tumors expressing a high amount of p53 (as measured by IHC) are more frequently ER-negative and PR-negative. They are also associated with a high proliferation rate, high histological and nuclear grades, aneuploidy and poorer survival. Shokouh TZ et al¹⁶ reported an inverse correlation between age and p53 mutation, however it was not statistically significant. The inverse association between ER, PR and p53 has also been demonstrated by Ahmed HG et al¹⁷ among Yemini women with breast cancer.

ER and PR should be measured on every primary invasive breast cancer and may be measured on metastatic lesions if the results would influence treatment planning. In both pre-and postmenopausal patients, steroid hormone receptor status should be used to identify patients most likely to benefit from endocrine forms of therapy in both the early breast cancer and metastatic disease settings.¹⁸

In the present study, HER2/neu positivity was seen in 6 cases comprising 12 % of the total cases. The human epidermal growth factor receptor-2 (HER2/neu), which is estimated to be overexpressed in 20%-30% of breast cancer patients, with regard to its role as a prognostic and predictive factor. Although many studies have suggested that HER2/neu overexpression may be associated with a poor clinical outcome, other studies have not fully supported this observation.¹⁹

HER2/neu expression and/or amplification should be assessed in every primary invasive breast cancer either at the time of diagnosis or at the time of recurrence, chiefly to guide selection of trastuzumab in the adjuvant and/ or metastatic setting. HER2/neu defines prognosis as HER2/neu amplification, overexpression, and the presence of HER2/neu extracellular domain are generally associated with a poorer prognosis. High levels of tissue HER2/neu expression or HER2/neu gene amplification should be used to identify patients for whom trastuzumab may be of benefit for treatment of breast cancer in the adjuvant or metastatic disease settings. HER2/neu is used for predicting response to specific chemotherapeutic agents and to determine sensitivity to endocrine therapy.¹⁸

CONCLUSION

Estrogen receptor positivity was seen in 36% cases. Progesterone receptor positivity was seen in 36% cases. ER PR positivity was seen in 24% cases, ER+PR- in 12%, ER- PR+ in 12% whereas ER PR negativity was seen in 52% cases. p53 positivity was seen in 62% cases. HER2/neu positivity was seen in 12 % of cases. Thus, it was concluded that p53 is inversely proportional to ER PR expression. Hence, it can be considered as a marker for prognosis and disease free survival rate.

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