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Defining Breast Cancer Prognosis Based on Correlation of Histomorphological Findings with Expression of Estrogen Receptor, Progesterone Receptor and Her 2neu Receptors.

[1]Drisya P.S, [2] Shaista Choudhary, [3] Manjunatha Y A,
DR B R AmbedkarMedical College, Bangalore, Karnataka
DR B R AmbedkarMedical College, Bangalore,Karnataka
DR B R AmbedkarMedical College, Bangalore, Karnataka
Corresponding Author: Drisya P.S

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ABSTRACT:
Introduction- Breast carcinoma is the most common cancer in Indian women, with an age-adjusted prevalence of 25.8 per 100,000 women and a fatality rate of 12.7 per 100,000 women[1]. Prognostic data is critical for advising patients on the anticipated course of their condition and planning future treatment. ER, PR, and Her-2neu are prognostic and therapeutic targets and existence of these is linked to a better outcome and is a key predictor of hormone therapy response.
OBJECTIVES: 1. To define breast cancer prognosis based on correlation of histomorphological findings with expression of estrogen receptor, progesterone receptor and her 2neu receptors
METHODS: All mastectomy specimens is fixed in 10% formalin, and several tissue bits will be taken during grossing according to protocol. Tissue is processed, and sections are cut at a thickness of 4-5 microns and stained with hematoxylin and eosin. Each section would be examined in detail for microscopic characteristics. Immunohistochemistry (IHC) for ER/PR and Her-2neu were performed on relevant sections. Histopathology and IHC findings were noted. Clinical data and investigations would be documented as well.
RESULTS: The A total of 52 cases of invasive breast cancer were included in the study. With 52 percent involvement, the right breast was more typically affected than the left. The study's most usually impacted age group was between 40 and 50 years old, with 30.8 percent overall, and the least common age group was under 30 years old, with only 3.8 percent. Invasive ductal carcinoma breast was the most common histologic type of breast cancer, accounting for 88.5 percent of all cases. Invasive lobular carcinoma is the second most prevalent carcinoma, accounting for 3.9 percent of all cases. Patients with lymph node metastasis, tumours smaller than 5cm, and grade 1 tumours (with ER/PR Her2 neu positive status) respond well to hormonal therapy and have a good prognosis, whereas patients with axillary lymph node metastasis, tumours larger than 5cm, and grade 3 tumours (with ER/PR negative status) do not respond to hormonal therapy and other treatments options are to be considered.
CONCLUSION: Histopathological grading and other clinicopathological characteristics are well correlated with ER, PR, and HER-2 status. A higher grade is associated with HER-2 positivity and ER/PR negative, larger tumour size, lymph node metastases, and a higher clinical stage.
KEYWORDS: Breast carcinoma, Estrogen receptor, Progesterone receptor, HER2 neu

I. INTRODUCTION

Breast carcinoma is the most common cancer in Indian women, with an age-adjusted prevalence of 25.8 per 100,000 women and a fatality rate of 12.7 per 100,000 women. The age-adjusted incidence rate of breast cancer was reported to be 41 per 100,000 women in Delhi, with Chennai (37.9), Bangalore (34.4), and Thiruvananthapuram district following closely behind (33.7). In rural registries, the mortality to incidence ratio was as high as 66, while in urban registries it was as low as 8. Aside from that, it has been discovered that young age is a key risk factor for breast cancer in Indian women. The number of women diagnosed with breast cancer in India is expected to reach 1797900 by 2020, according to projections. The estimates of cancer incidence show that existing diagnostic and treatment facilities, which are inadequate and unable to address the current burden of cancer in India, urgently need to be strengthened and supplemented. [1] The discovery that the presence of hormone (oestrogen and progesterone) receptors in tumour tissue correlates strongly with response to hormone therapy and chemotherapy has been a

key development in the treatment of breast cancer. In fact, oestrogen receptor status is now regarded as the most powerful predictive marker in the treatment of
breast cancer. [2] Prognosis is the key concern for surgeons, owing to late presentation at the outpatient department. Prognostic data is critical for advising patients on the anticipated course of their condition and planning future treatment. ER, PR, and Her-2neu are prognostic and therapeutic targets for (Estrogen Receptor) ER, (Progesterone Receptor)PR, and Her-2neu, respectively. The existence of these is linked to a better outcome and is a key predictor of hormone therapy response. The goal of this study was to see if there was a link between ER, PR, and Her-2neu expression and tumour histology. This would aid in the treatment of people with breast cancer.

II. METHODS:

All mastectomy specimens will be preserved in 10% formalin, and several tissue bits will be taken during grossing according to protocol. Tissue is processed, and sections are cut at a thickness of 4-5 microns and stained with hematoxylin and eosin. Each section would be examined in detail for microscopic characteristics. Immunohistochemistry (IHC) for ER/PR and Her-2neu will be performed on relevant sections. Histopathology and IHC findings would be noted. Clinical data and investigations would be documented as well**.**

III. RESULTS

A total of 52 cases of invasive breast cancer were included in the study. With 52 percent involvement, the right breast was more typically affected than the left. The age group between 40 and 50 was the most typically affected in the study, accounting for 30.8 percent of the total. The 50-60 age group is the next most common. The least prevalent age group is 30 years old, which accounts for 3.8 percent of the population.With 88.5 percent of all breast carcinoma cases, the most prevalent histologic type was invasive ductal carcinoma breast [**Figure 5(a)** histopathology, **5(b)** oestrogen receptor staining, **5(c)** progesterone receptor staining, **5(d)** Her2 neu receptor staining].

Invasive lobular carcinoma is the second most prevalent carcinoma, accounting for 3.9 percent of all cases. **(Figure1)**. 40(80%) tumors had desmoplasia, 38(73%) had necrosis, 39(75%) had Peritumoral retraction, 26(50%) had lymphovascular invasion(LVI), 27(52%) had calcification, 11 (21%) had perineural invasion. Necrosis, desmoplasia, LVI & perineural invasion were significantly more in highgrade tumors.

Basal like is the most common molecular type in the study, followed by luminal B. Invasive ductal carcinoma tumors were found in 39 percent of cases, with her2 neu positive tumours being the least common.

Cases were histologically graded, with 50% of carcinomas being classified as Grade II, 25% as Grade I, and 25% as Grade III. Seventy-five percent of patients had lymph node metastases, whereas just twenty-five percent were free of it. On gross inspection, 26 tumors (50%) measured >5cms and 26 tumors (50%) measured less than 5cms.The p value for the correlation of tumor size, tumor grade, and lymph node metastasis with those of different age groups was >0.05, indicating that there was no significant correlation.

All 52 cases were tested for ER, PR, and HER2/neu.

54% of tumors were ER negative and 46% were ER positive. 56% of tumors were PR negative and 44% were PR positive. 58% of tumors were HER 2 neu negative and 42% were HER 2 neu positive.

In the total instances, the majority of tumors were ER and PR negative (54.1%). Twenty cases (39%) showed ER -ve & PR -ve & HER2 –ve (Triple negative), followed by 14 cases (27%) displaying ER +ve & PR +ve & HER2 +ve (Triple positive), 17.1% showing ER +ve & PR +ve & HER2 –ve (Luminal A/ Normal breast-like), 15% exhibiting ER -ve & PR -ve & HER2 +ve (HER2 positive)

When lymph node metastasis was correlated with ER, PR, and HER2 neu status, 71.4 percent of cases with ER/PR/HER2 neu positive status had no lymph node metastasis, compared to 47.4% of cases with ER/PR negative status. With a substantial p value of 0.05, there is a positive significant connection between lymph node status and ER, PR, and HER2 neu status. Patients with lymph node metastasis (with ER, PR, and HER2 neu positive status) respond well to targeted therapy and have a good prognosis, whereas patients with lymph node metastasis (with ER, PR, and HER2 neu negative status) do not respond to targeted therapy and require additional therapeutic choices. **(Figure 3)**

When tumor size was compared to ER, PR, and HER2 neu status, 40 percent of patients with tumor size<=5cm were ER, PR, and HER2 neu positive, while 59.3% of cases with tumor size>5cm were ER, PR, and HER2 neu negative. With a substantial p value of 0.05, there is a positive significant association between tumour size and the ER, PR, and HER2 neu stats. This

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shows that tumors with a size of less than 5cm (with ER, PR, and HER2 neu positive status) respond well to targeted therapy and have a good prognosis, whereas tumours with a size of more than 5cm (with ER, PR, and HER2 neu negative status) do not respond to targeted therapy and require other treatment options.(Figure 2)

When comparing tumor grade to ER, PR, and HER2 neu status, 61.5 percent of grade 1 patients were ER/PR positive, but only 7.5 percent of grade 1 tumors were ER, PR, and HER2 neu negative. About 23% of grade 2 cases were ER, PR, and HER2 neu positive, compared to 46% of cases that were only ER, PR, and HER2 neu negative. About 2% of grade 3 patients were ER/PR positive, compared to 62% of those that were only ER, PR, and HER2 neu negative. With a substantial p value of 0.05, there is a positive significant correlation between tumor size and ER/PR status. This demonstrates that grade 1 cancers (with ER, PR, and HER2 neu positive status) react well to targeted therapy and have a favorable prognosis, but grade 3 tumors (with ER, PR, and HER2 neu negative status) do not respond to targeted therapy and require additional therapeutic choices.(Figure 4)

Figure 1: Pie chart depicting the frequency of various breast carcinoma in the present study.

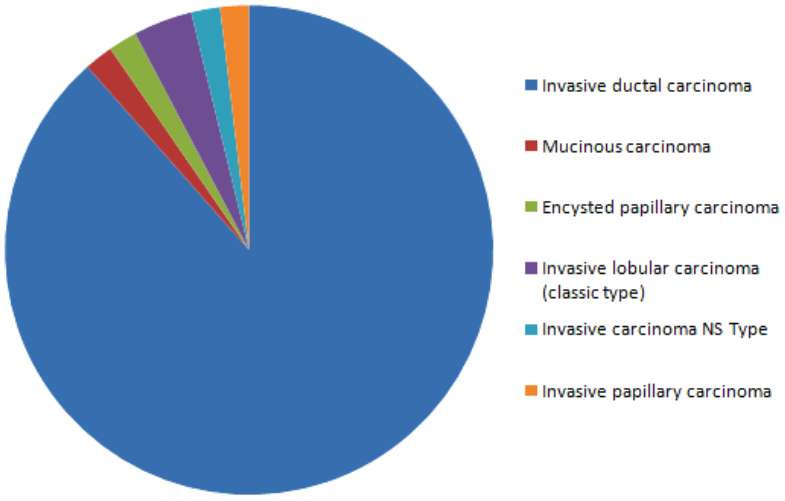

Figure 2: Correlation of ER/PR and HER2 neu with tumor size.

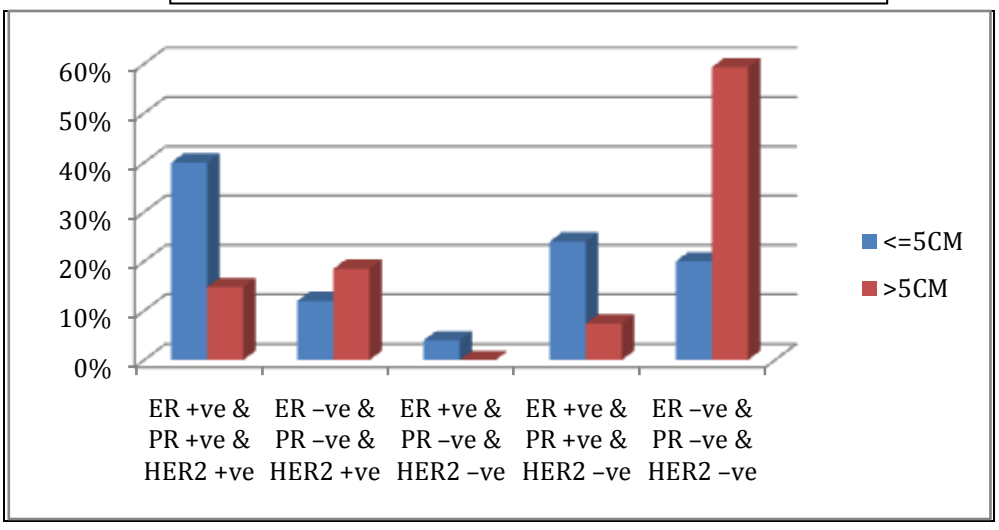

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Figure 3: Correlation of ER/PR and HER2 neu with lymph node status

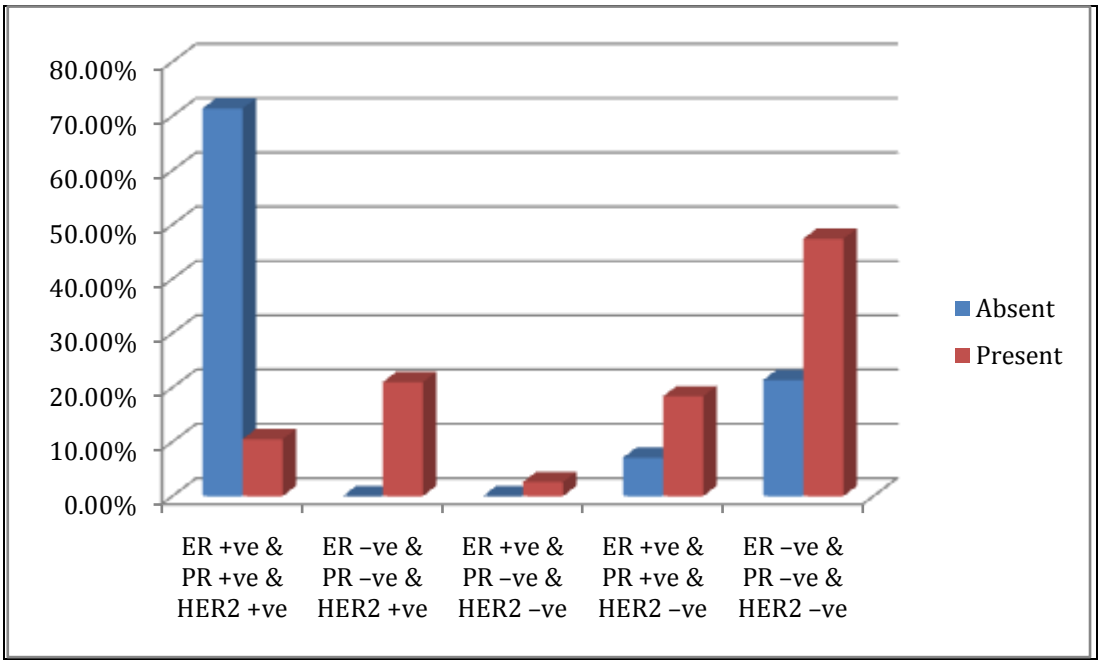
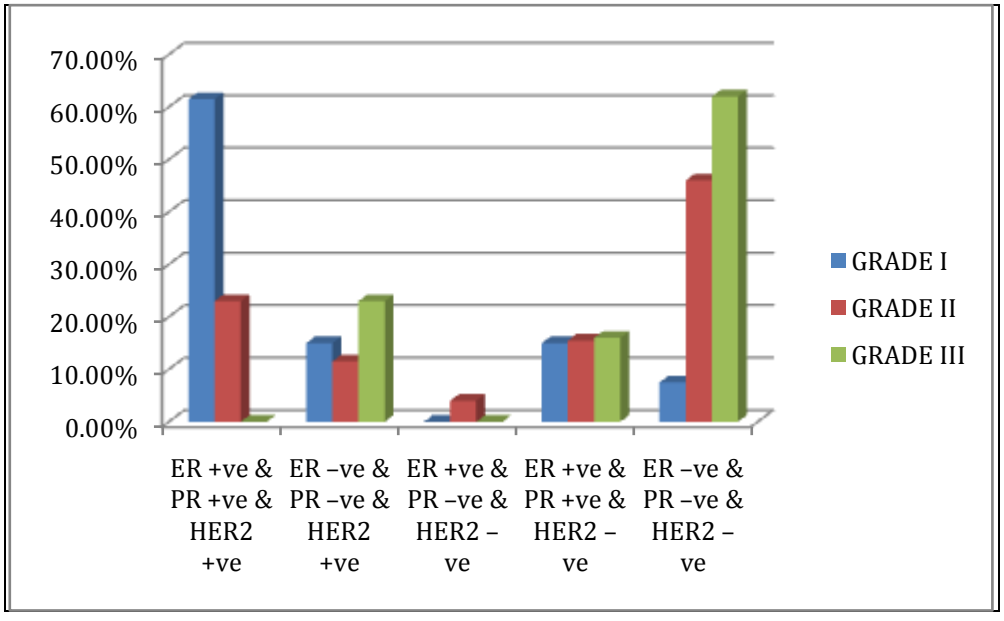


Figure 4: Correlation of ER/PR and HER2 neu with tumor grade.



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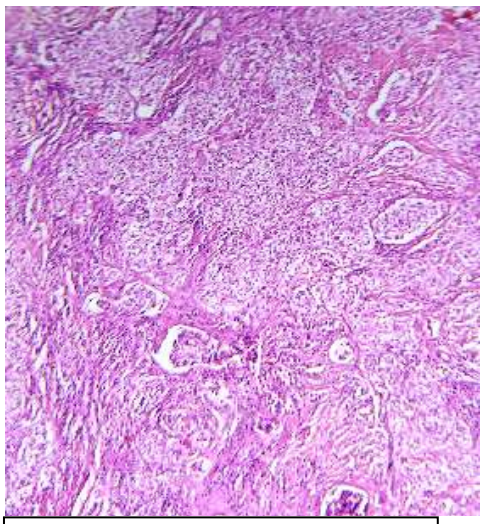

Figure 5(a): Section from a Grade II (moderately differentiated) IDC showing less tubule formation and tumor cells predominantly arranged in clusters and sheets with moderate nuclear pleomorphism. **(x40 H&E)**

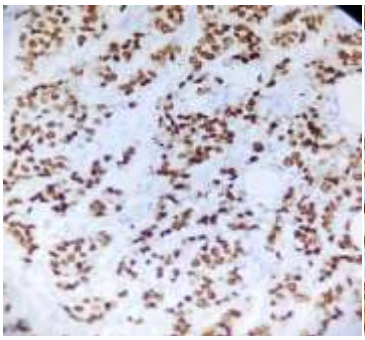

Figure 5(b): Section from a Grade II (moderately differentiated) IDC showing dense ESTROGEN RECEPTOR intense nuclear staining of almost 100% of malignant ductal cells. **(x40)**

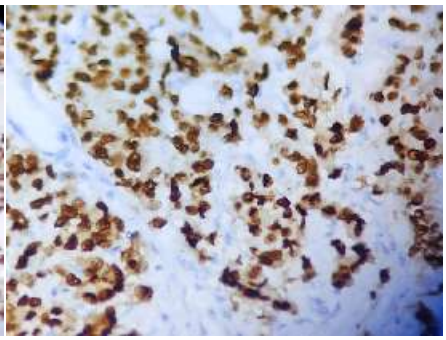

Figure 5(c): Section from a Grade II (moderately differentiated) IDC showing dense PROGESTERONE RECEPTOR intense nuclear staining of almost 100% of malignant ductal cells. **(x40)**

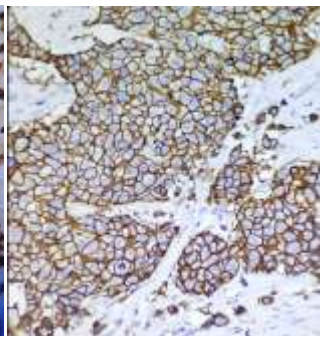

Figure 5(d): Section from a Grade II (moderately differentiated) IDC showing Complete membranous staining of HER 2 neu in >10% cells (HER2 positive) of strong intensity. **(x40)**

IV. DISCUSSION:

The age at presentation in this study ranged from 25 to 80 years, with a mean of 47.6 years, which is consistent with Joshi K et al[3] findings. The most prevalent age group affected by breast cancer was 41-50 years, which is also consistent with Singh Mahendra et al[4] findings (41-50). In the current study, 26 (50%) tumors were larger than 5 cm, and the percentage of common histological types was 88.5 percent of invasive ductal carcinoma (similar to Dayal et al[5] - 86.3 percent) and 3.9 percent of infiltrating lobular carcinoma (similar to Juneja S et al[6] - 3.64 percent) [6]

The majority of cases were grade II, similar to the observation reported by Le Doussal et al[7], and histological grading was done using modified Bloom Richardson grading.

75% tumors had lymph node metastasis.

Shreshta et al[8] and Ayadi L etal[9] demonstrated high ER, PR positivity with IDC (NOS), invasive lobular carcinomas similar to the present study. When HER-2 status was analyzed according to histologic features, HER-2 positivity showed higher expression of IDC and invasive lobular cracinoma in our present study compared to other studies. In our study 1 each of mucinous and invasive papillary carcinomas were positive for HER-2.

Geethamal aK et al[10], Mittal A et al[11], Emmanuel I et al[12] have shown that well differentiated tumors express hormone receptors with decreased expression of HER-2 in comparison with our study showed similar observation of ER and PR receptors but, also showed higher expression of HER 2 neu positivity in well differentiated tumors.

In our study, 76.9% of Grade I cancers had both ER, PR positivity and 77 percent positive HER-2 expression, whereas only 15.4% of Grade III tumors had both ER, PR, and 23 percent positive HER-2 expression, implying that poorly differentiated tumors have fewer hormone receptors and lower HER-2 expression. As a result, HER-2 over expression is related to the ER/PR state.

Bhagat et al[13] correlated tumor size with steroid receptor status. They concluded that there was a significant correlation between tumor size and ER/PR status, with tumors smaller than 5cm expressing more ER/PR than tumors larger than 5cm.

ER and PR expression in nuclear grade 1 tumors was significantly higher than that in nuclear grade III tumors (ER & PR). Our findings were similar to other studies as in Bhagat et al[13], Singh Mahendra et al[4], Onitilo AA et al.[14] However, higher HER-2neu positivity was also noted in nuclear grade-I tumors and lower expression in grade III tumors. 62% tumors of ER/PR-, HER-2-, subgroups were in stage III and 16% of tumors of ER/PR+, HER-2- subgroup were in stage I similar to the observation made by Onitilo AA et al.[14] This reflects the higher incidence of metastasis and aggressive biologic behavior with triple negative tumors.

V. CONCLUSION

In recent decades, breast cancer diagnosis and therapy have evolved substantially, allowing for earlier detection of the disease and the development of more effective treatments. As a result, the number of women dying from breast cancer has significantly decreased, while their quality of life has improved.

The prognosis and management of breast cancer are influenced by classic features such as histologic type and grade, tumor size, lymph node status, and hormone receptor status (ER, PR, and, more recently, HER-2 status). The goal of this study was to determine the relationship between ER, PR, and HER-2 status and histopathological grading and clinicopathological characteristics.

In the treatment of breast cancer, the connection between ER, PR, and HER-2 has become increasingly important. Anti-HER-2 antibodies (Herceptin) have recently been discovered to be effective in the treatment of breast tumors that over express HER-2.

In conclusion, the presence of ER, PR, and HER-2 correlates well with histological grading and other clinicopathological variables. A higher grade is associated with HER-2 and ER/PR negative, larger tumour size, lymphnode metastases, and a higher clinical stage.

SOME OF THE ADVANAGES FROM THE ABOVE RESULTS

a)Helps in prognosis.

b) Aids in molecular classification of breast carcinoma.

c) Aid in treatment protocols and targeted therapy thereby increasing the quality of life of the patient.

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