Section: Miscellaneous

Original Research Article

# CORRELATION OF HISTOLOGICAL TYPE AND GRADE WITH ER/PR AND HER-2/NEU STATUS IN BREAST CARCINOMA PATIENTS AT TERTIARY CARE HOSPITAL, NORTHERN INDIA

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## ABSTRACT

**Background:** Breast carcinoma is the most common malignancy among women worldwide and shows wide variation in clinical, histopathological, and molecular features. Evaluation of Estrogen receptor (ER), Progesterone receptor (PR), and HER-2/neu expression plays an important role in determining prognosis and guiding targeted therapy. Correlation of these markers with tumor size, histological grade, and lymph node status helps in assessing tumor behavior and planning appropriate management. **Materials and Methods:** This observational study was conducted in the Department of Pathology of a tertiary care hospital, Northern India, from June 2025 to March 2026. A total of 56 surgically treated cases of breast carcinoma were included. All specimens were examined histopathologically and graded using the Nottingham modification of Bloom–Richardson system. Immunohistochemistry for ER, PR, and HER-2/neu was performed using the peroxidase–antiperoxidase method. The receptor status was correlated with clinicopathological parameters including age, tumor size, histological grade, and lymph node involvement. **Results:** Most patients were in the age group of 41–50 years. The majority of tumors measured 2–5 cm and were grade II carcinomas. Invasive ductal carcinoma (NOS) was the most common histological type. ER and PR positivity was observed in 50% and 42.86% cases respectively, while HER-2/neu positivity was seen in 42.86% cases. ER and PR positivity showed significant association with smaller tumor size, lower tumor grade, and fewer lymph node metastases. HER-2/neu overexpression was associated with larger tumor size, higher grade, and increased lymph node involvement. Triple-negative tumors constituted a smaller proportion and were associated with poor prognosis. **Conclusion:** Immunohistochemical evaluation of ER, PR, and HER-2/neu provides valuable prognostic information in breast carcinoma. Hormone receptor positivity indicates better prognosis, whereas HER-2/neu overexpression is associated with aggressive tumor behavior, highlighting the importance of receptor status in therapeutic decision-making.

## INTRODUCTION

Breast cancer is the most common cancer and the leading cause of death in women, with more than one million cases occurring worldwide every year.[1] It accounts for 20% of all malignancies among females and 15% of all cancer deaths.[2] The incidence of breast cancer is greater in women of higher socio-economic background.[3] It is of serious concern owing to the rising incidence of the disease in the last 5-10 years.4 It is estimated that every year, around 78,500 cases of breast cancer are occurring in India.[5] The population-based cancer registry data from the various parts of the country, has revealed breast cancer as the commonest cancer among women in Delhi, Mumbai, Ahmedabad, Calcutta and Trivendram.[6]

Breast cancer is recognized to be a heterogenous group of diseases comprising of many biological subtypes with altered natural history and present with a varied spectrum of clinical, pathological and, molecular features with different prognostic and therapeutic implications. , Regarding the definitive prognostic/ predictive analysis, consensus has yet to be reached, but significant progress continues to be made in the search for a rigorous, specific and reproducible method of identifying successful treatment, utilizing biological markers.[7] It has been


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documented that factors such as age, age at menarche, marital status, age at menopause, place of residence (rural/urban), religion and family history of breast cancer can all play role as risk factor. Prognosis is related to a variety of clinical, pathological and molecular features which include classical prognostic factors that are histologic type, histologic grade, tumor size and lymph node metastasis, status of hormonal receptors- estrogen receptor (ER) and progesterone receptor (PR) and recently HER-2/neu status.[8] An imbalance precipitates abnormal processes like epithelial hyperplasia, intraductal and invasive carcinoma.[9] Over the last few decades of years there have been better, advances in breast cancer management leading to earlier detection of disease and the development of more effective treatment, resulting in significant decrease in number of deaths due to breast carcinoma and improved survival.[10] Estrogen is an important mitogen exerting its activity by binding to its receptor (ER) and found in 50-80% of breast cancers. PR is a surrogate marker of a functional ER and help in predicting the behavior of breast carcinoma and expressed in 60-70% of breast cancer with higher positivity in older age and postmenopausal women.[11] ER (Estrogen Receptor) & PR (Progesteron Receptor) status of breast cancer is now established as an excellent predictive marker & a weak prognostic marker. Breast cancers which express ER and PR can be effectively treated with anti-estrogen therapy with tamoxifen, prolonging disease-free survival.[12] ER positive tumors in 55-60% women respond to additive or ablative hormone therapy, compared with about 8% of women with ER negative tumors. Better differentiated tumors are more likely to be ER and PR positive and have a better prognosis.[13,14] HER-2/neu proto-oncogene (also known as c-erbB2) is located on chromosome 17q 11,[5-7] which encodes for p185 a transmembrane glycoprotein with tyrosine kinase activity, belongs to the family of epidermal growth factor receptors.15 The role of HER-2/neu (Human, Epidermal Growth Factor Receptor-2) for prognostication & for determining the optimal therapy in breast cancer is currently evolving. Amplification of the HER-2 gene leads to over expression of HER-2/neu protein on the surface of cells in approximately 25-30% of invasive primary breast cancers.[16] Association have been found to exist between overexpression of HER-2/neu and wide variety of different clinicopathological features of breast carcinoma that include: Large size, high histologic grade, lack of steroid receptor expression, lymphoid infiltration, p53 mutation, axillary lymphnode metastasis, advanced age, early relapse and reduced overall survival.[17,18] Breast cancers with HER-2/neu alterations are now treated with specific anti-HER-2/neu targeted therapies with transtuzumab(Herceptin) which have been shown to improve response rate and survival when added to chemotherapy or as monotherapy.[19] HER-2/neu is recognized to be a very good prognostic marker.[11,16] ImmunoHistochemistry (IHC) is the most reliable method for the determination of hormone receptor status in breast cancer. The interrelationship of ER, PR and HER-2/neu has become an important role in management of breast cancer. It has been shown that patients with breast carcinoma overexpressing HER-2/neu do not respond to tamoxifen therapy. Although HER-2/neu expression generally is inversely correlated with ER and PR expression.20 IHC-based classification of ER/PR and HER-2/neu status provides an information of therapeutic and prognostic importance, is inexpensive and readily available.[21]

Triple negative breast cancer(TNBC) is defined as a group of breast carcinomas that are negative for expression of hormone receptors(ER, PR, HER-2/neu), we can distinguish between two groups: basal-like (ER- , PR- , HER-2/neu- , cytokeratin(CK) 5/6+ and/or Her11+) and unclassified subtype (ER- , PR- , Her1- and CK5/6-).[22] The overall prevalence of TNBC in breast cancer patients 11-20%.[23] The BRCA1 mutations occur in close to 20% of sporadic TNBC and are associated with improved prognosis.[24] Triple negative breast cancer has distinct clinical and pathological features and is a clinical problem because of its relatively poor prognosis, aggressive behavior and cannot be treated with endocrine therapy or anti HER-2/neu therapy, leaving only chemotherapy as a mainstay treatment.[25]

**Aim and objectives**

1. To study the clinical profile of breast cancer in Tertiary Care Hospital.
2. To study the pattern of expression of Estrogen and Progesterone receptor (ER & PR) and HER-2/neu in cases of breast carcinoma operated in this hospital, using Immunochemistry method.
3. To correlate ER, PR status and HER-2/neu expression with

- Various clinical parameters like size of the tumor and lymph node status.
- Pathological aspects, like histological type and grade, tumor size.
- Association of ER, PR status with HER-2/neu status.

4. To compare results with other studies in India and abroad where similar immunohistochemistry method is used with internationally accepted scoring system.
5. To evaluate the role of ER, PR & HER-2/neu status in the management of breast cancer patients in Tertiary Care Hospital.

## MATERIALS AND METHODS

The present study was undertaken by the department of pathology, tertiary care hospital, Northern India, with collaboration of the department of surgery in this hospital.

**Design of study:** Observational study.

**Study period:** June 2025- March 2026


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**Inclusion Criteria:** Patients with breast carcinoma who were treated with surgery (Modified Radical Mastectomy and Lumpectomy).

**Exclusion Criteria**

1. Patients of breast carcinoma who were managed without surgery.
2. Patients with breast cancer in when adequate clinical data was not available.
3. Patients with metastasis of cancer in breast.

**Method**

56 Breast specimens were received at histopathology department for diagnosis with histopathological type, grade and the aid of immunohistochemistry (ER, PR, HER2/neu). After histopathological examination, immunohistochemical antibodies ER, PR and HER2/neu were applied using peroxidase ant peroxidase method. Gross examinations of specimens were done under heads of overall appearance, size of specimen and tumour, ulceration, fungation, appearance of cut surface. Tissue sections were taken from representative location -various level of lesion, from surgical margin, normal tissue &lymphnode number, if identified in received tissue. Specimens were fixed as early as possible by 10% neutral buffered formalin & processed preferably with in 24 hrs of surgery of patient. After routine paraffine processing, 3-5micron thick sections were cut and stained by Hematoxylin –Eosin method (H & E Method).

## RESULTS

The present study was conducted on the 56 Modified mastectomy specimens (mastectomies with axillary lymph node) received at histopathology section (Figure 1). Total 29 cases (51.79%) were below the age of 50 years, while the remaining 27 cases (48.21%) were 50-year-old or more. The age presentation of patients revealed that maximum cases 21 cases (37.5%) were seen between 41 to 50 years of age(Table-1). Tumor size ranged from 1.5-10 cm. Of the 56 breast cancer cases there were 3 cases (5.36%) of T1 (<2cm), 41 cases (73.21%) of T2 (2-5cm), 12 cases (21.43%) were T3 (>5cm). Majority of the tumors measured in the T2 range of 2-5 cms with a percentage of 73.21%. [Table-2]

In present study most of breast carcinoma (46 cases; 82.14%) were pure Invasive ductal carcinoma - Not otherwise specified (NOS) (Figure 2), while of total 10 cases (17.86%) included Invasive ductal carcinoma (IDC) with Invasive lobular carcinoma component (Figure 3), Mucinous carcinoma (Figure 8), and IDC with Paget's disease and IDC with tubular carcinoma and solid papillary carcinoma with invasion. [Figure 7, Table-3]

The present study showed Nottingham Modification of Bloom Richardson (BR) scoring system that 34 cases (60.71%) of the tumors had tubules formation in <10% of the tumor area. A moderate nuclear pleomorphism was seen in 36 cases (64.29%) and 28 cases (50%) showed mitotic index between 0-5 /10 hpf (0.44 mm of field diameter). [Table-4]

According to Nottingham Modification of Bloom Richardson Grading System, grade I was seen in 8 cases (14.29%) out of 56 cases, 35 cases (62.50%) were grade II and 13 cases (23.21%) were grade III. Majority of the tumors were histopathological grade II (62.50%), followed by grade III (23.21%). [Table-5]

In present study maximum cases (21 cases; 37.50%), showed >3 lymph node positivity, while 17 cases (30.36%) did not show\ lymph node metastasis.

ER and PR expression were positive in 28 (50%) and 24 (42.86%) cases respectively (Figure 4,5). Simultaneous positive expression of ER, PR were found in 23 cases (41.07%) and 27 cases (48.21%) out of 56 cases were ER, PR negative. HER-2/neu in the positive expression 24 cases (42.86%) (Figure 6) and 32 cases were negative (57.14%).

The percentage of ER and PR positivity was found to be higher (59.26%, 51.85% respectively) in the age group of >50 Years than in <50 years (41.38%, 34.48%, respectively). HER-2/neu positivity was found to be higher (44.44%) in the age group of >50 Years than in <50 years (41.38%). ER, PR & HER-2/neu receptor positivity was not significantly associated with the age.

ER and PR positivity was significantly associated with small tumor size & HER-2 positivity was significantly associated with large tumor size.

ER and PR expression was seen to be decreased with increased number of positive lymph nodes. HER-2/neu overexpression was increased as number of positive lymph nodes increased. [Table-6]

**Table 1: Age distribution of the Breast cancer patients**

| Age (yr) | Cases | Percent (%) |
|---|---|---|
| 21 – 30 | 1 | 1.79 |
| 31 – 40 | 7 | 12.5 |
| 41 – 50 | 21 | 37.5 |
| 51 – 60 | 16 | 28.57 |
| 61 – 70 | 7 | 12.5 |
| 71 – 80 | 4 | 7.14 |
| **Total** | 56 | 100 |

**Table 2: The frequency of the tumor sizes (T) of the Breast cancer**

| Tumor size(cm) | Cases | Percent (%) |
|---|---|---|
| T1 (<2) | 3 | 5.36 |
| T2 ( 2 – 5) | 41 | 73.21 |


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| | | |
|---|---|---|
| T3 ( >5) | 12 | 21.43 |
| **Total** | **56** | **100** |

**Table 3: The histological type of The Breast cancer**

| Histological type | Cases | Percent (%) |
|---|---|---|
| Invasive Duactal carcinoma (IDC), not otherwise specified (NOS) | 46 | 82.14% |
| Invasive carcinoma with medullary features | 3 | 5.35% |
| IDC+ Invasive lobular carcinoma (ILC) | 2 | 3.57% |
| Mucinous carcinoma | 2 | 3.57% |
| Solid Papillary carcinoma with invasion | 1 | 1.79% |
| Tubular carcinoma+ Ductal carcinoma | 1 | 1.79% |
| IDC+ Paget's Disease | 1 | 1.79% |
| **Total** | 56 | 100% |

**Table 4: Distribution of cases according to Nottingham Modification of Bloom Richardson (BR) scoring system**

| BR score | | Cases | Percent |
|---|---|---|---|
| Tubule formation | 1 point | 2 | 3.57 |
| | 2 point | 20 | 35.71 |
| | 3 point | 34 | 60.71 |
| Total | | 56 | 100 |
| Nuclear pleomorphism | 1 point | 2 | 3.57 |
| | 2 point | 36 | 64.29 |
| | 3 point | 18 | 32.14 |
| Total | | 56 | 100 |
| Mitotic count | 1 point | 28 | 50 |
| | 2 point | 23 | 41.07 |
| | 3 point | 5 | 8.93 |
| Total | | 56 | 100 |

**Table 5: The distribution of cases according to Histological Grade**

| Grade (BR score) | Differentiation | Cases | Percent |
|---|---|---|---|
| I (3-5) | Well differentiated | 8 | 14.29 |
| II (6-7) | Moderately differentiated | 35 | 62.50 |
| III (8-9) | Poorly differentiated | 13 | 23.21 |
| **Total** | | **56** | **100** |

**Table 6: Comparison of Lymph Node status and ER, PR and HER-2 /neu status**

| | Axillary lymph node involvement | | | | | |
|---|---|---|---|---|---|---|
| | Negative | | 1-3 Positive | | >3 Positive | |
| **ER Positive** | 09 | 52.94% | 09 | 50.00% | 10 | 47.62% |
| **PR Positive** | 08 | 47.06% | 08 | 44.44% | 08 | 38.10% |
| **HER-2/neu Positive** | 05 | 29.41% | 08 | 44.44% | 12 | 57.14% |
| **Total =56(100%)** | **17** | **30.36%** | **18** | **32.14%** | **21** | **37.50 %** |

**Figure 1: Gross Specimen of Breast Carcinoma**

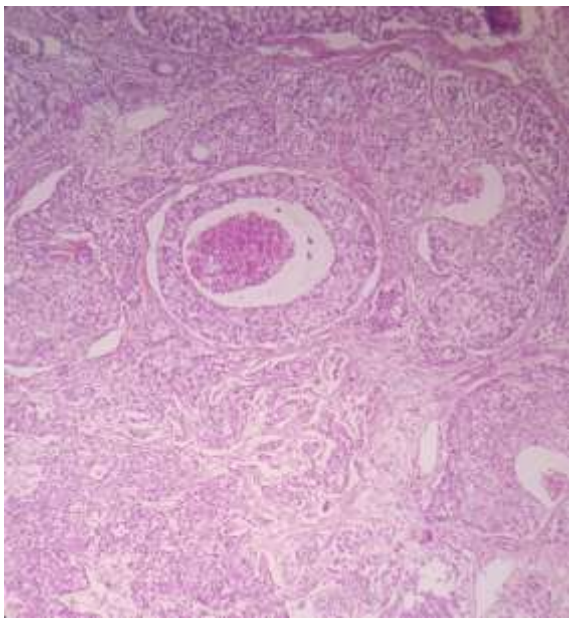

**Figure 2: Invasive Ductal Carcinoma NOS Type with Comedo necrosis (H&E Stain, 10x)**


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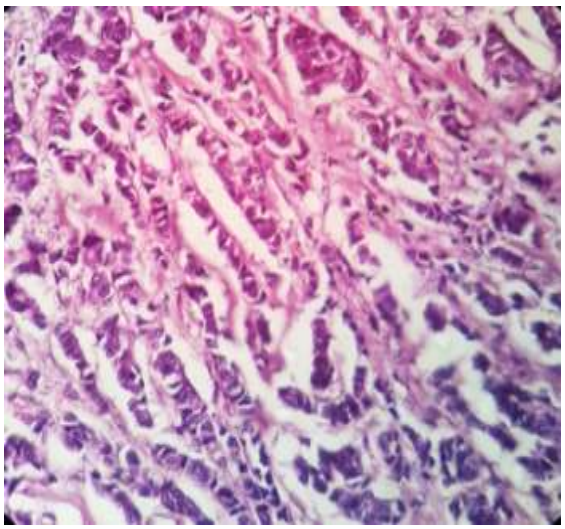

**Figure 3: Infiltrative Lobular Carcinoma (H&E Stain, 40x)**

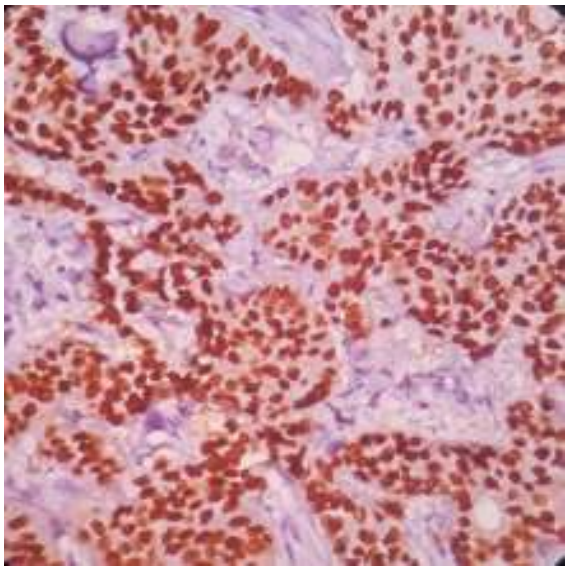

**Figure 4: Nuclear Positivity for Estrogen Receptor in Invasive Ductal Carcinoma (IHC, 40x)**

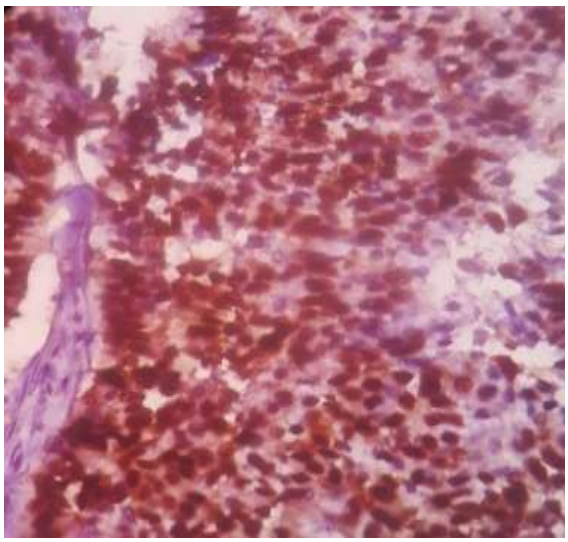

**Figure 5: Nuclear Positivity for Progesterone Receptor Positivity in Invasive ductal carcinoma (IHC, 40x)**

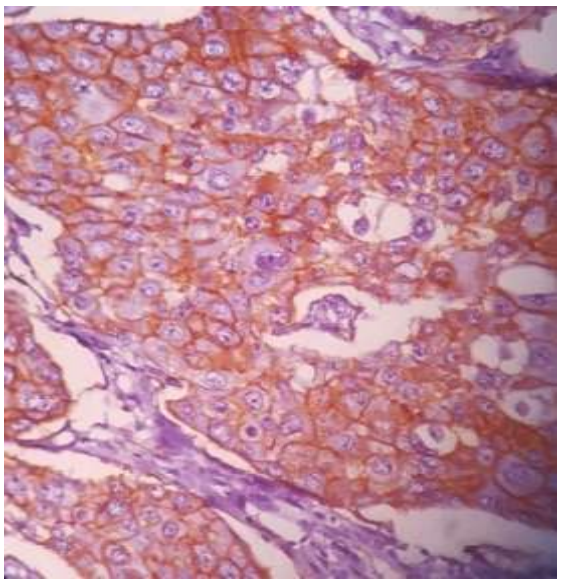

**Figure 6: Invasive Ductal Carcinoma, showing membrane positivity for HER-2/neu (IHC, 40x)**

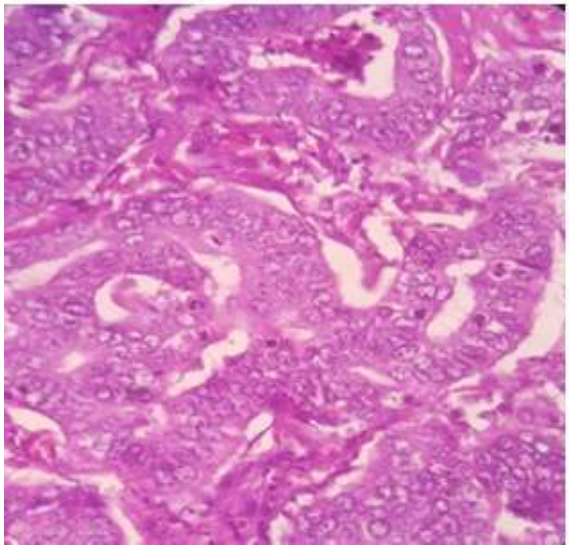

**Figure 7: Solid Papillary Carcinoma with invasion (H&E Stain, 40x)**

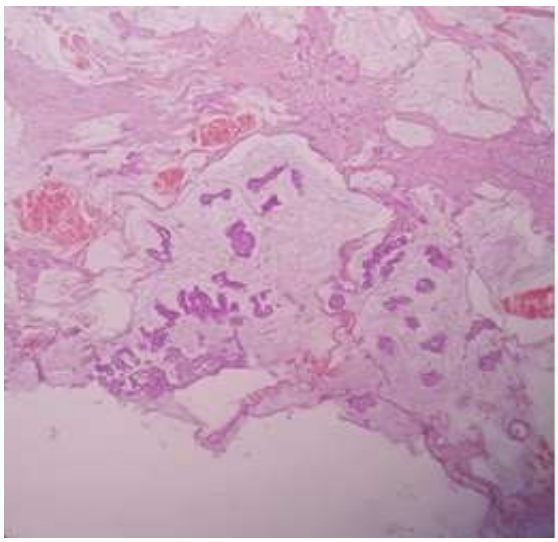

**Figure 8: Mucinous carcinoma (H&E Stain,10x)**


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## DISCUSSION

In the present study maximum cases were between 41-50 years of age which was similar to Bhagat et al,[30] and Mean age in present study was 47.26 yrs. Our findings were comparable to those of Azizun et al,[27] and Naeem et al,[25] and lower than Shafaq et al and Rashmi et al.[32] In present study maximum tumor size was between 2-5 cm which concurs with other studies.

In present study lymph node status is not in accordance with other studies in cases of nil lymph node status and 1-3 lymph node positive cases. However, in cases of >3 lymph nodes positive status, the present study is in accordance with Azizun et al,[27] and Naeem et al.[25]

In present study ER positive was less than studies done by Lal et al,[24] and Dutta et al,[31] but more than studies done by Azizun et al,[27] Naeem et al,[25] and Shafaq et al,[26] and was comparable to Bhagat et al,[30] and Rashmi et al,[32] studies. In present study PR positivity was less than Lal et al,[24] Naeem et al25, Dutta et al,[31] and Rashmi et al,[32] but higher than Azizun et al,[27] and slightly higher than Bhagat et al,[30] and Shafaq et al.[26] In present study HER-2/neu positivity was concur with Naeem et al,[25] but more than in all other studies.

In the present study ER/PR& HER-2 positivity was observed higher with well differentiated (grade 1) and very low with poor differentiation. Present study showed direct association between positive lymph node status and HER-2/neu expression, which was comparable with studies done by Almasri et al,[23] and Azizun et al.[27] However, in present study, ER and PR expression was decreased with increase in lymph node positivity status, which were not comparable to these studies. Present study showed % of triple negative breast cancers were lower than studies done by Ambroise et al and Bhagat et albut higher than Adedayo et al. Triple negativity is associated with poor prognosis.

## CONCLUSION

In the present study the maximum age distribution was in 5th decade of life. Most patients presented late with tumors larger than 2 cm and frequent lymphnode metastasis. The majority of tumors were invasive ductal carcinoma (NOS), predominantly Grade II. ER and PR positivity was associated with smaller tumor size, lower grade and fewer lymphnode metastasis, indicating a better prognosis. HER-2/neu over expression showed association with larger tumor size, higher grade and positive lymphnode status, suggesting aggressive tumor behaviour and poor prognosis. Triple-negative breast cancers were less common but were associated with unfavourable prognosis.

Overall, hormone receptor-positive tumors showed better prognostic features, whereas HER-2/neu positivity and triple negativity were associated with more aggressive disease.

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