

Research Article**A cross sectional study on HER-2 receptors in cases of breast cancer****¹Muhammad Umar Ijaz, ²Anum Anjum
and ³Arif Khaliq**¹Ex-House Officer, Mayo Hospital Lahore²Incharge Health Officer, Basic Health Unit 36 GB³Medical officer, Rural Health Center District Killa**ABSTRACT****Objective:** To study the HER-2 receptors positivity in cases of breast cancer.**Methods:** This was a cross sectional study and conducted at Department of Surgery, Mayo Hospital, Lahore from November 2016 May 2017. Total 120 consecutive women with breast cancer were recruited in this study. A tissue biopsy was sent for immune-histochemical (IHC) studies (HER-2/neu receptors and ER/PR receptors and detailed histo-pathological analysis including tumor subtype, histological grade.**Results:** All 120 female patients of breast cancer diagnosed on histopathology of tissue sample were selected for this study. Mean age of the patients was 43.3 ± 12.5 years. The Her-2/neu receptor, ER, PR receptor were found positive in 50 (42%), 94 (78.33%) and 81 (67.5%) of patients respectively. Majority our patients 108 (90%) tumor type was invasive ductal carcinoma on histopathology. In our study HER-2 Receptor status was not significantly associated with obesity ($p > 0.05$) but it was significantly associated with age of the patients ($p < 0.05$).**CONCLUSION:** There is high rates of positive expression Her-2 receptor in breast cancer patients and significant association was found between Her-2 receptor and age of the patients. Her-2/neu receptor status should be checked in all breast cancer along with estrogen and progesterone receptor especially in young female.**Key words:** HER-2/neu, breast carcinoma, ER/PR, over-expression, co-expression**INTRODUCTION:**

Breast cancer is one of the most common cancer in women and about 1 million women are diagnosed with breast cancer every year. It is one of the most common cancer related cause of death in women of middle age globally. There is a 10-fold variation in the prevalence of breast cancer among the different countries. Variations in the prevalence of breast cancer among multi-cultural populations suggest that etiological factors vary in biological expression and their impact on the outcome of disease. Breast cancer is commonly prevalent in Pakistani women.¹ The gradual increase in prevalence of breast cancer has created an urgent need to develop strategies for prevention. This disease have a complex etiology,

possibly with interplay of many causal factors including hormonal, genetic and environmental factors operating over a long period.²

Approximately 1 in every 9 Pakistani women suffers from breast cancer. This is the highest incidence rate of breast cancer in Asia. In Pakistani women the incidence of breast cancer is 50/100000 and in Indian women the incidence is 19/100000 with similar socio-cultural background.³

In molecular classification of the breast cancer, hormone receptor is a key parameter which serves as a marker of hormone-dependent growth and predictor of responsiveness to hormonal therapies.^{4,5} HER-2/Neu receptor is a trans-

membrane growth factor receptor which 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 motility, proliferation and resistance to apoptosis. This effect may be enhanced by the over-expression of HER-2/neu in cancer cells, leading to increased cell proliferation and decreased cell death, as well as changes in cell motility. It is expressed in 10% to 34% of breast carcinomas. Over-expression of HER-2/Neu receptor is associated with poor response to hormone receptor modulators. These patients are resistant to conventional treatment. They can opt for herceptin treatment which is highly efficient for these patients.¹

The aim of study is to determine the prevalence of HER-2/ neu receptor in Breast cancer patients. On literature search it has been observed that very limited data is available on this topic and no study available in our population especially in southern Punjab. So a study is planned to know the prevalence of HER-2/neu Receptor status in women with breast cancer. It may help us to adopt strategies regarding prevention and treatment modification.

MATERIAL AND METHODS:

This was a cross sectional study and conducted at Department of Surgery, Mayo Hospital, Lahore from November 2016 May 2017. Total 120 female patients having breast lump diagnosed as cancer on histopathology after tissue biopsy and having only lobular carcinoma / ductal carcinoma age range from 20-65 years were selected for study. Patients having recurrent breast cancer and patients who were not willing for immunohistopathology were excluded from the study. An approval was taken from institution review committee and written informed consent was taken from every patient.

HER-2/neu Receptors 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.

Weight and height of all the patients was measured to calculate BMI. Age at first live birth was also 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 laboratory findings were recorded along with demographic profile of the patients on pre-designed proforma. All the data were entered in SPSS version 17 and analyzed. Mean and SD was calculated for numerical variables and frequencies and percentages were calculated for categorical variable. Chi-square test was used to see the association between different study variables. P value ≤ 0.05 was considered as statistically significant.

RESULTS :

A total of 120 patients of breast cancer reporting to the Department of Surgery Bahawal Victoria Hospital (B.V.H) and Bahawalpur Institute of Nuclear Medicine & Oncology (BINO) were enrolled in the study. Diagnosis in all the patients was made on histopathology of tissue sample. All patients were female. Age ranged from 20 to 70 years with a Mean \pm SD of age 43.3 \pm 12.5 years.

The Her-2/neu receptor status was found positive in 50 (42%) patients and negative in 70 (58 %) patients. (Fig. 1)

Twenty three (19%) patients found with Grade-I tumor followed by 36 (30%) Grade-II and 61 (51%) had Grade-III tumor. (Fig. 2)

Out of 120 patients with breast cancer, ductal carcinoma was present in 108 (90%) patients and lobular carcinoma was present in 12 (10%) patients. (Fig. 3)

Stratification in relation to age was done and two age groups were made, age group 20-45 years and 46-70 years. In age group 20-45 years, out of 44 (36.67%) patients HER-2/neu receptor was found positive in 11 (25%) patients and out of 76 (63.33%) patients of age group 46-70 years, HER-2/neu receptor was found positive in 39 (51.32%) patients. HER-2/neu receptor status significantly

($P = 0.006$) associated with age of the patients. (Table 1)

Among the 43 (35.83%) obese patients, HER-2/neu receptor was found positive in 20 (46.51%) patients. In 77 (64.17%) non-obese patients,

HER-2/neu receptor was found positive in 30 (38.96%) patients. Insignificant ($P = 0.446$) association of HER-2/neu receptor with obesity was seen. (Table 2)

Fig. 1: Frequency of HER-2/Neu receptor status

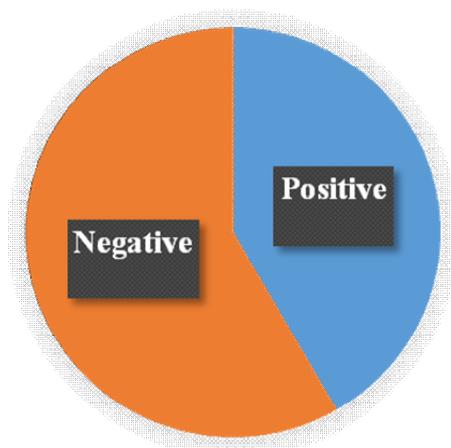


Fig. 2: Histopathological Grades of tumor in respondents

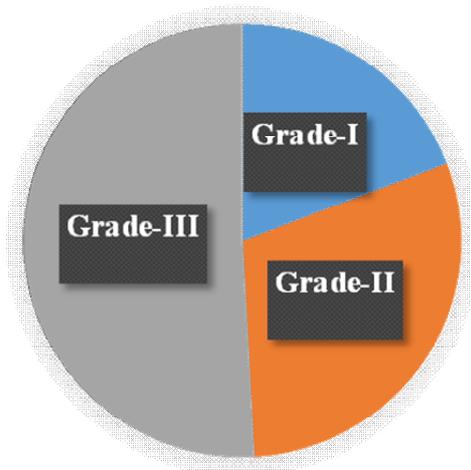


Fig. 3: Histopathological type in Breast cancer Patients

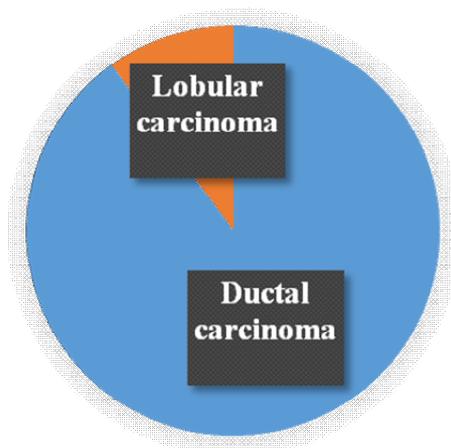


Fig. 4: ER/PR Status

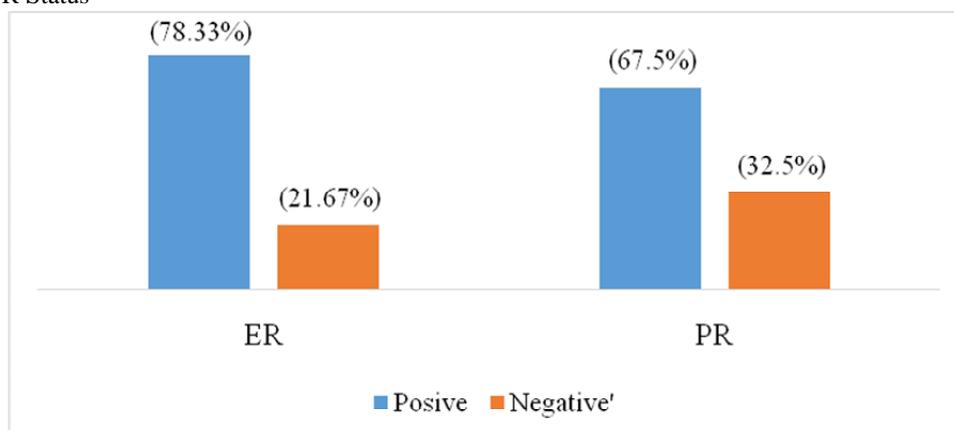


Table 1: Association of HER-2/neu receptor status with age

Age	HER-2/neu receptor status		Total	P. value
	Positive	Negative		
20-40	11 (25)	33 (75)	44 (36.67)	0.006
41-60	39 (51.32)	37 (48.68)	76 (63.33)	
Total	50 (42%)	70 (58%)	120	

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

Obesity	HER-2/neu receptor status		Total	P. value
	Positive	Negative		
Obese	20 (46.51)	23 (53.49)	43 (35.83)	0.446
Non-obese	30 (38.96)	47 (61.04)	77 (64.17)	
Total	50 (42%)	70 (58%)	120	

DISCUSSION:

HER-2/Neu receptor is a trans-membrane growth factor receptor belonging to type I receptor tyrosine kinase family of proteins. HER-2/Neu receptor over-expression is associated with poor response to hormone receptor modulators. These patients are resistant to conventional therapy. Over expression of the HER2 receptor is associated with poor prognosis in patients with breast cancer, as well as with aggressive tumor growth and metastases.¹⁰

Our study comprised of 120 cases of invasive breast cancer with a mean age of 43.3±12.5 years. Similar mean age of patients of breast cancer was reported by Favret et al,¹²Naeem et al¹³ and Sandhu et al.¹⁴

In my study HER- 2/neu was positive in 42% patients and negative in 58%. Naeem et al,¹³ found HER-2/neu receptor positive in 45.8% patients of breast cancer which is in agreement with our study. On the other hand Naqvi et al⁴ reported positive overexpression of HER-2/neu receptor in 31% patients. Alahwal MS¹⁵ found 28.3% patients of breast positive for HER-2/neu receptor. Arigaet al¹⁶ reported in their study that 15% patients was 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.

Our study showed that 78.33 % of cases had positive estrogen receptor expression while 67.5

% expressed Progesterone. Expression of estrogen and progesterone in my study is high as compared to a study in yamen with estrogen receptors expressed in 43.8 % and progesterone receptors in 27% patients.¹⁸ This is similar when compared to some Western studies which have reported 73% ER positivity and 58% PR positivity. Similar result also found in a study in bangladesh where Estrogen Receptor expression was positive in 69.0%, PR expression was positive in 72.3% of patients.¹⁹ This variation may be because of different biological expression of breast cancer in different demographic profile.

In this study HER-2/neu receptor found positive in 25% patients of age group 20-40 years and 51.32% in age group 41-60 years. Al-ahwal¹⁵ has documented 34.1% of his young patients (≤ 40 years) positive for HER-2/neu receptor and 65.9% of those above 40 years of age. These findings are comparable with our findings.

Majority of our breast patients were found with invasive ductal carcinoma on histopathology. This is similar as compared to other studies where more than 90% of breast cancers were invasive ductal carcinoma.¹³ The commonest histological grade was III 51% followed by Grade II 30% and Grade I was 19%. These findings are in contrast with a study conducted in yamen in 2011 where majority of patient presented with grade II (55.2%) followed by grade I (25.3%).¹⁸ 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 etiologic factor in different demographic profile.

In present study out of 43 obese patients, HER-2/neu receptor was found positive in 46.51% patients and out of 77 non-obese patients, HER2/neu receptor was found positive in 38.96% patients. The association of HER-2/neu receptor status with obesity was not statistically significant ($P = 0.446$). This was different to a study where HER-2receptor status was positively correlated with increasing BMI among post-menopausal women ($p=0.048$).²¹

CONCLUSION:

In conclusion, study of Her2/neu receptor in breast cancer patients indicates that there are high rates of positive expression of these receptors. There is a significant correlation between Her-2 receptor and younger age group. Her-2/neu receptor status should be checked in all breast cancer along with estrogen and progesterone receptor especially in young people because it has a great impact on further management with trastuzumab and anthracycline based chemotherapeutic agents. There is also need to explore Her-2 receptor correlation with other etiologic factors especially in young people.

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