FREQUENCY OF ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, AND HER2/NEU EXPRESSION IN BREAST CANCER PATIENTS AT QUETTA – A HOSPITAL-BASED STUDY

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ABSTRACT

Objective: To determine the frequency of Estrogen receptor (ER), Progesterone receptor (PR) and HER2/Neu expression in breast cancer patients.

Methods: Retrospective observational study conducted at Combined Military Hospital, Quetta, from 01 Jan 2022 to 30 March 2025. The study included 100 patients aged 22 to 88 years, all with comprehensive clinical and histopathological data. Data analysis was performed using SPSS version 20, employing chi-square tests to evaluate associations. Statistical significance was determined at $p<0.05$.

Results: Among the 100 patients, 91% (n=91) were diagnosed with Invasive ductal carcinoma (IDC NST), followed by 4% (n=4) with Invasive lobular carcinoma (ILC), 4% (n=4) with Mucinous carcinoma, and 1 case of Metaplastic carcinoma. ER was positive in 64% (n=64) of cases, PR was positive in 54% (n=54), and Her2 was positive in 24% (n=24). Of these cases, 54% (n=54) were ER+/PR+, 12% (n=12) were ER+/PR-, 1 case was ER-/PR+, and 33% (n=33) were negative for both ER and PR, including 20% (n=20) cases of triple-negative breast cancer (TNBC). Hormone receptor expression was analyzed in relation to different age groups, histological subtypes, and histological grades.

Conclusion: The study identified a significant correlation between histological grade and hormone receptor expression with lower grades exhibiting higher hormone receptor positivity. However, no statistically significant association was observed between hormone receptor expression and histological subtype or specific age groups.

Keywords: Hormone receptors, Modified radical mastectomy, Triple negative breast cancers.

INTRODUCTION

Breast cancer is one of the most common cancer diagnosed worldwide. In 2020, 2.26 million new cases of breast cancer were reported.[1] It is the main cause of cancer related deaths in females worldwide. The global burden of breast cancer will rise, particularly in developing countries, due to socioeconomic factors and tumor biology variations associated with genetic ancestry.[2]

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Breast cancer incidence has increased 57.8% over three decades, with an annual growth rate of 0.5%.[3] In Asia, breast cancer comprised 10.8% of cancer cases in 2020, ranking second most prevalent in the region.[4] Breast cancer is among the most common cancers in females in Pakistan, affecting one in nine females.[5] In Pakistan, the age-standardized incidence rate of breast cancer was recorded at 7.60 per 100,000 women, with around 6,166 new cases each year.[6] The burden of breast cancer in Pakistan necessitates enhanced awareness, early detection, and comprehensive treatment.

The prognosis and decision of treatment for breast cancer rely on multiple important factors. Axillary lymph node status remains a key prognostic indicator, with larger tumor size and age less than 60 years associated with higher lymph node positivity.[7] Tumor grade, lymphovascular invasion (LVI), and the size of the tumor are recognized as risk factors for metastasis to the sentinel lymph node.[8]

Hormone receptors, Estrogen receptor (ER), Progesterone receptor (PR), and Human epidermal growth factor receptor 2 (HER2) are integral to breast cancer classification, prognosis, and therapeutic decisions. These receptors inform management strategies and impact patient outcomes.[9] Their presence or absence delineates breast cancer's molecular subtype, influencing treatment modalities. Tumors that are ER and PR positive typically respond well to hormone treatments, whereas cancers with HER2 positivity might be effectively treated with anti-HER2 targeted therapies. The interaction among these receptors, particularly in single hormone receptor positivity or low expression, can influence prognosis and treatment response, necessitating accurate receptor status assessment.[10]

In Pakistan, the expression of ER, PR, and HER2 in breast cancer patients shows varying frequencies. In remote areas of Pakistan, breast cancer presents a major health issue due to the scarcity of diagnostic and treatment resources. This study evaluates these biomarkers' prevalence in breast cancer patients in Quetta, emphasizing diagnostic and treatment access disparities. Identifying receptor expression patterns will help customize therapeutic strategies, enhance awareness, and advocate for improved oncological care in underserved areas to enhance survival rates and quality of life.

MATERIALS AND METHODS

Our study was a retrospective observational. It was conducted at Combined Military Hospital Quetta, on patients who presented with breast lesions between 01 Jan 2022 and 30 Mar 2025 (CMH QTA-IERB/107/2025).

Inclusion Criteria: The study population included adults of both genders aged 22 years to 88 years who presented with breast lumps and were diagnosed with a malignant diagnosis following trucut biopsies, incisional biopsies, and mastectomies. Also, the patients for whom immunohistochemical markers for hormone receptors ER, PR, and HER2 were applied were included. Cases with complete clinical and histopathological details were included in the study.

Exclusion criteria: The cases in which there was incomplete biopsy data or inadequate tissue samples for histological evaluation were excluded. Patients with benign diagnoses and on whom no Immunohistochemical markers were applied were also excluded. Specimens that were poorly fixed or not representative were excluded as well.

In our study 100 cases were included in total. All trucut, incisional biopsies, and mastectomies were reported using the RCPath guidelines. ER and PR staining was interpreted using the Allred scoring system. Data was collected from hospital electronic records and histopathology archives. Variables included patient demographics (age, gender), tumor size, histological grade, histopathological results, and hormone receptors and HER2/Neu status. Ethical approval was obtained (CMH QTA-IERB/107/2025). Data confidentiality was maintained. SPSS version 20 was used for analysis of data. Chi-square tests were used to check for any association between age, histological diagnosis, and histological grade with hormone receptor status. We divided patients into four age groups: group I (< 25 years), group II (26–40 years), group III (41–60 years), and group IV (>60 years). A p-value less than 0.05 was taken as statistically significant.

RESULTS

The patients in our study ranged in age from 22 years to 88 years. Mean age was 48.86 years with a standard deviation of 14.03. Most of the cases were between 35 and 60 years of age. Females comprised the predominant group, representing 99% (n=99) of the sample, while only one male accounted for 1% (n=1). The samples primarily consisted of trucut biopsies (n=72) and modified radical mastectomy (MRM) specimens (n=16), followed by incisional biopsies (n=11) and one case of wide local excision. Among all breast cancer cases, 91% (n=91) were classified as invasive ductal carcinomas, no special type (IDC NST), 4% (n=4) as invasive lobular carcinomas (ILC), 4% (n=4) as mucinous carcinomas, and 1% (n=1) as metaplastic carcinoma. Ductal carcinoma in situ (DCIS) was observed in 12% (n=12) of cases, and lymphovascular invasion (LVI) was noted in 13% (n=13) of cases. Immunohistochemical analysis of tumor samples revealed distinct expression profiles for estrogen receptor, progesterone receptor, and Human Epidermal Growth Factor Receptor 2 (Her2/Neu). A comprehensive overview of hormonal receptor and Her2/Neu status, are also summarized in Table 1.

Table 1: Distribution of Hormone Receptors and Her2/Neu (n=100)

Hormone Receptor	Positive	Negative	Total	Remarks
ER	64 (64%)	36 (36%)	100 (100%)	
PR	54 (54%)	46 (46%)	100 (100%)	
Her2/Neu	24 (24%)	74 (74%)	100 (100%)	2 (2%) Equivocal

On analyzing data, 54% of cases were ER+/PR+, 12% were ER+/PR-, 1 case was ER-/PR+, and 33 cases were negative for both ER and PR, including 20 cases of triple-negative breast cancer, as shown in Figure 1.

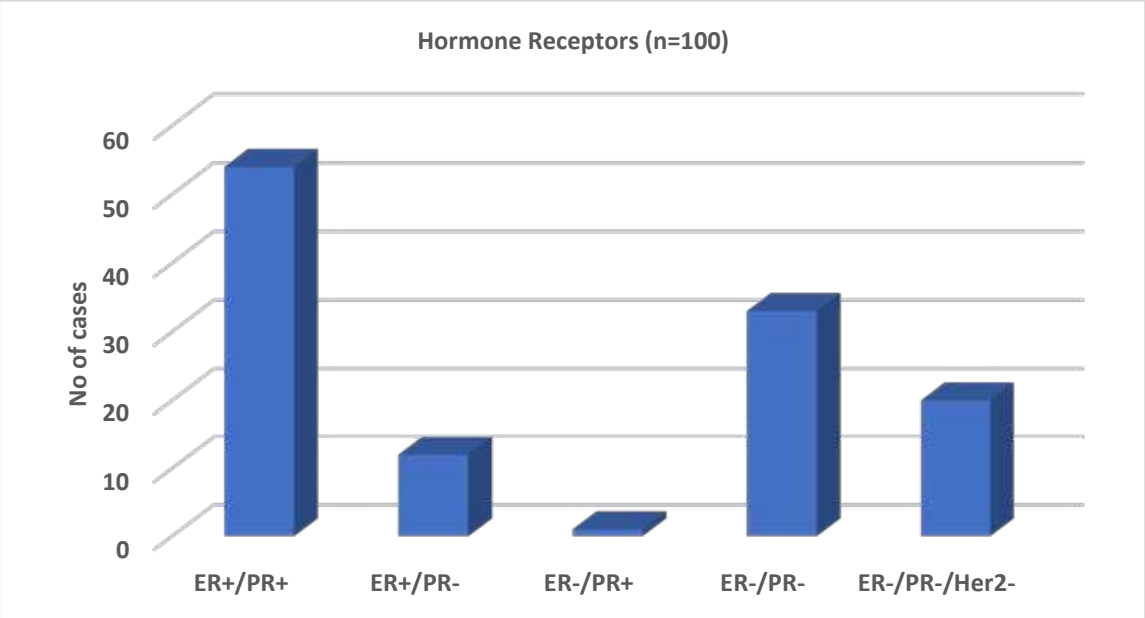

Figure 1: Distribution of Hormone receptors and Her2/Neu (n=100)

The distribution of hormone receptors (ER, PR) and HER2/Neu was compared across various histological breast cancer groups. Group III showed a higher number of ER-positive cases, 61.4% (n=27), while Group IV demonstrated a higher number of ER and PR positivity, 76.2% (n=16) and 61.9% (n=13), respectively. However, no statistically significant differences were observed in the distribution of hormone receptors and HER2/Neu, as the p-value exceeded 0.05, as shown in Table 2. Group III also exhibited the highest HER2/Neu positivity at 34.9% (n=15), yet these findings were not significant statistically.

Table 2: Distribution Of Hormone Receptors And HER2/Neu Across Different Age Groups

Hormone Receptor	Age Groups	Hormone Receptor Status		Total	P value
		Positive	Negative		
ER	Group I	0	2 (100%)	2 (2%)	0.184
	Group II	21 (63.6%)	12 (36.4%)	33 (33%)	

	Group III	27 (61.4%)	17 (38.6%)	44 (44%)	
	Group IV	16 (76.2%)	5 (23.8%)	21 (21%)	
	Total	64 (64%)	36 (36%)	100 (100%)	
PR	Group I	0	2 (100%)	2 (2%)	0.396
	Group II	19 (57.6%)	14 (42.4%)	33 (33%)	
	Group III	22 (50%)	22 (50%)	44 (44%)	
	Group IV	13 (61.9%)	8 (38.1%)	21 (21%)	
	Total	54 (54%)	46 (46%)	100 (100%)	
Her2/Neu	Group I	0	2 (100%)	2 (2.04%)	0.276
	Group II	6 (18.2%)	27 (81.8%)	33 (33.7%)	
	Group III	15 (34.9%)	28 (65.1%)	43 (43.8)	
	Group IV	3 (15%)	17 (85%)	20 (20.4%)	
	Total	24 (24.5%)	74 (75.5%)	98 (100%)	

Hormone receptor (ER, PR) and HER2/Neu status were also compared across specific histological subtypes of breast cancer to identify any associations between receptor expression and histological subtype. The majority of cases were invasive ductal carcinoma (IDC), accounting for 91% (n=91), with ER expression in 61.5% (n=56) and PR expression in 52.7% (n=48) of cases. Mucinous and invasive lobular carcinoma (ILC) cases exhibited 100% ER and PR positivity, although these cases were limited in number. Metaplastic carcinoma showed no receptor positivity and was therefore classified as triple-negative. No statistically significant differences were found between histological type and all three hormone receptor status (ER, PR, HER2/Neu), as indicated in Table 3.

Table 3: Distribution Of Hormone Receptors (ER, PR) And HER2/Neu Across Various Histological Subtypes of Breast Cancers (n=100)

Hormone Receptor	**Histological Type**	**Hormone Receptor Status**		**Total**	**P value**
		Positive	Negative		
ER	IDC	56 (61.5%)	35 (38.%)	91 (91%)	0.189
	ILC	4 (100%)	0	4 (4%)	
	Mucinous Ca	4 (100%)	0	4 (4%)	
	Metaplastic Ca	0	1 (100%)	1 (1%)	

	Total	64 (64%)	36 (36%)	100 (100%)	
PR	IDC	48 (52.7%)	43 (47.3%)	91 (91%)	0.423
	ILC	2 (50%)	2 (50%)	4 (4%)	
	Mucinous Ca	4 (100%)	0	4 (4%)	
	Metaplastic Ca	0	1 (100%)	1 (1%)	
	Total	54 (54%)	46 (46%)	100 (100%)	
Her2/Neu	IDC	24 (26.9%)	65 (73.1%)	89 (90.8%)	0.915
	ILC	0	4 (100%)	4 (4.1%)	
	Mucinous Ca	0	4 (100%)	4 (4.1%)	
	Metaplastic Ca	0	1 (100%)	1 (1.02%)	
	Total	24 (24.5%)	74 (75.5%)	98 (100%)	

The expression of hormone receptors (ER, PR) and HER2/Neu was subsequently compared with the histological grade (Grade 1 to 3) of breast cancer, accompanied by P-values to assess statistical significance. The expression of ER and PR was found to be significantly associated (p-value <0.05) with tumor grade, with lower grades exhibiting higher hormone receptor positivity. In contrast, there was no statistically significant correlation of grade with HER2/Neu expression in this cohort, as shown in Table 4.

Table 4: Distribution Of Hormone Receptors And Her2/Neu Across Different Histologic Grades (n=100)

Hormone Receptor	**Histological Grade**	**Hormone Receptor Status**		**Total**	**P value**
		Positive	**Negative**		
ER	Grade 1	6 (85.7%)	1 (14.3%)	7 (7%)	0.002
	Grade 2	53 (71.6%)	21 (28.4%)	74 (74%)	
	Grade 3	6 (31.6%)	13 (68.4%)	19 (19%)	
	Total	65 (6%)	35 (35%)	100 (100%)	
PR	Grade 1	6 (85.7%)	1 (14.3%)	7 (7%)	0.011
	Grade 2	43 (58.1%)	31 (41.9%)	74 (74%)	
	Grade 3	5 (26.3%)	14 (73.7%)	19 (19%)	

	Total	54 (54%)	46 (46%)	100 (100%)	
Her2/Neu	Grade 1	0	7 (100%)	7 (7.1%)	0.480
	Grade 2	18 (25%)	54 (75%)	72 (73.5%)	
	Grade 3	6 (31.6%)	13 (68.4%)	19 (19.4%)	
	Total	24 (24.5%)	74 (75.5%)	98 (100%)	

DISCUSSION

The prevalence of ER, PR, and HER2 in breast cancer shows variation worldwide and regionally. A comprehensive study conducted in the United States reported that 75.1% of cases were ER+PR+, 9.7% were ER+PR-, 0.9% were ER-PR+, and 14.3% were ER-PR-.[11] This distribution highlights the dominance of hormone receptor positive breast cancers among Western populations. Similarly, a study in South Asia focusing on HER2-negative breast cancers found that 90.5% of HER2-low cases were hormone receptor-positive, while 62.4% of HER2-0 cases were hormone receptor-positive.[12] Our study revealed that 67% (n=67) of hormone receptor-positive cases were ER+/PR+, while 33% (n=33) were hormone receptor-negative, aligning with these studies. In our study, 20% (n=20) of cases were TNBCs, which are biologically aggressive. These tumors do not respond to hormonal therapy, and chemotherapy remains as the only mode of treatment in such patients. Around 12-20% of all breast cancer cases globally are TNBCs.[13] A study conducted in Lahore, Pakistan, reported 18.7% of cases as TNBCs which also correlates with our study.[14] The slightly lower hormone receptor positivity and higher incidence of TNBCs in our study may be attributed to the occurrence of breast cancers at relatively younger ages and advanced stages at presentation, genetic factors, and inadequate screening protocols. These findings highlight the necessity of understanding regional variations in breast cancer subtypes to tailor appropriate screening and treatment strategies.

Histologic subtypes of breast cancers possess distinct characteristics and prognostic significance. The most common subtype, invasive carcinoma of no special type (IDC NST), represents the majority of cases. However, special subtypes such as invasive lobular carcinoma (ILC), mucinous, tubular, medullary, metaplastic, and micropapillary carcinomas exhibit unique features.[15] We found in our study that the majority of cases, 91%, were of the IDC NST type, followed by 4% (n=4) cases of ILC, 4% (n=4) mucinous carcinoma, and 1% cases of metaplastic carcinoma. These findings were consistent with other local and international studies.[15] While ILC is classified as luminal A with favorable prognostic features, some studies suggest a higher risk of late distant recurrence compared to IDC, NST.[16] Mucinous carcinoma of the breast is characterized by elevated expression of ER and PR, alongside reduced expression of HER2 when compared to other breast cancer subtypes.[17] This pattern was corroborated in our study, where all 4% (n=4) of cases were positive for hormone receptors. Metaplastic breast carcinomas, known for their aggressive nature, are predominantly TNBCs.[18] The single case in our study was also triple-negative.

Different age groups significantly influence the expression of ER, PR, and HER2 in breast cancer, thereby affecting prognosis and treatment strategies. In women under 40, the behaviour of breast cancer is more aggressive. These patients have an increased incidence of ER-negative and HER2-positive tumors.[19] Our study demonstrated increased hormone receptor expression with advancing age, with ER positivity observed in 76.2% (n=16) and PR positivity in 61.9% (n=13) of group 4, compared to younger patients. Recent studies have underscored the importance of independently considering PR status, as low PR expression in young breast cancer patients (under 40) correlates with a poorer prognosis compared to those with strong PR expression.[20] This suggests that PR status may serve as a critical prognostic factor in young breast cancer patients. HER2 expression is seen across all age groups and is associated with advanced-stage disease and increased mortality. A study utilizing data from the National Clinical Database-Breast

Cancer Registry in Japan found that HER2-positive breast cancer in elderly patients (aged 65 and older) was linked to elevated 10-year mortality rates across all stages.[21] Another study involving younger patients (<40 years) with HER2-positive breast cancer indicated a tendency towards more aggressive tumor characteristics and poorer prognosis.[22] In our study, HER2 expression was noted in 24.5% (n=24) of cases, with the majority occurring in age group 3 (34.9%, n=15).

The expression of ER, PR, and HER2 is also closely associated with the histologic grades of tumors. Research indicates that tumors that show hormone receptor positivity are generally of lower grade, whereas HER2-positive and TNBCs are often of higher grade.[17,23] A study carried out in Iraq between 2018 and 2021 found grade II (low grade) tumors in 64.44% of the cases, making them the most common. The hormone receptor status indicated that 46.67% of cases were ER-positive and 42.22% were PR-positive, while 62.22% were HER2-negative.[24] The relationship between receptor status and tumor grade has significant implications for treatment strategies. Similar findings were observed in our study, where ER and PR expression were highest (85%) in grade 1 tumors. In grade 2 tumors, 71.6% (n=53) were ER positive, and 58.1% (n=43) were PR positive.

CONCLUSION

These biomarkers are crucial in formulating treatment strategies and determining prognosis for breast cancer patients. Understanding their frequency within this specific population can aid in tailoring treatment approaches and enhancing patient outcomes. The expression of these receptors may vary across populations and can be influenced by factors such as ethnicity and environmental conditions. Such studies will enable healthcare providers to gain a deeper understanding of the local breast cancer landscape and adapt treatment strategies accordingly. Furthermore, these studies highlight the necessity for improved breast cancer screening, awareness, and treatment strategies in such remote areas of Pakistan.

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