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Research Article

**AN AUDIT OF HER-2/NEU RECEPTOR STATUS IN
INVASIVE BREAST CANCER PATIENTS****¹Dr. Umair Ahmad, ²Dr. Mian Moeed Ahmad, ³Dr. Muhammad Zoha**¹Associate Professor, Department of Surgery, Quaid-e-Azam Medical College, Bahawalpur²House Officer, Bahawal Victoria Hospital, Bahawalpur³House Officer, Bahawal Victoria Hospital, Bahawalpur**Article Received:** March 2020**Accepted:** April 2020**Published:** May 2020**Abstract:****Objective:**

To find out the frequency of HER-2/Neu receptor status in invasive breast cancer patients.

Material and methods:

This cross-sectional study was conducted at Department of Surgery, Bahawal Victoria Hospital, Bahawalpur from January 2019 to June 2019 over the period of 6 months. Total 100 patients with breast cancer (having only lobular carcinoma / ductal carcinoma) as per operational definition and having age from 20-65 were selected. HER-2/Neu receptor status was assessed in selected patients.

Results:

In present study, mean age of the patients was 43.78±12.67 years. HER-2/Neu receptor was found positive in 40 (40%) patients and negative in 60 (60%) patients. Grade-I tumor was found in 21 (21%) patients followed by grade-II in 35 (35%) patients and grade-III tumor was found in 44 (44%) patients. Total 13 (13%) found with lobular carcinoma and 87 (87%) found with ductal carcinoma. ER was found positive in 75 (75%) patients and negative in 25 (25%) patients. PR was found in 65 (65%) patients and negative in 35% (35%) patients.

Conclusion:

Results of this study showed a higher rate of over expression of HER-2/Neu receptor. Most of the cases found with grade-III tumor. There was no association of HER-2/neu receptor status with age and obesity. In most of the patients, ER and PR was found positive.

Key words: HER-2/neu, breast carcinoma, ER/PR, over-expression, co-expression

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INTRODUCTION:

Breast cancer is the most common cancer in women. Invasive breast cancer is still the most common female malignancy worldwide and more than 1 million women are diagnosed with breast cancer each year. It is the most common cancer related cause of death in middle-aged women all over the world.¹ There is a 10-fold variation in breast cancer incidence among different countries worldwide. Variations in incidence of breast cancer among multicultural populations suggest that etiological factors vary in biological expression and their impact on disease outcome. The gradual increase in incidence of breast cancer has created an urgent need to develop strategies for prevention. Breast cancer appears to have a complex etiology, possibly with interplay of many causal factors including hormonal, genetic and environmental factors operating over a long period.²

Increased exposure to estrogen is associated with an increased risk for developing breast cancer, whereas reducing exposure is thought to be protective.² Correspondingly, factors that increase the number of menstrual cycles, such as early menarche, nulliparity, and late menopause, are associated with increased risk. Moderate levels of exercise and a longer lactation period, factors that decrease the total number of menstrual cycles, are protective. Approximately one in every nine Pakistani women is likely to suffer from breast cancer. This is one of the highest incidence rates in Asia. Amazingly Pakistani women show an incidence of 50/100,000 and in the neighboring country India with similar socio-cultural background the incidence is 19/100,000. Differences in diet, racial or genetic factors may provide a partial explanation but it needs to be sorted out.³

Hormone receptor status is a key parameter in molecular classification of breast cancer, which serves as a marker of hormone-dependent growth and predictor of responsiveness to hormonal treatments.^{4,5} A recent literature review found evidence that nulliparity, late age at first birth and postmenopausal obesity are associated with increased risk for estrogen receptor- α (ER- α)-positive cancers as compared with ER- α -negative tumors, and that early menarche was more strongly linked to tumors co-expressing ER- α and progesterone receptor (PR).⁶ Subsequently, a meta-analysis updating this review affirmed the heterogeneous associations for nulliparity and late age at first birth, but not for age at menarche.^{7,8,9}

Due to high prognostic significance and frequency in Pakistani females with breast cancer, HER-2/neu receptor should be checked in all patients with breast cancer so that the positive cases should have specific anti HER-2 therapy which can improve survival in these patients. The purpose of present study is to find

out the frequency of HER-2/neu receptor in Breast cancer patients. The result of my study will provide a current magnitude of HER-2/neu Receptor in Breast Cancer patients. Variations in incidence of breast cancer among multicultural populations suggest that etiological factors vary in biological expression. On literature search it has been observed that very limited study available on this topic and no study available in our population. If the result of our study shows high prevalence of HER-2/neu Receptors in breast cancer it will indicate poor prognosis of our breast cancer patients. It will also help us to adopt strategies regarding prevention and treatment modification.

OPERATIONAL DEFINITIONS:

Breast Cancer: Patients having breast lump diagnosed as cancer on histopathology after tissue biopsy.

HER-2/neu Receptors positive:

Positive patients were those who were confirmed after immunohistochemical (IHC) staining of tissue biopsy. A Hercep test score of 3+ was considered as positive and a score less than this (0+, 1+,2+) was taken as negative for HER-2/neu receptor.

MATERIAL AND METHODS:

This cross-sectional study was conducted at Department of Surgery, Bahawal Victoria Hospital, Bahawalpur from January 2019 to June 2019 over the period of 6 months. Total 100 patients with breast cancer (having only lobular carcinoma / ductal carcinoma) as per operational definition and having age from 20-65 were selected. Patients having recurrent breast cancer. Patients who were not willing for immunohistopathology were excluded from the study.

Study was approved by the ethical committee of the hospital and written informed consent was taken from every patient.

Weight and height of all the patients was measured to calculate BMI. Age at first live birth was noted. Tissue of tumor was send to laboratory for estrogen and progesterone status, grade of tumor, histological type, histopathological grade and HER-2/neu Receptors status. All the data was recorded along with demographic profile of the patients on pre-designed proforma.

The data was analyzed by computer software SPSS Version 16. Mean and Standard Deviation was calculated for numerical data i.e. age of the patient, Age at first live birth in years and BMI. The qualitative data like HER-2/NEU receptor status (Positive or Negative), type of cancer (ductal / lobular) and hormone receptor status was labeled as frequency distribution table. Stratification will be done for age of the patient, Age at first live

birth in years and obesity. Post stratification chi-square test will be applied to see the association of these with outcome variable i.e. HER-2/NEU receptor status (Positive or Negative). P value ≤ 0.05 was considered to be considered as significant.

RESULTS:

Mean age of the patients was 43.78 ± 12.67 years. HER-2/Neu receptor was found positive in 40 (40%) patients and negative in 60 (60%) patients. (Fig. 1) Out of 100 patients, grade-I tumor was found in 21 (21%) patients followed by grad-II in 35 (35%) patients and grade-III tumor was found in 44 (44%) patients. (Fig. 2) Total 13 (13%) found with lobular carcinoma and 87 (87%) found with ductal carcinoma. (Fig. 3) ER was found positive in 75 (75%) patients and negative in 25 (25%) patients. PR was found in 65 (65%) patients and negative in 35% (35%) patients. (Fig. 4)

Patients were divided into two age groups i.e. age group 20-40 years and age group 41-60 years.

Total 38 (38%) patients belonged to age group 20-40 years and 62 (62%) patients belonged to age group 41-60 years. HER-2/neu receptor status was positive in 14 (36.84%) patients of age group 20-40 years and in 26 (41.94%) patients of age group 41-60 years. statistically insignificant association of HER-2/neu receptor status with age group was noted with p value 0.6772. (Table 1) Total 34 (34%) patients were obese and HER-2/neu receptor status was positive in 14 (41.18%) patients. Total 66 (66%) patients were non-obese and HER-2/neu receptor status was positive in 26 (39.39%) patients. Statistically insignificant association between obesity and HER-2/neu receptor status was noted with p value 1.000. (Table 2)

Fig. 1: Frequency of HER-2/Neu receptor status (positive/negative)

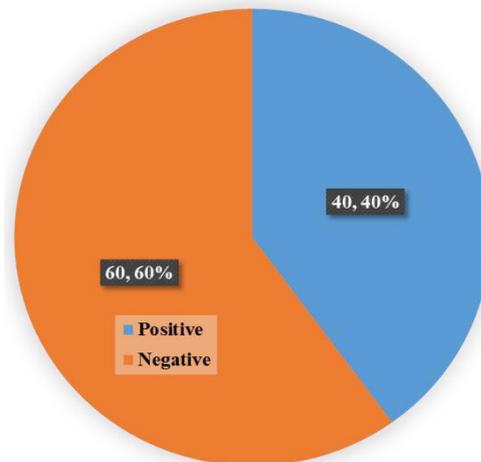


Fig. 2: Grades of tumor

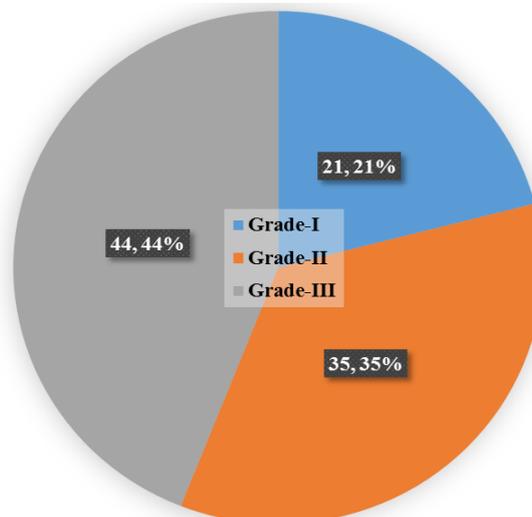


Fig. 3: Histopathological type in Breast cancer Patients

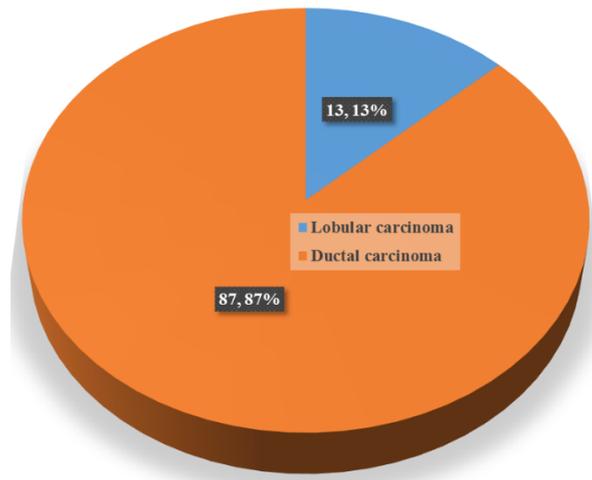


Fig. 4

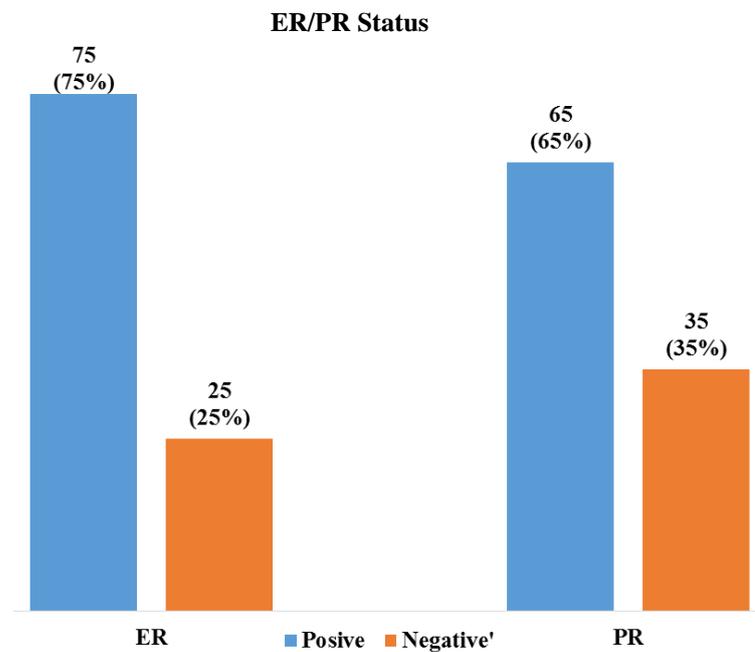


Table 1: Association of HER-2/neu receptor status with age

Age	HER-2/neu receptor status		Total	P. value
	Positive	Negative		
20-40	14 (36.84)	24 (63.16)	38 (38)	0.6772
41-60	26 (41.94)	36 (58.06)	62 (62)	
Total	40 (40%)	60 (60%)	100	

Table 2: Association of HER-2/neu receptor status with obesity

Obesity	HER-2/neu receptor status		Total	P. value
	Positive	Negative		
Obese	14 (41.18)	20 (58.82)	34 (34)	1.0000
Non-obese	26 (39.39)	40 (60.61)	66 (66)	
Total	40 (40%)	60 (60%)	100	

DISCUSSION:

HER-2/Neu receptor is a trans-membrane growth factor receptor belonging to type I receptor tyrosine kinase family of proteins. Because of its function as an activator of signaling pathways, HER2 plays a central role in a number of cellular processes, including proliferation, motility, and resistance to apoptosis.¹⁰ This effect may be enhanced by the overexpression of HER2 in cancer cells, leading to increased cell proliferation and decreased cell death, as well as changes in cell motility.¹¹

In present study, mean age of the patients was 42.88 ± 13.47 years. Favret *et al*,¹² Naeem *et al*¹³ and Sandhu *et al*.¹⁴ also reported comparable mean age of patients.

In our study, HER-2/Neu receptor was found positive in 40 (40%) patients and negative in 60 (60%) patients. Similar (45.8%) rate of positive HER-2/Neu receptor status was reported by Naeem *et al*.¹³ In one study, Naqvi *et al*⁴ reported positive overexpression of HER-2/Neu receptor in 31% patients which is not correlate with our findings. In another Alahwal MS¹⁵ reported HER-2/Neu receptor status positive in 28.3% patients. Ariga *et al*¹⁶ reported in their study that 15% patients were found positive for HER-2/Neu receptor. Naqvi *et al*,¹⁷ in 2002 reported that positive over-expression of HER-2/Neu receptor was found in 33% patients of breast cancer. These studies are in contrast with our findings for HER-2/Neu receptor status.

ER was found positive in 75 (75%) patients and negative in 25 (25%) patients. PR was found positive in 65 (65%) patients and negative in 35% (35%) patients. Similar results were found in a study conducted in Bangladesh, where Estrogen Receptor expression was positive in 69.0% patients and PR expression was positive in 72.3% patients.¹⁸ This variation may be because of different biological expression of breast cancer in different demographic profile. In one study conducted at Yamen, ER was positive in 43.8% patients and PR was positive in 27% patients.¹⁹

Patients were divided into two age groups i.e. age group 20-40 years and age group 41-60 years.

Total 38 (38%) patients belonged to age group 20-40 years and 62 (62%) patients belonged to age group 41-60 years. HER-2/neu receptor status was positive in 14 (36.84%) patients of age group 20-40 years and in 26 (41.94%) patients of age group 41-60 years. Statistically insignificant association of HER-2/neu receptor status with age group was noted with p value 0.6772. Al-ahwal¹⁵ has reported 34.1% of his young patients (≤ 40 years) positive for HER-2/neu receptor and 65.9% of those above 40 years of age. Majority of our breast patients were found with invasive ductal carcinoma on histopathology This is similar as compared to other studies where more than ninety percent of breast cancers were invasive ductal carcinoma.¹

Grade-I tumor was found in 21 (21%) patients followed by grad-II in 35 (35%) patients and grade-III tumor was found in 44 (44%) patients. These findings are in contrast with a study conducted in Yemen in 2011 where majority of patient presented with grade II (55.2%) followed by grade I (25.3%).¹⁹ This is almost close to study conducted in India in 2011 where majority of histological grade was III (44%).²⁰ This difference in studies might be due to interplay of different etiological factor in different demographic profile.

CONCLUSION:

Results of this study showed a higher rate of over expression of HER-2/Neu receptor. Most of the cases found with grade-III tumor. There was no association of HER-2/neu receptor status with age and obesity. In most of the patients, ER and PR was found positive.

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