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A Prospective Randomised Observational Study To Assess The Impact Of Receptor Status On Prognosis Of Breast Cancer: Single-Institution Study

Dr. M.Ramula
Prof. Of Surgery
Karpaga Vinayaga Institute Of Medical Sciences & Research
Chengalpattu District, Tamil Nadu

Sanjay Kannaa V,
CRMI,

Sangari M,
CRMI,

Praveen Kumar,
CRMI,

Ekambar,
CRMI,

Lakshana,
CRMI,

Praveen FMG,
CRMI,

Abstract

Background

Breast cancer is rapidly becoming a major public health issue and continues to be the most frequently screened and diagnosed cancer among women universally, with a rising incidence in developing countries due to changing socioeconomic and reproductive patterns, lifestyle factors, and improved screening and diagnostic capabilities. Despite advances in screening and treatment, a significant proportion of patients in resource-limited settings still present with locally advanced disease, which adversely affects prognosis and survival outcomes.

Aim

To assess the role of immunohistochemistry as a prognostic indicator of breast carcinoma

Methodology

Prospective observational study with a study population of 90 patients over 1 year, in which comparisons between receptor-positive and receptor-negative groups for continuous variables were performed using the student's t-test. The associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test, wherever appropriate. Survival outcomes were analysed using Kaplan–Meier, for disease-free survival. and the long-rank test was used to assess differences between survival curves

Results

Triple-negative breast lumps are reportedly more associated with less favourable histological grade, locally advanced breast cancer, with more axillary nodal group involvement, with or without distant metastasis. In triple-positive cases, the prognosis is comparatively better in terms of survival rate and long-term disease-free interval.

Conclusion

Receptor-positive tumours tend to exhibit lower tumour load, lower metastatic potential, and a favourable response to endocrine therapy. Patients with ER- and PR-positive tumours generally have better outcomes, including improved overall survival and disease-free survival, compared with hormone receptor–negative

counterparts. In HER2/neu negative contrast, is associated with aggressive tumour behaviour, increased likelihood of axillary nodal metastasis, and poorer clinical outcomes in the absence of targeted therapy

Keywords: *Breast carcinoma, ER, PR, HER2/neu, prognosis, immunohistochemistry*

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I. Introduction

Although there are many prognostic indicators, in breast carcinoma, axillary lymph node infiltration remains one of the most significant predictors of disease outcome, directly influencing staging, therapeutic decision-making, and long-term survival [1]. The extent and number of axillary nodal group metastasis are associated with increased risk of recurrence and reduced overall survival, stressing the importance of understanding factors that predispose tumours to nodal spread. While primary clinicopathological parameters such as tumour size, grade, and nodal status provide valuable prognostic information, they do not give a clear picture of the biological heterogeneity of breast cancer [2]. In the last decade, advances in tumour biology at the molecular level, and the prominence of immunohistochemical receptor studies in refining prognostic prediction, treatment response, and survival rates, have complemented conventional histopathological and radiological assessment.[3]

The main predictors, oestrogen receptor and progesterone receptor expression, form key biomarkers in breast cancer, as hormone receptor–positive or negative tumours. Receptor-positive tumours tend to exhibit less tumour load, lower metastatic potential, and a favourable response to endocrine therapy [4]. Patients with ER- and PR-positive tumours generally have better results, improved overall survival and disease-free survival when compared to hormone receptor–negative counterparts. In HER2/neu negative contrast, receptor 2 (HER2/neu) is associated with aggressive tumor behaviour, increased likelihood of axillary nodal metastasis, and poorer clinical outcomes in the absence of targeted therapy. The advent of anti-HER2 agents has significantly altered the prognosis of HER2-positive breast cancer, emphasising the importance of accurate HER2 assessment in practice[5] The holistic receptor evaluation of three receptors namely, ER, PR, and HER2 status has resulted in the classification of carcinoma breast into characteristic molecular immunohistochemical subtypes, with each receptor identifiable by specific anticipated patterns of disease advancement, response of axillary nodes to the proposed treatment. Patient tailored management has now come down to molecular level and has become the base for tailoring individualistic treatment plans. [6] Triple negative breast lumps are reportedly more associated with less favourable histological grade, locally advanced breast cancer, with more axillary nodal group involvement, with or without distant metastasis. In view of these considerations, the present study was designed to evaluate the immunohistochemical profile of breast carcinoma to compare prognosis, survival outcomes, and treatment response between IHC-positive and IHC-negative groups, thereby addressing clinically relevant gaps in prognostic assessment and therapeutic decision-making

AIM

Immunohistochemical profile of breast carcinoma and determining the prognosis by comparing the IHC-positive and IHC-negative groups

Determine the proportion of patients with axillary node metastasis, categorised by their IHC profile (ER, PR, and HER2 status) and the association of IHC with survival rate.

II. Materials And Methods

This prospective observational study was conducted in the Department of General Surgery at KIMS & RC for one year, from May 2025 to April 2026, after it was approved by the institution's ethics committee. Institutional approval. The entire enrolled population n=90) was categorised into IHC-positive and IHC-negative groups based on receptor expression.

Study Design and Study Population

The study was designed as a prospective observational study using non-probability purposive sampling. The study population comprised female patients diagnosed with breast carcinoma with clinically and/or radiologically proven axillary lymph node involvement who attended the Surgery Outpatient Department and were subsequently admitted for further management.

Sample Size

Based on previously published literature and using a 95% level of confidence with an absolute precision of around 8%, the required sample size was calculated using the formula:

$N = Z^{1}{}^{\alpha/22} \times p\,(1 - p) / d^{2}$

Given the available patient population and feasibility, a sample size of 50 to 70 cases was planned, and patients were recruited accordingly during the study period.

Inclusion Criteria
• Patients with histopathologically confirmed as carcinoma breast
• Patients willing for the chosen procedure

Exclusion Criteria
• Patients with recurrent breast carcinoma
• Patients with distant metastasis at presentation

Data Collection

The study population underwent core needle biopsy to confirm diagnosis, and specimens were used for receptor study and Ki index to determine receptor status. The combined evaluation of ER, PR, and HER2 status enables classification of breast carcinoma into distinct immunohistochemical subtypes, each characterized by unique patterns of disease. The immunohistochemistry correlation was used to identify the primary receptors, ER,PR and HER 2 /NEU used to assess prognosis

All relevant clinical data were collected in Microsoft Excel using a structured pro forma. Information documented includes demographic details, socioeconomic, clinical presentation at the time of diagnosis, tumour size, laterality, clinical stage, and axillary nodal status. Comorbidities, if any and previous treatment modalities relevant to this study, such as surgery, chemotherapy, radiotherapy, and hormonal therapy, were documented.

Statistical Analysis

All collected and verified data were tabulated date-wise in Microsoft Excel, and subsequently transferred into SPSS for statistical analysis. Continuous variables were reported as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages

.Comparisons between receptor-positive and receptor-negative groups for continuous variables were performed using Student's t-test. The associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test, wherever appropriate. Survival outcomes were analysed using Kaplan–Meier, for disease-free survival. The log-rank test was used to assess differences between survival curves

The relationships between these two immunohistochemical profiles and clinicopathological grading were analysed depending on variable type. Impact of tumour markers on complete recovery and disease-free interval was analysed, with a two-tailed p-value of <0.05 taken as statistically significant

III. Results

Immunohistochemical Analysis

Histopathological examination to confirm diagnosis, diagnosis along with IHC for receptor status sections from primary breast tumors obtained by core needle biopsy.ER, and HER2/neu, along with Ki Index, are used for positive cases. For prognosis and disease-free survival, Interpretation of ER and PR status was performed based on nuclear staining in tumour cells, while HER2/neu expression was assessed .

Outcome Measures

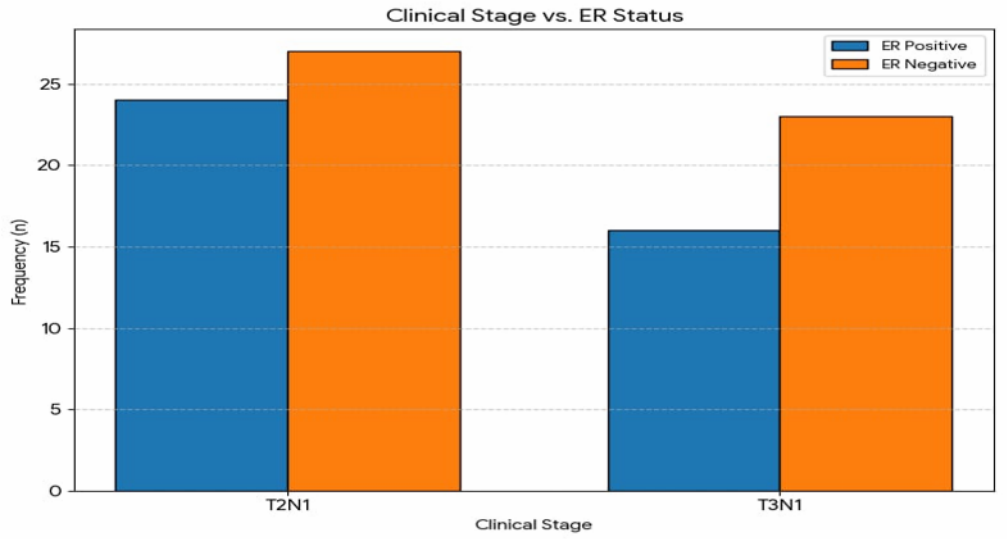
Based on the nodal status of axillary node involvement, the study population was grouped as either triple-positive or Her2/neu-negative. The measure was the proportion of patients with axillary node metastasis, categorised by immunohistochemical profile (ER, PR, and HER2 status). Secondary outcome measures considered were the association of IHC profile with overall survival, disease-free survival, and response to treatment options including surgery, chemotherapy, and radiotherapy.

Among the 90 study participants, the largest proportion was in the 61–70 years age group (30.0%), followed by the 41–50 years and 51–60 years age groups, each accounting for 28.9% of cases. Only 12.2% of patients were younger than 40 years. Overall, 87.8% of patients were above 40 years of age, indicating that node-positive breast cancer was primarily a disease of middle-aged and elderly women in the present cohort. The patient's age at diagnosis is highly significant. This is a well-recognised risk factor for breast cancer due to cumulative exposure to hormonal influences, progressive accumulation of genetic mutations, and age-related alterations in immune surveillance. In previous decades, the incidence was higher in older age groups than in the current scenario. This may be due to greater awareness, increased screening availability, and greater accessibility. Though in this study we found that advancing age may contribute not only to breast cancer development but also to disease progression, resulting in axillary lymph node involvement.

The association between age group and estrogen receptor (ER) status demonstrated a relatively uniform distribution of ER positivity across all age categories. ER-positive tumors were observed in 45.5% of patients younger than 40 years, 42.3% of patients aged 41–50 years, 42.3% of those aged 51–60 years, and

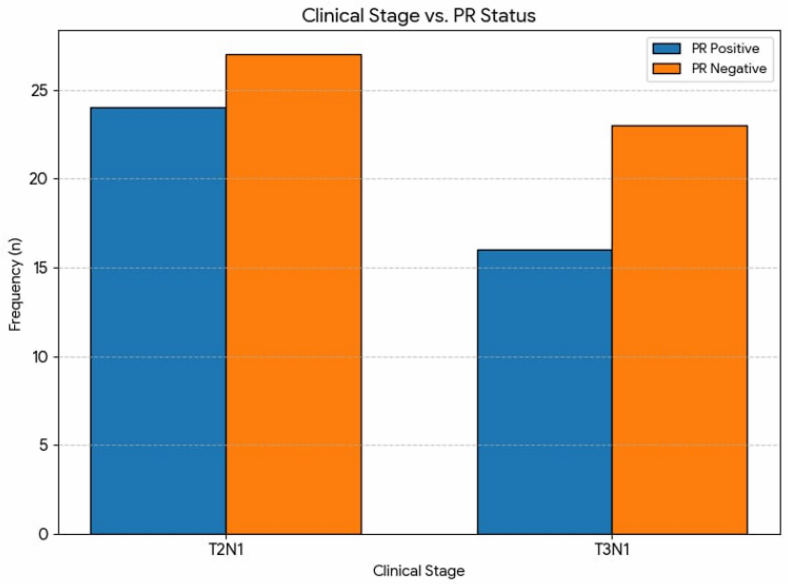
48.1% of patients aged 61–70 years. Similarly, ER-negative tumors accounted for approximately half of the cases in each age group. In our study we observed no significant association between age and ER status (χ^2 = 0.22, p = 0.974). These findings indicate that estrogen receptor expression was independent of patient age in the present study population and remained relatively consistent across different age groups (Graph 1)

Graph1.Association Between Clinical Stage and Estrogen Receptor Status



The association between clinical stage and PR receptor status demonstrated that 24 of 51 patients (47.1%) with T2N1 disease were PR-positive, while 27 (52.9%) were PR-negative. Among patients with T3N1 disease, 16 of 39 (41.0%) were PR-positive and 23 (59.0%) were PR-negative. PR-negative tumors were slightly more prevalent in both clinical stages. Our, study analysis revealed no significant association between clinical stage and PR status (χ^2 = 0.33, p = 0.566). These findings suggest that progesterone receptor expression was not influenced by disease stage in the present cohort, indicating a relatively similar distribution of PR positivity and negativity across both T2N1 and T3N1 breast cancer cases.(Graph 2)

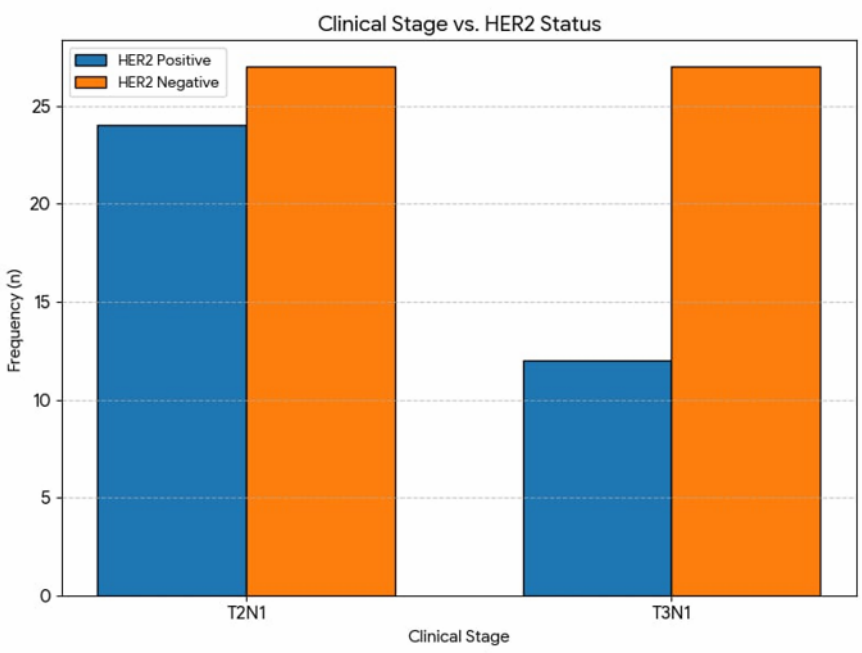
GRAPH 2. Association Between Clinical Stage and Progesterone Receptor Status



The relationship between clinical stage and HER2 status showed that among patients with T2N1 disease, 24 (47.1%) were HER2-positive and 27 (52.9%) were HER2-negative. In contrast, among patients with T3N1 disease, only 12 (30.8%) were HER2-positive, while 27 (69.2%) were HER2-negative. Although HER2 positivity appeared more common in T2N1 patients and HER2 negativity predominated in T3N1 patients, the observed difference was not statistically significant (χ^2 = 2.43, p = 0.119). These findings suggest that HER2

expression did not show a significant association with clinical stage in this study population, despite a trend toward lower HER2 positivity in more advanced disease.(Graph 3)

GRAPH 3. Association Between Clinical Stage and HER2 Status



IV. Discussion

The present study was undertaken to evaluate the immunohistochemical (IHC) profile of breast carcinoma with axillary lymph node metastasis and to determine the significance of hormone receptors on the prognosis of breast carcinoma with lymph node metastasis. Our study compared the IHC makers in two groups: one with triple-negative patients and the other with triple-positive patients. Although we compared these two groups based only on receptor status, in particular three receptors, namely estrogen,[7]ER, progesterone receptor (PR), and HER2/neu, and examined how their expression on biomolecules influences complete recovery, disease-free interval, survival rate and how they affect treatment response.[8] Understanding the relationship between molecular markers and clinical outcomes is essential for risk stratification and individualised treatment planning.[9] This study is significant, because it highlights the prognostic value of immunohistochemical profiling in node-positive breast cancer and supports the use of molecular characteristics to guide therapeutic decisions, predict outcomes, and optimize patient management.[10]

Although younger patients represented a smaller proportion of cases, in the past, currently, more breast cancers occurring in younger women are often found to be more biologically aggressive and associated with poorer outcomes. Liao et al. demonstrated that aggressive molecular subtypes, particularly triple-negative breast cancers, exhibit unique immune microenvironment characteristics and enhanced metastatic potential within axillary lymph nodes [11]This may partly explain the occurrence of axillary metastasis even among the small proportion of younger patients identified in the present study. The majority of patients are above and beyond, hence the group underscores the importance of screening and early detection programs. Earlier diagnosis may reduce the incidence of axillary nodal involvement and improve long-term survival outcomes[11]. Overall, the age distribution observed in this study supports previous literature and confirms that breast carcinoma with axillary node metastasis predominantly affects middle-aged and elderly women.

The most significant factor in assessing the prognosis is the clinical stage at the time of presentation. In this present study, T2N1 disease was observed in 56.7% of patients, while T3N1 disease accounted for 43.3%. These findings indicate that although most patients were diagnosed before progression to more extensive local disease, a substantial proportion still presented with advanced-stage tumours accompanied by axillary nodal involvement. The high frequency of T3N1 disease reflects delayed presentation and emphasises the need for increased awareness and timely diagnosis.

Patients with T2N1 axillary metastasis are more commonly observed, as documented by Babu et al., who found that tumour size, with or without palpable axillary nodes, was significantly associated with axillary metastasis and noted it as a notable independent predictor of nodal involvement in breast carcinoma patients [13]. Kim et al. further demonstrated that a smaller post-treatment tumour size (≤1.5 cm) significantly increased the likelihood of axillary pathological complete response following neoadjuvant chemotherapy (OR=2.83), stressing that tumour burden is also of prognostic importance in tumour stage and burden [14]. Similarly, Weber et

al. in their research on a similar topic reported that patients with clinically palpable axillary node disease indicate the need for intense axillary management, as residual nodal disease was identified in an average of 70% of patients undergoing further adjuvant radio or chemotherapy. [15].

Early detection favours the possibility of curative treatment; hence, the clinical stage distribution observed in this study reinforces the importance of early detection and appropriate systemic therapy in reducing disease progression and nodal metastasis. The findings are consistent with previously published studies demonstrating the strong relationship between tumour stage and axillary disease burden.

V. Conclusion

In the present study, the three tumour markers, namely ER, PR, and HER2/neu, were assessed by immunohistochemistry in patients clinically diagnosed with breast carcinoma, and nodal metastasis status was evaluated. In patients with breast carcinoma along with lymph node metastasis in the axilla, their prognosis is based on whether they are triple negative or triple positive. Our results have shown that,in patients with breast cancer and axillary nodal involvement, which is more common in relatively younger age groups, in the 3rd or 4th decade, middle-aged and elderly women with clinical staging of T2N1. These triple-negative tumours indicate a high tumour load and a biologically poor prognosis. prognosis within the study population. Immunohistochemical profiling proved to be an important tool for prognostic assessment. Although ER-positive and PR-positive tumours showed lower recurrence rates than receptor-negative tumours, these differences were not statistically significant. In contrast, HER2 status emerged as a major determinant of clinical outcome. HER2-positive patients experienced significantly lower recurrence rates and superior recurrence-free outcomes compared with HER2-negative patients, emphasising the prognostic importance of HER2 expression and the beneficial impact of targeted therapeutic approaches.

Limitations Of The Study

The small sample size (90) and single-institution study are the main limitations of the study, and these results need further validation. Although the sample size of 90 patients was deemed sufficient for this study, it fell short of the objectives to identify definitive associations between relevant IHC markers and clinical outcomes.

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