

CORRELATION OF ER, PR, AND HER2 WITH HISTOLOGICAL GRADES OF INVASIVE DUCTAL CARCINOMA OF BREAST

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ABSTRACT

Objective: To study the correlation of histological grades of breast cancer with the expression of hormone receptors ER, PR, and HER2/neu in patients of invasive ductal carcinoma breast.

Material and Methods: A Descriptive, cross-sectional study was conducted at the Department of Pathology, PNS Shifa Hospital, Karachi from 13th February 2021 to 12th August 2021. 77 cases of invasive ductal carcinoma breast were included in this study with subjects falling between the age groups of 25 and 85. On H&E-stained sections, The Nottingham Scarff Bloom Richardson System variant was used to grade the histology of the samples. The formalin-fixed paraffin-embedded (FFPE) tissues were subjected to immunohistochemistry for ER, PR, and HER-2 receptors using the DAKO Envision kit.

Results: In our study, histological grading of invasive ductal carcinoma was found to be as follows; grade I in 01 (1.30%), grade II in 53 (68.83%), and grade III in 23 (29.87%) patients. Among the hormone receptors, the ER receptors revealed non-significant correlation i.e. 0.090. Also, PR receptors revealed 0.192 and HER-2 showed 0.410 values respectively in accordance to the grades of invasive breast carcinoma.

Conclusion: According to the study's findings, grade II (75.71%) and grade III (22.86%) had the highest prevalence among invasive ductal carcinoma cases. Additionally, the estrogen receptor (ER) expression was higher than that of HER-2 and the progesterone receptor (PR).

Keywords: Histologic grade, Invasive ductal carcinoma, ER, PR, HER-2.

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INTRODUCTION

Breast cancer is one of the most common cancers causing mortality in women between the ages of 45 and 55 years. It is the most frequently diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer for both incidence and mortality [1]. The incidence in Pakistan is 34.6%, placing it at the top position among Asian countries [2]. Factors that govern the prognosis for breast carcinoma include tumor size, lymph node involvement, histologic subtype, and histologic grade. Different subtypes of breast carcinoma were generated based on expression of ER, PR, Ki67 and HER2, positive and/or negative [3]. The human epidermal growth factor receptor-2 (HER2), progesterone receptor (PR), and estrogen receptor (ER) are frequently employed biomarkers for predictive and prognostic purposes [4]. In women with operable invasive breast cancer, the hormone

receptor subtype is a significant independent prognostic predictor [5]. They support therapeutic decisions that are trustworthy and economical and are affordable substitutes for more expensive molecular subtyping techniques [6,7]. With a view to reducing mortality, it is essential to maintain efficient procedures and protocols for the early detection and screening of the disease [8,9].

The status of ER, PR, and HER2 receptors in breast cancer has become pertinent to determining prognosis in contemporary medical practice [10]. For patients with breast cancer, immunohistochemical examination of receptors like ER, PR, and HER2 is frequently done to forecast therapy outcomes [11]. The objective of the current study was to correlate ER, PR, and HER2/neu markers immunohistochemistry status in breast cancer. Correlation with histological grading was also carried out to look at any links between these markers and the severity of the disease.

MATERIAL AND METHODS

A Descriptive, cross-sectional study was conducted at the Department of Pathology, PNS SHIFA

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Hospital, Karachi from 13th February 2021 to 12th August 2021. Between the ages of 25 and 85, 77 cases of invasive ductal carcinoma, including both males and females, were included in the study. Patients below and above this age group were excluded from this study.

A sample size of 77 was calculated with the WHO calculator by taking a 95% confidence interval, 7% margin of error, and prevalence of invasive ductal carcinoma of the breast, grade I = 11% (from a Pakistani study). For this study's non-probability, consecutive sampling was used. The study includes Trucut, incisional or and excisional biopsy, mastectomy specimens diagnosed as invasive ductal carcinoma with ≥ 500 tumor cells. Whereas poorly fixed tissue with extensive necrosis post-chemotherapy tumors and metastatic tumors were excluded from the study. After approval from the College of Physicians and Surgeons of Pakistan and an ethical permission certificate from the Institutional Ethical Committee, the patients who fulfilled the inclusion criteria were included in the study. The formalin-fixed paraffin-embedded (FFPE) tissues were used to create slides that were stained with hematoxylin and eosin. The histologic type and grade of the tumor were determined by a microscopic examination performed by a histopathologist.

ER, PR, and HER2 status were stained using the DAKO Envision kit in accordance with the manufacturer's instructions. The Allred criteria were used to evaluate ER and PR. The HER2 status was disclosed in accordance with the ASCO/CAP recommendations.

Statistical analysis was done using SPSS version 23.0. Continuous variables including age and BMI were presented as mean $\pm$ standard deviation. Tumor grading and hormone receptors were compared by using the Chi-square test. Post-stratification Chi-square test was used. A p-value of ≤ 0.05 was taken as statistically significant.

RESULTS

The age range in this study was from 25 to 85 years with a mean age of 50.89 ± 14.14 years. The majority of the patients 47 (61.04%) were >55 years of age. The majority of the patients were females (97.4%). Table-I revealed Immuno histochemical analysis of the breast cancer cases with respect to estrogen receptors (ERs), progesterone receptors (PRs), and the human epidermal growth factor receptor-2 (HER2/neu). The frequencies of positively expressed cases for ER, PR & HER2 receptors are found to be 41 %, 36.2% and 51% respectively. Figures I, II & III also showed the

positive immune expression of these hormone receptors.

In our study, the histological grading of invasive ductal carcinoma was found to be as follows; Grade I in 01 (1.30%), Grade II in 53 (68.83%), and Grade III in 23 (29.87%) patients. Stratification of grades with respect to ER, PR, and HER2 are shown in Tables-II, III and IV respectively, revealing the correlation of these receptor with the histological grades of invasive ductal carcinoma. The study found no significant correlation of these hormonal receptors with the histological grades of invasive breast carcinoma.

Table-I: Distribution of patients with status of receptors (n=77).

Types of Receptors	Expression	No of cases	Frequencies
ER	Positive	41	53.25
	Negative	36	46.75
PR	Positive	33	42.86
	Negative	44	57.14
HER-2	Positive	51	66.23
	Negative	26	33.77

Table-II: Correlation of histological grade with respect to ER.

ER	Histologic grade			p-value
	I	II	III	
Positive	01	31	09	0.090
Negative	00	22	14	

Table-III: Correlation of histologic grade with respect to PR.

PR	Histologic grade			p-value
	I	II	III	
Positive	01	26	06	0.192
Negative	00	27	17	

Table-IV: Correlation of histologic grade with respect to HER2.

HER2	Histologic grade			p-value
	I	II	III	
Positive	01	37	13	0.410
Negative	00	16	10	

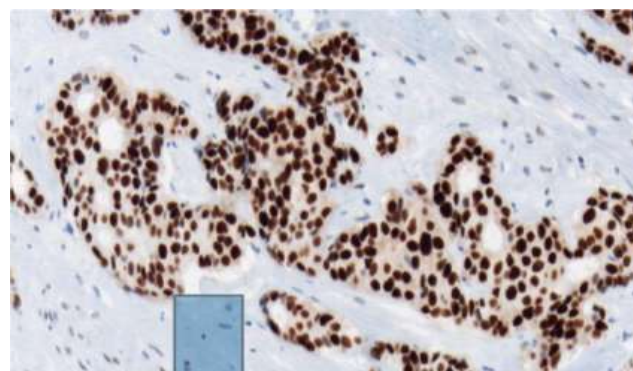


Figure-I: Estrogen receptor staining.

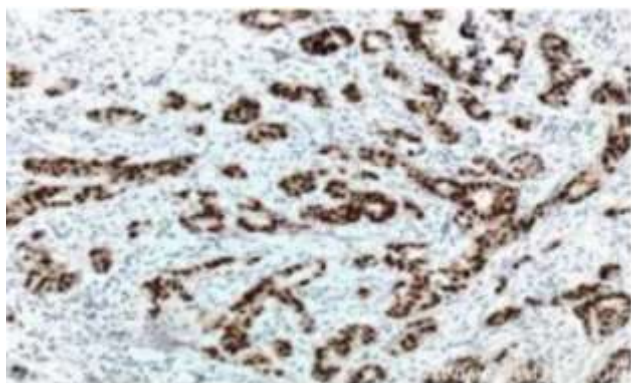


Figure-II: Progesterone receptor staining.

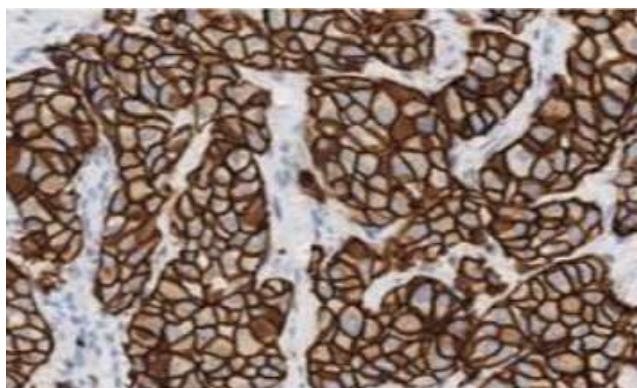


Figure-III: HER2 staining.

DISCUSSION

This study was carried out at PNS Shifa Hospital in Karachi and involved 77 patients diagnosed with invasive ductal breast cancer. The need to combine clinical pathology and cancer biology is emphasized in order to determine the optimum course of treatment and prognosis for breast cancer patients. The evaluation of hormone receptors, such as ER, PR, and HER2/neu, is frequently used to guide adjunct hormonal and targeted therapy for breast cancer patients. Better outcomes will be obtained by adopting treatment decisions on this knowledge. The ages of the participants in this study who took part in the analysis ranged from 25 to 85. The average age of the patients was calculated to be 50.89 years. The majority of the patients 47 (61.04%) were >55 years of age which is almost comparable to other studies in Pakistan [12,13].

We have conducted this study to determine the histological grading of invasive ductal carcinoma and to compare histological grades of invasive ductal carcinoma with hormone receptors in patients of invasive ductal carcinoma. In our study, histological grading of invasive ductal carcinoma was found to be as follows; grade I in 01 (1.30%), grade II in 53 (68.83%), and grade III in 23 (29.87%) patients.

In the present study the expression of ER was found in 41 (53.25%) patients, PR expression

was 33 (42.86 %) and HER -2 was found to be 51(66.23%) in cases of invasive breast carcinoma.

Similar observations were made by Tummidu Santosh *et al* in a prospective study conducted at MKCG MCH Brahmapur, Odisha, India on 82 cases for a period of one year [14]. According to histological grading, ER, PR and HER-2 receptors reveals non-significant correlation. These results are partially consistent with a study [15].

Our findings are not consistent with another study conducted by Ablavi Adani in Togo (West Africa), who assessed negative ER and PR expression, and HER2 positivity. The study also revealed a significant correlation of HER-2 receptor subtype types with the stage ($p=0.025$) and the histological grade ($p < 0.0001$) [16].

Similar observations were made by Carol A. Parise and Vincent Caggiano in the California Cancer Registry. According to the ER/PR/HER2 subtype is simple, inexpensive, easy to interpret, reliable, reproducible, and readily available for clinicians without additional tests [16]. Similar findings were made by Montemurro F Cosimo S, and Arpino G in a study [17].

Our findings are not consistent with a study conducted by Hou W, Yao Q, Niu DF, Xue WC in China, who assessed negative ER and PR expression, and HER2 positivity [18].

Our study findings co relate with a study carried out at university of Rothak where 150 samples were studied and similar expression of ER, PR and Her 2 receptors was seen in the study [19].

The most crucial element of breast cancer prognostication is histopathological grades which could be assimilated into staging systems and algorithms to choose the most appropriate treatment for patients with breast cancer [20,21].

The current study's observation of a direct association between ER, PR, and HER-2 positivity and histological grade highlights the importance of these markers as effective breast cancer prognostic tools. These results underline how crucial it is to evaluate the expression of ER, PR, and HER-2 in figuring out the tumor's grade, which in turn helps in choosing the correct treatment options. These indicators can be effective tools for management and therapy decisions. In this regard, we recommend that immune staining of the hormone receptors should be used routinely for breast cancer diagnosis as it will help in the early and timely management of high-risk patients to reduce the morbidity and mortality associated with breast carcinoma.

CONCLUSION

The histological grade is an important determinant of breast cancer prognostication and should be incorporated into staging systems and algorithms to choose the most appropriate treatment for patients with breast cancer.

STRENGTHS AND LIMITATIONS

Strengths: The main strength of this study is the fact that it establishes a direct histological correlation between the expression of hormone receptors and different histological grades of invasive ductal carcinoma breast. This significance can be employed for assessing the prognosis as well as determining the need for adjuvant chemotherapy in the patients.

Limitations: The study done at Karachi's P.N.S. Shifa Hospital admits several restrictions. First off, only patients treated at that hospital were included in the investigation of biomarkers, which may not accurately reflect the region's full population of breast cancer patients. The study's sample size was very modest, which may limit how far the results may be applied

CONFLICT OF INTEREST

None

RECOMMENDATIONS

It may be possible to gain additional knowledge and chances to examine histopathological correlations in greater detail by doing the study on a bigger sample size. Future research can improve our comprehension of breast cancer and its histological characteristics by addressing these shortcomings

AUTHORS CONTRIBUTION

Yusra Saleem: Conceived idea, study design, data collection, immunohistochemical analysis, Result interpretation,

Hona Wati: Literature review, manuscript writing, data analysis, result interpretation, proofreading & correction of entire manuscript

Beenish Hussain Nomani: Manuscript writing, data analysis, proofreading and correction of entire manuscript

Misbah Riaz: Data analysis, immunohistochemical analysis.

Shaista Bakhat: Helped to draft the manuscript, proofreading and correction

Hira Faisal: Data collection, helped to draft the manuscript, proofreading and correction

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